Molecular and metabolic investigation into the fungal-fungal interaction between the soilborne plant pathogen *Rhizoctonia solani* and the mycoparasite *Stachybotrys elegans*

Rony Chamoun

Plant Science Department

McGill University, Montreal

April 2013

A thesis submitted to McGill University in partial fulfillment of the requirements of the degree of Ph.D.

TABLE OF CONTENTS

TABLE OF CONTENTS II
LIST OF TABLES VIII
LIST OF FIGURES IX
LIST OF ABBREVIATIONS XI
ABSTRACT XIII
RÉSUMÉ XV
ACKNOWLEDGMENTS XVII
PREFACE AND CONTRIBUTIONS OF AUTHORS XIX
Contribution to Science XIX
CHAPTER 1 1
1. INTRODUCTION 1
1.1. HYPOTHESES 2
1.2. OBJECTIVES 3
CHAPTER 2 4
2.1. LITERATURE REVIEW 4
2.1.2. BIOLOGICAL CONTROL 4
2.1.3. IMPROVEMENT OF BIOCONTROL MECHANISMS 5
2.1.4. ANTAGONISTIC MECHANISMS 6
2.1.4.1. Mycoparasitism 6
2.1.4.1.1. Cell Wall Degrading Enzymes (CWDEs) and their encoding genes 7
2.1.4.1.2. Genes induced during mycoparasitism 9
2.1.4.1.3. Host reaction in response to mycoparasitism 11
2.1.5. *RHIZOCTONIA SOLANI* 12
2.1.5.1. Biocontrol of *R. solani* 12
2.1.6. *STACHYBOTRYS ELEGANS* 13
2.1.7. MYCOPARASITISM OF SCLEROTIA 14
2.1.8. SIGNAL TRANSDUCTION GENES 16

2.1.8.1. G-PROTEIN 16
2.1.8.2. Cyclic Adenosine Monophosphate (cAMP) 17
2.1.8.3. MAP kinase 18
2.1.9. METABOLISM 20
2.1.9.1. Classes of secondary metabolites 21
2.1.9.1.1. Terpenes 21
2.1.9.1.2. Polyketides 21
2.1.9.1.3. Non-ribosomal peptides (NRP) 22
2.1.9.1.3.1. Gliotoxin and gliovirin 22
2.1.9.1.3.2. Peptaibols 22
2.1.9.2. Metabolic profiling of pathosystems 23
2.1.10. CONCLUSION 25
CONNECTING STATEMENT BETWEEN CHAPTERS 2 AND 3 26
CHAPTER 3 Expression of genes of *Rhizoctonia solani* and the biocontrol *Stachybotrys elegans* during mycoparasitism of hyphae and sclerotia 27
3.1. ABSTRACT 28
3.2. INTRODUCTION 29
3.3. MATERIALS AND METHODS 30
3.3.1. Organisms and cultures conditions 30
3.3.2. Confrontation assays 31
3.3.3. Dual culture of *S. elegans* with hyphae of *R. solani* 31
3.3.4. Dual culture of *S. elegans* with the sclerotia of *R. solani* 32
3.3.5. Light microscope observation of the mycoparasitic process 32
3.3.6. RNA extraction and retrotranscription (RT) 33
3.3.7. Primer design 33
3.3.8. Transcripts abundance by real time quantitative RT-PCR 34
3.3.9. Data quantification 34
3.4. RESULTS 35
3.4.1. Light microscopy 35
3.4.2. Quantification of target and reference genes transcripts 36
3.4.3. *S. elegans* transcript abundance during interaction with the host's hyphae and sclerotia 36

3.4.5. *R. solani* transcript abundance during interaction with the mycoparasite 37
3.5. DISCUSSION 48
3.5.1. Mycoparasitism-associated genes 48
3.5.2. Host response genes 50
3.6. ACKNOWLEDGMENTS 52
CONNECTING STATEMENT BETWEEN CHAPTERS 3 AND 4 53
CHAPTER 4 Characterization and transcriptional regulation of *Stachybotrys elegans* mitogen-activated-protein kinase gene s*mkA* following mycoparasitism and starvation conditions 54
4.1. ABSTRACT 55
4.2. INTRODUCTION 56
4.3. MATERIALS AND METHODS 58
4.3.1. Fungal strains, media and culture conditions 58
4.3.2. Experimental set up 58
4.3.3. Protein extraction 59
4.3.4. Western blot 60
4.3.5. Targeted proteomics analyses 61
4.3.5.1. Sample preparation for proteomics 61
4.3.5.2. Liquid chromatography-MS/MS 61
4.3.5.3. Protein identification 62
4.3.6. Protein sequence alignment and primers design 62
4.3.7. Nucleic acid extraction and manipulation 63
4.3.8. Southern blot analysis 64
4.3.9. Phylogenetic analysis 64
4.3.10. Isolation of RNA and reverse transcription 64
4.3.11. Quantitative RT-PCR conditions 65
4.4. RESULTS 66
4.4.1. Activation of ERK1/2 during interaction with *R. solani* and in response to starvation condition 66
4.4.2. A phosphoproteomic approach identified one phosphopeptide with a TXY motif, which is activated during mycoparasitism and in response to nutrient starvation 67
4.4.3. *smkA* is a homologue of the ERK1 subfamily 67

4.4.4. *smkA* is member of a small gene family 68
4.4.5. Differential induction of *smkA* transcripts during mycoparasitism and carbon starvation.....69
4.5. DISCUSSION.....80
4.6. ACKNOWLEDGMENTS 83
CONNECTING STATEMENT BETWEEN CHAPTERS 4 AND 5.....84
CHAPTER 5 Transformation of *Stachybotrys elegans* by polyethylene glycol and *Agrobacterium tumefaciens* 85
5.1. ABSTRACT.....86
5.2. INTRODUCTION 87
5.3. MATERIALS AND METHODS.....88
5.3.1. Strain and culture conditions 88
5.3.2. Protoplast formation.....89
5.3.3. Protoplast transformation.....89
5.3.4. Transformation by *Agrobacterium tumefaciens* AGL-1.....90
5.3.5. Assessment of protoplast viability and transformation efficiency.....90
5.3.6. Primers design.....91
5.3.7. Generation of *S. elegans* MAP kinase overexpression mutant lines: pSMKA.....91
5.3.8. RNAi vector construction: pSMKAi 91
5.3.9. Analysis of transformants 92
5.4. RESULTS 92
5.4.1. Sensitivity to hygromycin B 92
5.4.2. Protoplasts isolation, transformation and regeneration.....92
5.4.3. *Agrobacterium tumefaciens*-mediated transformation (ATMT).....93
5.5. DISCUSSION.....101
5.6. ACKNOWLEDGMENTS 104
CONNECTING STATEMENT BETWEEN CHAPTERS 5 AND 6.....105
CHAPTER 6 Metabolic biomarkers associated with the mycoparasitic process between the plant pathogen *Rhizoctonia solani* and the mycoparasite *Stachybotrys elegans* 106
6.1. ABSTRACT.....107
6.2. INTRODUCTION 108

6.3. MATERIALS AND METHODS....110
6.3.1. Chemicals and reagents....110
6.3.2. Fungal cultures....110
6.3.3. Experimental design....110
6.3.4. Optic microscopy....111
6.3.5. Sampling, quenching and metabolite extraction....111
6.3.6. Direct infusion mass spectrometry analysis (DI-MS) and DI-tandem MS (DI-MS/MS)....112
6.3.7. Data processing and analyses....112
6.3.8. Metabolite identification....113
6.4. RESULTS....115
6.4.1. Morphological and microscopical observations....115
6.4.2. Multivariate analysis highlights different metabolic profiles between pure and parasitized cultures of *Rhizoctonia solani* and corresponding biomarkers....115
6.4.2.1. DI-Orbitrap MS analysis reveals differences in the chemical groups detected in *R. solani* single cultures and during mycoparasitism in co-cultures....116
6.4.2.2. Metabolites detected in the fungal pathogen *R. solani*....117
6.4.2.3. Metabolites detected in cocultures and during mycoparasitism....117
6.4.2.4. Changes in the metabolic content of *R. solani* monoculture and mycoparasitism....117
6.5. DISCUSSION....132
6.5.1. Biomarkers belonging to the carboxylic acids and terpenoids groups....134
6.5.2. Biomarkers belonging to fatty acids (FAs) group....134
6.5.3. Biomarkers belonging to alkaloids group....135
6.5.4. Biomarkers belonging to heterocyclic compounds and their implication in metabolism of *R. solani*....136
6.5.5. Biomarkers belonging to cyanogenic glucosides and indoles groups....137
6.6. ACKNOWLEDGMENTS....137
CHAPTER 7 General Conclusions and Future Work....138
7.1. General Conclusions....138
7.2. Future Work....140
REFERENCES....142

APPENDICES 176

Appendix I. LC-MS/MS analytical conditions 177

Appendix II- Target in-house-built protein library in FASTA format 178

Appendix III. Setup parameters for proteomic analysis using the software SIEVE v1.3. 270

Appendix IV. Target in-house-built metabolite library 271

Appendix VI. Relative intensities of detected metabolic biomarkers applying direct infusion Orbitrap MS analyses in positive (ESI^+) and negative (ESI^-) electrospray modes in *R. solani* monoculture and during interaction after 120 h of growth.....291

Appendix VII. Mass to charge ratios (m/z) of metabolic biomarkers detected during the interaction after 120 h of growth applying direct infusion Orbitrap MS analyses in positive (ESI^+) electrospray mode 292

Appendix VIII. Mass to charge ratios (m/z) of metabolic biomarkers detected during the interaction after 120 h of growth applying direct infusion Orbitrap MS analyses in negative (ESI^-) electrospray mode. 293

Appendix IX. Mass to charge ratios (m/z) of metabolic biomarkers detected in the monoculture of *R. solani* after 120 h of growth applying direct infusion Orbitrap MS analyses in positive (ESI^+) electrospray mode 294

Appendix X. Mass to charge ratios (m/z) of metabolic biomarkers detected in the monoculture of *R. solani* after 120 h of growth applying direct infusion Orbitrap MS analyses in negative (ESI^-) electrospray mode.....295

Appendix XI. Relative intensities of mass to charge ratios (m/z) of detected metabolic biomarkers applying direct infusion Orbitrap MS analyses in positive (ESI^+) and negative (ESI^-) electrospray modes in *R. solani* monoculture and during interaction after 120 h of growth.....296

LIST OF TABLES

CHAPTER 3

Table 3.1. Primers used in QRT-PCR assays to amplify target genes of *S. elegans* (mycoparasite) and *R. solani* (pathogen) belonging to different functional categories.....38

CHAPTER 4

Table 4.1. Primers used in this study.....70

Table 4.2. Normalized intensities of MAP Kinase in *S. elegans* in response to nutrient starvation and mycoparasitism of *R. solani*.....71

CHAPTER 5

Table 5.1. Primers used in this study 94

CHAPTER 6

Table 6.1. Adducts for which databases were searched.....119

Table 6.2. Putatively identified metabolites detected only in monocultures of *Rhizoctonia solani* after 120 h of growth.....120

Table 6.3. Putatively identified metabolites detected exclusively in the interaction between *Stachybotrys elegans* and *Rhizoctonia solani* after 120 h of contact 125

LIST OF FIGURES

CHAPTER 3

Figure 3.1. Microscopic images of mycoparasitism between *S. elegans* and *R. solani* 42

Figure 3.2. Relative transcript abundance of *S. elegans* genes during mycoparasitism of *R. solani* hyphae and sclerotia over 5 d inoculation normalized by the *histone-4* encoding gene.....44

Figure 3.3. Relative transcript abundance of *R. solani* genes during mycoparasitism of *R. solani* hyphae and sclerotia by *S. elegans* during 5 d inoculation normalized by the *gpd11* encoding gene.....46

CHAPTER 4

Figure 4.1. Alignment of 13 MAP kinase protein sequences belonging to different Ascomycetes 72

Figure 4.2. Western analysis of ERK 1/2 protein at different time points.....74

Figure 4.3. Sequence of *smkA* ….....75

Figure 4.4. A rooted phylogenetic tree based on the distances among protein sequences of MAP kinases from various Ascomycetes, Basidiomycetes and Arabidopsis calculated using the maximum likelihood method 77

Figure 4.5. Southern blot analysis showing the *smkA* gene copy number in *S. elegans*.....78

Figure 4.6. Relative transcript abundance of *smkA* in response to mycoparasitism of *R. solani* and starvation conditions.....79

CHAPTER 5

Figure 5.1. Overexpression vector for *smkA* MAP kinase in *S. elegans* 95

Figure 5.2. RNAi silencing vector for *smkA* MAP kinase in *S. elegans*.....96

Figure 5.3. *S. elegans* protoplasts labelled with FDA and observed under UV light (epifluorescence).....97

Figure 5.4. *Agrobacterium tumefaciens*-mediated transformation (ATMT) of *S. elegans* conidia.....98

Figure 5.5. *S. elegans* transformation 99

Figure 5.6. Epifluorescence microscopic visualisation for GFP expression 100

CHAPTER 6

Figure 6.1. Mycoparasitism between *S. elegans* and *R. solani* after 120 h of growth 127

Figure 6.2. Partial least squares-discriminant analyses (PLS-DA) PC1/PC2 score plots of direct infusion Orbitrap MS metabolite profiles of *Rhizoctonia solani* (■) and *Rhizoctonia solani-Stachybotrys elegans* interaction (●) culture extracts, recorded in positive (ESI^+) and negative (ESI^-) electrospray modes (A and B) 120 h following inoculation. 128

Figure 6.3. Venn diagram for metabolic biomarkers detected during the experiment.....129

Figure 6.4. Percentages of chemical groups detected in *Rhizoctonia solani* monoculture (a) and during the interaction between *Stachybotrys elegans* and *Rhizoctonia solani* (b) after 120 h of growth applying DI-MS analysis.....130

Figure 6.5. Partial least squares (PLS) coefficient plots for direct infusion mass spectrometry selected common metabolites in *R. solani* single cultures and during mycoparasitism in co-cultures with values of scaled and centered PLS regression coefficients (CoeffCS). 131

LIST OF ABBREVIATIONS

AG	Anastomosis group
ATMT	Agrobacterium tumefaciens mediated transformation
ATP	Adenosine triphosphate
BCA	Biocontrol agent
cAMP	Cyclic adenosine monophosphate
CWDEs	Cell wall degrading enzymes
DI-MS	Direct infusion mass spectrometry
DI-MS/MS	Direct infusion tandem mass spectrometry
ERK	Extracellular regulated kinase
ESI	Electrospray ionization
EST	Expressed sequence tag
GFP	Green fluorescent protein
GTP	Guanosine triphosphate
HOG	High osmolarity glycerol
HYG	Hygromycin
JNK	Jun amino-terminal kinases
KEGG	Kyoto encyclopedia of genes and genomes
LC-MS	Liquid chromatography mass spectrometry
LIPID MAPS	Lipid metabolites and pathways strategy lipidomics gateway

LTQ	Linear trap quadrupole
MAPK	Mitogen activated protein kinase
MS	Mass spectrometry
MSMA	Minimal synthetic medium agar
PCA	Principal component analysis
PEG	Polyethylene glycol
PlantCyc	Plant metabolic pathway database
PLS-DA	Partial least squares-discriminant analyses
RNAi	RNA interference
ROS	Reactive oxygen species
SAPK	Stress activated protein kinase
TCA	Trichloroacetic acid
T-DNA	Transfer DNA
Thr	Threonine
Tyr	Tyrosine
YERK	Yeast extracellular regulated kinase
YMDB	Yeast Metabolome Database

ABSTRACT

Mycoparasitism, the direct attack of one fungus on another, is a complex process that involves sequential events, including recognition, attack and subsequent penetration and killing of the host. The cellular interaction between *Stachybotrys elegans* a mycoparasite of the soilborne plant pathogen *Rhizoctonia solani* begins with molecular and chemical interactions that lead to expression of several genes or components of signaling pathways, and secretion of many metabolite biomarkers. Transcriptional changes of several mycoparasitism-induced genes (oxidoreductase, cytochrome P450 monooxygenase, carboxylesterase, and *O*-methyltransferase) during an extended period of interaction were associated with the formation of excessive coils and infection pegs which are required for limiting the growth of the pathogen. Hyphae and sclerotia of *R. solani* triggered different expression patterns of these genes, which is a clear indication that multiple regulatory mechanisms might be involved during the mycoparasitic process. In response to attack, hyphal and sclerotial cells of *R. solani* had elevated expression of pyridoxal reductase, a precursor of vitamin B6 or its derivatives which are known as antioxidants and quenchers of reactive oxygen species. The high elevated expression of some genes belonging to the mycoparasite and the host suggests that these genes play an important role during the mycoparasitic process and host defense, respectively. As a first step toward understanding the molecular basis of signal transduction during the cross talk between *S. elegans* and *R. solani*, the cloning and complete characterization of *smkA*, the first MAP kinase (MAPK/ERK1/2) gene from *S. elegans* was accomplished. At the transcriptional level, *smkA* was significantly induced in response to hyphal parasitism compared to parasitized sclerotia. However, under starvation condition, *smkA* levels were significantly induced at a later stage of growth. Western blot analysis against ERK1/2 showed an increase in their phosphorylated forms when *S. elegans* was grown under starvation condition compared to that detected in response to mycoparasitism. A higher abundance of phosphorylated ERK1/2 at the third day of interaction compared to that estimated

under starvation condition was detected by applying LC–MS/MS. Direct Infusion Orbitrap MS (DI-MS) and robust bioinformatics tools highlighted a total of 486 metabolites as biomarkers in parasitized cells of *R. solani*, and in cells from monocultures of *R. solani*. Carboxylic acids and alkaloids were the predominant chemical groups in parasitized cells compared to those in *R. solani* monocultures indicating their role in the mycoparasitism. The increase in relative intensity of *R. solani*-derived indole biomarker, 11-hydroxycanthin-6-one, is indicative of a defense reaction against *S. elegans*. This study provides new knowledge that can be exploited for plant disease management strategies and for research dealing with biotechnology such as genetic engineering and/or biomarker-assisted plant breeding.

RÉSUMÉ

Le mycoparasitisme est un procédé complexe par lequel un champignon en attaque un autre par une série d'événements, soit l'identification, l'attaque et la pénétration subséquente et la mort de l'hôte. L'interaction cellulaire entre *Stachybotrys elegans*, un mycoparasite du cryptogame *Rhizoctonia solani*, est caractérisée par des interactions moléculaires et chimiques résultant en l'expression de plusieurs gènes ou composantes de mécanismes de transduction du signal ainsi que la sécrétion de plusieurs métabolites biomarqueurs. Des changements dans la transcription de plusieurs gènes (oxydoréductase, cytochrome P450 monooxygénase, carboxylesterase, et *O*-méthyltransférase) activés par le mycoparasitisme durant une longue période d'interaction sont associés à l'enroulement et au développement de tubes pénétrants de type infectieux tous deux requis pour limiter la croissance du pathogène. Les hyphes et les sclérotes de *R. solani* ont initié différents patrons d'expression génique indiquant clairement que plusieurs mécanismes de régulation sont impliqués lors du mycoparasitisme. En réponse à l'attaque, des cellules d'hyphes et de sclérotes ont exprimé abondamment la pyridoxal réductase qui est un précurseur de la vitamine B6 ou de ses dérivés connue pour leur effet antioxydant. Une augmentation dans l'expression de certains gènes appartenant au mycoparasite et à l'hôte suggère que ceux-ci jouent un rôle important lors du mycoparasitisme et de la défense de l'hôte, respectivement. Afin de comprendre la base moléculaire de la transduction du signal durant l'échange entre *S. elegans* et *R. solani*, le clonage et la caractérisation complète de *smkA*, le premier gène codant pour une MAP kinase (MAPK/ERK1/2) chez *S. elegans*, ont été accomplis. Au niveau de la transcription, *smkA* a été induit significativement en réponse au parasitisme des hyphes en comparaison avec les sclérotes parasités. Toutefois, en absence de nutriments, les transcrits de *smkA* ont été induits significativement à un stade de croissance plus avancé. Une analyse par immunobuvardage contre ERK1/2 a démontré une augmentation de la traduction des formes phosphorylées de ces protéines lorsque *S. elegans* était cultivé en absence de nutriments en comparaison

avec la quantité détectée lors du mycoparasitisme. Grâce à la méthode LC–MS/MS, une plus grande concentration des formes phosphorylées de ERK1/2 a été détectée au troisième jour d'interaction en comparaison avec celle estimée en absence de nutriments. À l'aide de la spectrométrie de masse Orbitrap (DI-MS) et d'outils de bioinformatique, 486 métabolites biomarqueurs ont été détectés dans les cellules parasitées de *R. solani* et dans les cellules provenant de monocultures de *R. solani*. En comparaison avec les monocultures de *R. solani*, les groupes chimiques prédominants dans les cellules parasitées étaient les acides carboxyliques et les alkaloids ce qui les associe au mycoparasitisme. L'augmentation de l'intensité relative du biomarqueur d'alkaloid dérivé de *R. solani*, 11- hydroxycanthin-6-one, est un indicateur de la réaction défensive contre *S. elegans*. Les résultats de cette recherche apportent de nouvelles connaissances utiles à la phytoprotection et à la recherche en biotechnologie comme le génie génétique et/ou la sélection végétale assistée par biomarqueurs.

ACKNOWLEDGMENTS

I would like to express my gratitude to my supervisor, Dr. Suha Jabaji, whose expertise, understanding, and patience, added considerably to my graduate experience. Working with her has been a real pleasure. Professor Jabaji has supported me with care, and always encouraged me to think outside the box and come up with new challenging idea. She provided moral support in times difficulties. Her ability to approach compelling research problems along with, her high scientific standards, and her hard work set an example. Above all, Dr. Jabaji became a friend, which I appreciate from my heart. I am thankful for her continuous financial assistance through NSERC grant throughout my Ph.D. program.

I would like to thank the members of my committee, Dr. Ajjamada Kushalappa, and Dr. Jean-Benoit Charron for the assistance and technical help they provided at all levels of the research project.

In addition, I have been very privileged to get to know and to collaborate with Dr. Konstantinos Aliferis who became a faithful friend. It has been a pleasure to work with you and I learned a lot from you about life, research and how to tackle problems.

I am thankful for Lynn Bachand, Carolyn Bowes, and Guy Rimmer for their help and cooperation throughout my PhD studies in the Plant Science Department.

I would like to acknowledge the Funlab fellows, Huilan Chen, Claudia Maios, Mamta Rani, Tanya Copley, François Gagné-Bourque, David Bernard Perron, and Jamil Samsatly, for their help and support during my Ph.D. I am thankful to my friends and colleagues who have been an invaluable support during all these years: Dr. Georges Rammouz, Dr. Hicham Chibli and my friends at the Plant Science Department. Thanks to all of you! This thesis would not have happened without your help.

This thesis would also not be possible without the love, courage and enthusiasm of my parents Elias and Nadia, my brother Georges and his family, my sister Juliana and her family, and my sister Diana. My happiness would have

been fulfilled if my grandmother were still with us. She always wanted to see me as a Dr. and she always encouraged me to pursue my dreams. Although she is not present physically with me, I know that her spirit is with me and that she is proud of what I have accomplished.

Most importantly, I am so indebted and grateful to the newest addition to my family, my fiancé Katia Colton-Gagnon, as well as her wonderful family, Daniel and Nancy, who all have been supportive and caring. The best outcome from these past five years is finding my best friend, soul-mate, partner and the love of my life. There are no words to convey how much I love her. Her support, encouragement, quiet patience and unconditional love are undeniably the foundation upon which my life is built. Katia is an idol for me; she taught me discipline, inspired and motivated me when I did not have faith in myself. She is a true and great supporter and has unconditionally loved me during my good and bad times. I could not have asked God for a better gift in my life than her. We both strengthen our commitment and determination to each other to live life to the fullest.

PREFACE AND CONTRIBUTIONS OF AUTHORS

This thesis is written in the form of manuscripts according to the "Guidelines Concerning Thesis Preparation". It contains four chapters (3 to 6) representing three separate manuscripts, all of which are either published (chapters 3 and 4), or will be submitted soon (chapter 6). Each co-author is mentioned, along with his/her corresponding address at the beginning of each chapter. Below is a general description of the contribution of each co-author. A detailed description of contribution is provided in the connecting statements at the beginning of each chapter.

My role in all chapters was to design experimental strategies, conduct and plan all of the work pertaining to experimental procedures including data mining and analysis, and the preparation of the first draft of each manuscript. Dr. Suha Jabaji provided supervision, technical assistance and NSERC funds throughout this study. She contributed significantly to the edition and correction of several versions of the manuscripts. Dr. Konstantinos Aliferis provided substantial help and assistance in proteomic (chapter 4) and metabolomic analysis (chapter 6). Using bioinformatic tools in addition to softwares (Proteome Discover, SIEVE, and MZmine), he helped in the protein library construction and the identification of phosphorylated proteins and their intensities in Chapter 4, and in constructing fungal metabolic library, detecting metabolic biomarkers and their identification in Chapter 6. He also reviewed and edited the manuscripts in chapters 4 and 6. Dr. Neena Mitter has provided a significant contribution and help in constructing the RNAi silencing plasmid in Chapter 5.

Contribution to Science

The chapters of this thesis represent a significant contribution to knowledge on the interaction between a biological control and a fungal pathogen during their confrontation.

1. Chapter 3 focuses on the mycoparasitic interaction between *S. elegans* and *R. solani* employing QRT-PCR technique. We are among the first to explore the molecular basis of a mycoparasitic relation over an extended period of dual interaction through kinetic studies of transcript levels of mycoparasitism-induced and pathogen-defense genes belonging to different pathways. This study has enabled us to understand the efficacy of the biocontrol agent on two different morphological structures of the fungal pathogen. Microscopic and molecular investigations have indicated *S. elegans* potential to be a suitable biocontrol for *R. solani*.

Additionally, Chapter 3 presented the first evidence that the parasitized pathogen responds to the attack by the mycoparasite at the transcriptomic level by the induction of genes encoding host response during mycoparasitism and highlighted the presence of a defense reaction that could be the basis for future investigations.

2. Chapter 4 reports on the cloning and the complete characterization of the first MAPK gene *smkA* in the mycoparasite *S. elegans.* Applying QRT-PCR, differential temporal expression of *smkA* allowed us to provide evidence of its implication in direct mycoparasitism with the fungal pathogen *R. solani* (biotic stress) and also its possible role in fungal nutrition.

3. Chapter 5 describes the effort to transform *S. elegans* for the first time applying two different methods (protoplasting and *Agrobacterium tumefaciens*). In spite of the unsuccessful several attempts, our contribution to science in the construction of plasmids that over-express or down regulate MAPK protein in fungi is an accomplishment. Future studies should be targeted to test factors that affect transformation and define optimal conditions that will lead to successful and stable transformants. These are required to understand the in-depth role of MAPK proteins in the transduction of signals from different elicitors and

their functions in activating transcription factors and other downstream genes.

4. Chapter 6 profiles the metabolome of *R. solani* in response to attack by *S. elegans*. Several metabolites belonging to chemical groups related to protein, toxin and antioxidant biosynthesis were detected in *R. solani* monocultures with the majority of them being absent during interaction. One particular pathogen-derived antimicrobial metabolite whose role may be implicated in defense against the mycoparasite was detected at elevated levels during interaction. These results represent the basis for future studies in developing strategies for biocontrol and plant disease management by targeting the chemical groups that were suppressed during the interaction.

CHAPTER 1

1. INTRODUCTION

Interest in biological control has increased over the last decade fuelled by public concerns over the use of chemicals in the environment in general and the need to find alternatives to the use of chemicals for disease control (Berg 2009; Gerhardson 2002). Biological control is the direct inoculation of microbial living organisms (also called antagonists) into soils or onto host surfaces to control plant pathogens, insects, nematodes and weeds (Pandya and Saraf 2010). Antagonists are generally naturally occurring, mostly soil microorganisms, and possess some traits or characteristics that enable them to interfere with pathogen growth, survival, infection, or plant attack. Necrotrophic mycoparasites are opportunistic fungi that parasitize other fungi, quickly destroying their hosts by releasing toxins or enzymes, and then feed exclusively on their dead host cells for nutrients. *In vitro*, mycoparasitic interactions typically follow a predictable sequence of events, comprised of: (1) the mycoparasite detecting its target and chemotropically growing towards it; (2) recognition of the host, either by physical (thigmotropism) or chemical mechanisms (chemotropism); (3) attaching to and coiling around host hyphae; (4) degrading the host cell walls with lytic enzymes released by the mycoparasite; and (5) nutrients acquiring from its host (Chet et al. 1998; Steyaert et al. 2003; Whipps 2001). Moderation of this typical sequence of events implies involvement of a number of genes and their products (Howell and Stipanovic 1983; Mukherjee et al. 2011; Reino et al. 2008; Sharma et al. 2011; Viterbo et al. 2007).

Among the mycoparasites that have shown a good potential in controlling Rhizoctonia disease of potato is the necrotrophic ascomycete *Stachybotrys elegans* (Benyagoub et al. 1994). This mycoparasite has the ability to colonize the hyphae and the sclerotia of *Rhizoctonia solani*, and the process entails the activity of cell wall degrading enzymes, mostly chitinases and glucanases

(Archambault et al. 1998; Morissette et al. 2003; Tweddell et al. 1995), and the upregulation of several mycoparasitism-related genes encoding pathogenic processes, toxin metabolism, translation, transcription and DNA repair (Morissette et al. 2008), some of which are modulated by MAP kinases. Despite these advances, we still have not monitored the expression and regulation of these genes over an extended period of mycoparasitism of different infective structures of the host, nor explored the potential and the capabilities of *S. elegans* to produce antibiotics and toxins during interaction with its host.

The processes that determine the outcome of an interaction between a fungal pathogen and its host are complex. To date, biocontrol is typically viewed from the perspective of how antagonists affect pathogens. Microbial antagonists use a diverse arsenal of mechanisms to dominate interactions with pathogens, and in a similar behavior pathogens apply diverse means to overcome microbial antagonism (Duffy et al. 2003). We believe that understanding pathogen self-defense mechanisms could provide a novel and innovative approach to improve the durability of biologically based disease control strategies. The possible roles of signal transduction genes and the factors they activate are investigated in this thesis. Additionally, we will be applying a metabolic approach to study the fungal pathogen response to attack by mycoparasites.

The overarching goal of this thesis is to develop a comprehensive platform for the characterization of transcript and metabolite level changes that can be targeted to decrease the negative impacts of diseases and support the development of alternative crop protection strategies. This platform will be used to monitor molecular and metabolic changes during mycoparasitic interaction of *S. elegans* with *R. solani.*

1.1. HYPOTHESES

This thesis is based on the following hypotheses:

i. Over the course of the mycoparasitic interaction between the mycoparasite and the pathogen, the alteration of several attack and defense genes that belong to the parasite and the host respectively occurs.
ii. The signal transduction pathway is a crucial step in the establishment of the mycoparasitic interaction between *S. elegans* (mycoparasite) and *R. solani* (pathogen).
iii. Metabolic profiles of the mycoparasite and the pathogen change as the two fungi interact.

1.2. OBJECTIVES

The objectives are the following:

i. To monitor over an extended period of mycoparasitism, the expression patterns of selective novel mycoparasitism-induced and pathogen genes and associate the transcriptional changes with the formation of different mycoparasitic structures.
ii. To examine whether transcriptional changes in both the pathogen and the mycoparasite markedly differed under different mycoparasitism situations.
iii. To characterize the first MAPK gene from *S. elegans* and conduct comparative expression studies of the gene during extended periods of mycoparasitism of *R. solani* and in response to nutritional stress.
iv. To conduct a high-throughput metabolomics approach for the study of the mycoparasitic interaction between *S. elegans* and *R. solani*

CHAPTER 2

2.1. LITERATURE REVIEW

2.1.2. BIOLOGICAL CONTROL

Plant diseases need to be controlled to maintain the quality and abundance of food, feed, and fiber produced by growers around the world. Different approaches may be used to prevent, mitigate or control plant diseases. Beyond good agronomic and horticultural practices, growers often rely heavily on chemical fertilizers and pesticides. Such inputs to agriculture have contributed significantly to the spectacular improvements in crop productivity and quality over the past 100 years (Pimentel et al. 1993; Ridgway et al. 1978; Sattler et al. 2007). However, the environmental pollution caused by excessive use and misuse of agrochemicals (Chiu et al. 2004; Engel et al. 2005) as well as fear-mongering by some opponents of pesticides, has led to considerable changes in people's attitudes towards the use of pesticides in agriculture. Today, there are strict regulations on chemical pesticide use and there is political pressure to remove the most hazardous chemicals from the market. Consequently, researchers have focused their efforts on developing alternative inputs to synthetic chemicals for controlling pests and diseases (Mandeel and Baker 1991; Van Loon et al. 1998; Whipps 2001). Among these alternatives are those referred to as biological controls.

Biological control of plant diseases is considered a viable alternative method to manage plant diseases and is defined as the inhibition of growth, infection or reproduction of one organism using another organism (Chet and Inbar 1994; Denoth et al. 2002; Jeffries 1995). Biological control employs natural enemies of pests or pathogens to eradicate or control their populations. This can involve the introduction of exotic species, or harnessing whatever form of biological control existing naturally in the ecosystem (Harman et al. 2004; Whipps 2001). This approach is the most compatible approach with no detrimental effect on the environment and a lower cost compared to chemical pesticides or mechanical

harvesting (Yudelman et al. 1998). Moreover, the combination of biological control agents (BCAs) with reduced levels of fungicide promotes a degree of disease suppression similar to that achieved with full fungicide treatments (Adejumo 2005; Rehman et al. 2012). Applications of antagonists of phytopathogenic fungi have been used to control plant diseases, and 90% of such applications have been carried out with different strains of the fungus *Trichoderma*. The success of *Trichoderma* strains as BCAs is due to their high reproductive capacity, ability to survive under very unfavorable conditions, efficiency in the utilization of nutrients, capacity to modify the rhizosphere, strong aggressiveness against phytopathogenic fungi, and efficiency in promoting plant growth and defense mechanisms (Amin et al. 2010; Ha 2010). Understanding the mechanisms at the molecular and the cellular levels used by these BCAs towards their hosts is an essential step in the selection of the appropriate agent, and how it can be used in disease management strategies.

2.1.3. IMPROVEMENT OF BIOCONTROL MECHANISMS

BCAs are living organisms whose activities depend mainly on the different physicochemical environmental conditions to which they are subjected (Larkin and Fravel 2002). Understanding the mechanisms of biocontrol will lead to improved application of BCAs. These mechanisms are complex, and what has been defined as biocontrol is the final result of different mechanisms acting synergistically to achieve disease control (Jamalizadeh et al. 2011). Biocontrol results from competition for nutrients and space or as a result of the ability of BCAs to resist and/or produce diffusible and/or volatile metabolites that either impede spore germination (fungistasis) (De Boer et al. 2003; Wicklow and Zak 1979), or kill the cells (antibiosis) (Whipps 2001). Biocontrol may also result from a direct interaction between the pathogen and the BCA, as in mycoparasitism, which involves physical contact and synthesis of hydrolytic enzymes (i.e. chitinases and glucanases), toxic compounds and/or antibiotics that act synergistically with the enzymes (Adams 1990; Archambault et al. 1998;

Jeffries 1995; Morissette et al. 2008; Steyaert et al. 2003). BCAs can even exert positive effects on plants with an increase in plant growth and the stimulation of plant-defense mechanisms (Chang et al. 1986; Lo and Lin 2002; Yedidia et al. 1999). Recent findings suggest that plant development and biochemistry are strongly affected by *Trichoderma* strains. Specific *Trichoderma* strains colonize and penetrate plant root tissues and initiate a series of morphological and biochemical changes in the plant, considered to be part of the plant defense response, which in the end leads to induced systemic resistance (ISR) in the entire plant (Ha 2010; Howell 2003; John et al. 2010).

2.1.4. ANTAGONISTIC MECHANISMS

Different types of interactions can occur between two microbes in a compatible confrontation: mutualism (benefit to both organisms), commensalism (benefit to one, no harm to the other), and antagonism in which the outcome is detrimental to one of the microbes. This type of relation includes mycoparasistim, antibiosis, competition, induced plant resistance, and predation. This review will focus on mycoparasitism. Readers are directed to several excellent reviews on the remaining topics (Adams 1990; Fravel 1988; Hammerschmidt 1999; Lucas 2010; Walters et al. 2005; Whipps 2001).

2.1.4.1. Mycoparasitism

Among the antagonistic forms of biocontrol, mycoparasitism is extensively studied (Benyagoub et al. 1994; Li et al. 2004; Martin et al. 2006; Morissette et al. 2003; Rotem et al. 1999; Sun et al. 2006). It is a complex process that is characterized by several steps, beginning with recognition, followed by attack and penetration, and ending with destruction of the host. This process involves the production and coordinate secretion by the mycoparasite of cell-wall degrading enzymes (CWDEs) such as chitinases, glucanases, proteases and cellulases (Brand and Alsanius 2004; de la Cruz et al. 1995; Tweddell et al. 1995) and the

expression of non cell-wall encoding genes (such as peptaibol synthetase, peptide synthetase, G-protein, MAP kinases, cAMP) that are believed to be involved in fungal metabolic processes (Carpenter et al. 2005; Morissette et al. 2008; Mukherjee et al. 2003; Mukherjee et al. 2004; Mukherjee et al. 2007; Muthumeenakshi et al. 2007; Suárez et al. 2007; Vizcaino et al. 2007; Wiest et al. 2002; Wilhite et al. 2001). These molecular studies have investigated the interaction between different structures of the mycoparasite and the host.

2.1.4.1.1. Cell Wall Degrading Enzymes (CWDEs) and their encoding genes

The purification and the sequencing of CWDEs of mycoparasites have made it possible to clone their corresponding genes and study their regulation under several carbon sources. Most of the work has been done on the model mycoparasite genus *Trichoderma* (Sharma et al. 2011).

Several chitinases genes were cloned and their expression was studied under simulated parasitism in which different stress and nutrient sources were applied to the medium and also in confrontation assays (Garcia et al. 1994; Morissette et al. 2003). The corresponding cDNA gene encoding CHIT42 was identified through cDNA library construction and its expression was studied through northern analysis when the parasite was grown under different carbon sources. The study revealed that *chit42* expression is induced by chitin (either present in host fungal cell walls or used as a substrate) and is strongly catabolite-repressed by glucose (Garcia et al. 1994). Disruption of *ech42* (endochitinase encoding gene) in *T. atroviride* showed reduced biocontrol activity (40 % compared to the wild) of the culture filtrate against *Botrytis cinerea* and *R. solani* (Woo et al. 1999). Similar function for the same gene was confirmed when *ech42* was deleted or over-expressed in *T. virens* leading to significant decrease or enhanced biocontrol activity against *R. solani* in cotton, respectively (Baek et al. 1999).

In mycoparasitic interactions between *Trichoderma* and *R. solani*, a diffusible factor released from the host is responsible for induction of *ech42* (endochitinase 42-encoding) gene transcription before physical contact (Zeilinger et al. 2005).

Upon direct contact, lectins in the host's cell wall can induce coiling of the mycoparasite around the host hyphae. Both enzyme production and infection structure formation are induced responses triggered by heat stable unidentified molecules released from the cell walls of the host fungus or located on its surface (e.g. lectins) (Zeilinger et al. 2005).

Glucanases have also been implicated in the mycoparasitism process. In-vivo and in-vitro assays have revealed the biocontrol ability of *tvbgn3*, a gene encoding β-1,6-glucanase, in the biocontrol of *P. ultimum* by *T. virens.* Deleting *tvbgn3* significantly reduced the ability to inhibit *Pythium* growth (87%) compared to that of the wild type (63.8%) (Djonovic et al. 2006).

The expression of *prb1*, the most studied protease-encoding gene, is induced by chitin, autoclaved mycelia, and fungal cell wall preparation, and its regulation is dependent on cell wall composition of the host. Over-expressing *prb1* in *T. harzianum* has improved its biocontrol activity against cotton plants grown in *R. solani*-infested soil (Flores et al. 1997). Mycoparasite/host studies demonstrated that the expression of *prb1* is induced during the interaction of *T. hamatum*/*Sclerotinia sclerotiorum* and *T. atroviride*/*R. solani*, even before physical contact for the latter interaction, and by diffusible factors produced by the host.

In the case of *sechi44,* a gene encoding an endochitinase of the mycoparasite *Stachybotrys elegans* (Morissette et al. 2006), its temporal expression in confrontation assays with its host under induced and non-induced conditions was measured by real-time quantitative RT-PCR. The study showed that the expression of *sechi44* during an extended period of mycoparasitism (i.e. 12 days) followed a cyclical pattern with an upregulation every two days, a period that coincides with the growth and hyphal extension of the mycoparasite on its host. Interestingly, the down-regulation of *sechi44* after few hours before contact of the mycoparasite with its host was believed to be likely triggered by a diffusible molecule(s) originating from the *R. solani* cells in order to offset attack.

Through an European Union (EU) functional genomic project "TrichoEST", several CWDEs (chitinases, glucanases and proteases) encoding genes have been

identified in *Trichoderma* sp. by generating cDNA libraries for different *Trichoderma* species grown on artificial induced conditions (chitin, and fungal cell walls) for the purpose of isolating genes with high biotechnological values for different industrial sectors (Suárez et al. 2007; Vizcaino et al. 2007). Thus, characterization of genes, other than those encoding CWDEs, during the mycoparasitic process needs to be explored in order to provide insight into the mechanisms of attack and defense that regulate the mycoparasitic process.

2.1.4.1.2. Genes induced during mycoparasitism

Although the aforementioned studies had a great impact on isolating genes involved in the biocontrol mechanism of the mycoparasites, the main drawback of the above studies is that the cDNA libraries generated were constructed from *Trichoderma* strains that were grown under different nutrient conditions, in the presence of cell wall preparation (i.e. starvation or simulated mycoparasitism), or in confrontation with a host but without direct contact.

The cellular interaction between a pathogenic microorganism and its host starts at the molecular interaction between the two partners and the expression of some of the genes involved in mycoparasitism may require the direct contact of a live host (Carpenter et al. 2005; Iakovlev et al. 2006; Liu and Yang 2005; Morissette et al. 2008; Muthumeenakshi et al. 2007; Zhang and Yang 2007).

Iakovlev et al. (2006) applied mRNA differential display and characterized genes encoding diverse putative functions (i.e. transcriptional repressor, hypothetical protein, mitochondrial inner membrane protein, cystathionine gamma-lyase, homologous recombination, DNA repair and stress responses) that were identified in either the antagonist *Physisporinus sanguinolentus* (total 10 genes) or the conifer pathogen *Heterobasidion annosum* (total 11 genes). Carpenter and coworkers (2005) applied suppression subtractive hybridization (SSH), and explored differential transcript abundance of the mycoparasite *T. hamatum* LU593 in the presence of the living host *S. sclerotiorum*. Only 19 genes were identified resulting in an incomplete view of genetic regulation during mycoparasitism. While Muthumeenakshi et al. (2007) identified 251 unisequences

representing genes associated with signaling and cellular communication, degradation of host cell walls and energy reserves, nutrient utilization, detoxification and stress response were preferentially expressed by *Coniothirium minitans* during sclerotial mycoparasitism.

To explore the putative genes' functions in the biocontrol agent *Chaetomium cupreum* during confrontation with its host *S. sclerotiorum*, Zhang and Yang (2007) constructed a cDNA library and generated 3,066 ESTs, with identification of 874 unigenes belonging to different categories with the most abundant ones responsible for: metabolism (22.7 %); cellular physiological process (15.4%); and oxidoreductase activity (11%).

Suppressive subtractive hybridization (SSH) technique was applied to isolate several transcripts during the interaction between the mycoparasite *S. elegans* and its host *R. solani* (Morissette et al. 2008). Novel genes belonging to different functional classifications (toxin metabolism, pathogenic processes, stress response, apoptosis, transport, respiration chain, translation, transduction, lipid metabolism, protein degradation, mitochondrial RNA and hypothetical proteins) were shown to be involved during the mycoparasitism process and some of them belonged to *R. solani*. This study has highlighted the importance of dual confrontation assays implicating living organisms in which a host defense reaction is expressed and a repressor role was suggested as a result of transcript abundance (Morissette 2006).

The different functional categories reported by Morissette et al. (2008) and Muthumeenakshi et al. (2007) underline the fact that a broader range of genes, other than those encoding for CWDEs is involved in the mycoparasitic process. Among those, the genes involved in the signal transduction pathways constitute a very essential component of the interaction process involving the binding of a host molecule to its corresponding receptor site on the mycoparasite cell walls, and therefore leading to the initiation of the mycoparasitic process by activating a series of relay proteins (Zeilinger and Omann 2007).

The role of signal transduction genes originates from the fact that the host recognition mechanism may involve the activation of one or multiple pathways

simultaneously (e.g., infection structure formation, transcript abundance of mycoparasitic genes, and antibiosis) (Zeilinger and Omann 2007), which will affect the efficiency and outcome of the mycoparasitism process. The transcriptomic study of Morissette et al. (2008) on the interaction between the mycoparasite *S. elegans* and its host *R. solani* demonstrated that a MAP Kinase transduction gene is present and expressed throughout the interaction process. From what has been stated above regarding the role of such genes, and that no such genes have been studied in the mycoparasite *S. elegans*, chapter 4 of this thesis will characterize and study the expression of the signaling gene, named *smkA*, under biotic (confrontation with *R. solani*) and abiotic (carbon starvation) stresses.

2.1.4.1.3. Host reaction in response to mycoparasitism

The majority of the studies on mycoparasitism have focused on the expression of genes that belong to the mycoparasite rather than the host. As the host is able to attack and suppress the effect of the mycoparasite, it has the capability to counteract the antagonist via several means (Duffy et al. 2003). The fungal host can overcome the mycoparasite attack by releasing compounds such as cyanide hydratase to degrade hydrogen cyanide, or by detoxification of active oxygen species such as 2,4-diacetylphloroglucinol, and 1-hydroxyphenazine (Levy et al. 1992). In the case of a competition, the host can alter the pH of the surrounding environment by producing specific compounds (i.e. oxalate) leading to a decrease in the activity of the parasite through diminishing the amount of antibiotics that it can release (Dutton and Evans 1996); or by the production of a broad range of toxins (Lewis and Lumsden 1995). During the parasitic interaction, the host can resist the mycoparasite due to the occurrence of a physical/chemical barrier resulting from the presence of melanin that confers resistance against the various classes of the cell wall degrading enzymes CWDEs) (Bell and Wheeler 1986).

To date, biocontrol is typically viewed from the perspective of how antagonists affect pathogens. Just as microbial antagonists use a diverse arsenal of mechanisms to dominate interactions with pathogens, pathogens also have diverse

responses to counteract antagonism (Duffy et al. 2003). Understanding pathogen self-defense mechanisms provides a novel and innovative approach to improving the durability of biologically based disease control strategies. This will be addressed in Chapter 3.

2.1.5. *RHIZOCTONIA SOLANI*

Rhizoctonia disease of potato can lead up to 30% reduction in marketable yield of potato tubers in Canada. Although several *Rhizoctonia* species were reported to infect potato plants, *R. solani* AG-3 is considered an important destructive pathogen for *Solanum tuberosum* in several countries around the world (Liu et al. 2003; Tsror et al. 2001; Yanar et al. 2005). The characterization of the disease is based on the symptoms caused by the pathogen on the below and above-ground parts of the plants and grouped into two stages. Stem canker, not easily detectable as it occurs early in the growing season beneath the soil surface, is represented by the emergence of poor stands and the presence of sunken lesions on stolons, roots and stems that can develop with maturity to be necrotic; whereas black scurf is noticeable at the end of the growing season and after harvest by the occurrence of irregularly shaped, brown to dark black superficial vegetative resting bodies called sclerotia on potato tubers. These are formed by the aggregation of melanized cells and can overwinter in the infected soil, in the plant residues, and on potato tubers during storage, and they are considered to be the major source of inoculum for disease outbreak in the next growing season (Errampalli and Johnston 2001; Woodhall et al. 2007) when suitable environmental factors (i.e. high soil moisture, cool temperatures, high soil fertility and a neutral to acid soil) are present.

2.1.5.1. Biocontrol of *R. solani*

To date, no potato varieties with complete resistance have been reported to exist. Currently, several cultural practices are used to decrease the severity of the

disease and its economic outcome on the agricultural sector, but with no complete efficiency (Bains et al. 2002; Grosh et al. 2005). These include, planting certified sclerotia-free tubers at shallow depth and at warm temperatures in dry soils in order to prevent the emergence of the disease, and crop rotation mainly with cereals is usually recommended when a severe stem canker infection has been detected in the field. In addition, other management techniques such as soil fumigation, cattle manure application (Tsror et al. 2001), an immediate harvesting after tuber vine desiccation have been used.

Jager and Velvis (1998) studied the efficiency of the mycoparasite *Verticillium biguttatum* on the viability of *R. solani* sclerotia on tubers under different temperature and relative humidity regimes. They concluded that in order to meet the commercial specification for exporting potato tubers (sclerotium index < 12.5), the optimal conditions for the mycoparasite activity were the application of the conidial suspension at a temperature of 20^{o}C and a relative humidity of 99%. The mechanism by which *V. biguttatum* suppresses *R. solani* is believed to be caused by the action of the CWDEs, chitinases, glucanases and proteases (McQuilken and Gemmell 2004). Other antagonists have shown a high efficiency on controlling *R. solani*, among them is the Ascomycete *Stachybotrys elegans* (Benyagoub et al. 1994).

2.1.6. *STACHYBOTRYS ELEGANS*

Stachybotrys elegans is a destructive mycoparasite of *R. solani* and is considered to be a potential biocontrol agent (Morissette et al. 2003, 2008). The mycoparasitic process is accomplished by several successive steps: production of an extracellular matrix that surrounds *R. solani* cell; coiling and the formation of appressoria that aid in penetrating the pathogen's cell wall followed by intracellular colonization (Benyagoub et al. 1994). Applying cytochemical and immunocytochemical techniques, Benyagoub and co-workers (1996) examined morphologically the interaction between *S. elegans* and *R. solani* (hyphae and sclerotia). Their findings clearly showed that the colonization of the host by *S.*

elegans during the course of the interaction is attributed to combined enzymatic action and mechanical pressure involving the secretion of certain enzymes that are implicated in the degradation of the host's cell walls. The absence of N-acetylglucosamine at the penetration sites provided evidence that the mycoparasite produces chitinases in the presence of its host.

Several CWDEs were characterized from *S. elegans*, and their kinetics studied. They include glucanases (Archambault et al. 1998; Tweddell et al. 1995) and chitinases (Taylor et al. 2002). All purified enzymes degraded the hyphal tips of *R. solani*. As with *Trichoderma* species, the expression of genes encoding some CWDEs in *S. elegans* is stimulated by carbon and nitrogen sources as well as by the presence of a live host (Morissette et al. 2006). The temporal expression of several mycoparasite's genes selected from an SSH-library generated from the interaction between *S. elegans* and its host *R. solani* was studied during live confrontation between *S. elegans* and *R. solani* and between *S. elegans* and a non-host *S. sclerotiorum* (Morissette 2006). The results showed a higher expression of genes when *S. elegans* was in direct interaction with the host fungus compared to the non-host. Interestingly, the study also showed that some genes were down-regulated during interaction with the non-host fungus. The authors believe that such an effect may be related to production of repressor molecules secreted by the non-host as counterattack.

2.1.7. MYCOPARASITISM OF SCLEROTIA

For a mycoparasite to be classified as an effective biocontrol agent, it should be able to suppress the disease caused not only by the mycelium of the pathogen but also by its resting vegetative structures. Sclerotia, the vegetative structures of many fungi are considered to be the main source of inoculum as they overwinter in the rhizosphere of the infected plant. This has led several studies to test the ability of some mycoparasites to colonize these structures.

Mischke (1998) studied the interaction between the mycoparasite *Sporidesmium sclerotivorum* and several potential hosts belonging to the same

lineage, the Sclerotiniaceae under in vitro and in soil conditions. They speculated that an unknown signal could be secreted from the host sclerotia to achieve a complete mycoparasitism of *Sclerotinia minor, S. sclerotiorum* and *Amphobotrys ricini* by the mycoparasite. The interaction between the mycoparasite *Pythium oligandrum* and two morphologically different types of sclerotia, the plano-convexoid sclerotium of *Botrytis cinerea* and the tuberoid sclerotium of *S. minor* has been examined (Rey et al. 2005). The study revealed that the melanized rind cells of the sclerotia in both hosts constituted a rough barrier to be crossed and that colonization occurred only in the case of *Botrytis*. The difference in the colonization of the two types of sclerotia was attributed to the melanin deposited on the surface of these structures, forming a superficial layer in the *B. cinerea* host, whereas it enveloped the whole outer cells in *S. minor*.

The mode of parasitism underlying the interaction between the mycoparasite *Aspergillus terrus* and the pathogen *S. sclerotiorum* was studied using the sclerotial bait technique (Melo et al. 2006) in which sclerotia of the host were dipped in a conidial solution of *A. terrus* and incubated on an antibiotic amended potato dextrose agar (PDA). *A. terreus* manifested a mycoparasitic behavior in colonizing the sclerotia of *S. sclerotiorum* by producing small hyphal branches that penetrated host cell wall, grew inside the cells and sporulated outside the host. Total mortality of the sclerotia was confirmed by Scanning Electron Microscopy (SEM) showing a complete invasion of the sclerotia, a massive destruction of the medullary cells and a sporulation outside the host indicating that *A. terrus* is a destructive mycoparasite for *S. sclerotiorum*.

The structural anatomy of the sclerotia has shown to affect the mycoparasitic interaction and the expression of mycoparasitic-related genes (Willetts and Bullock 1992). Interaction studies of the mycoparasite *S. elegans* with its host *R. solani* and a non-host *S. sclerotiorum*, demonstrated that the expression of some genes such as, calmodulin, acetylcholinesterase and *sechi44* was influenced by the structural anatomy of the sclerotia suggesting that a component of the sclerotia stimulates the expression of these genes (Morissette et al. 2006).

In contrast to the hyphal parasitism, not much work has been done on the genetics of sclerotia degradation by *Trichoderma* spp. The role of a *T. virens* laccase gene *lcc1* in mycoparasitism of two types of sclerotia was studied using gene knock-out studies. Strains with loss of function of *lcc1* had reduced ability to degrade *B. cinerea* sclerotia whereas the same mutants had enhanced ability to degrade *S. sclerotiorum* sclerotia (Catalano et al. 2011). These results reconfirm that the architecture and anatomy of sclerotia plays an important role in host defense.

Collectively, the above findings indicate the need of in-depth studies in which the expression of attack and defense genes is studied simultaneously during the mycoparasitic interaction.

2.1.8. SIGNAL TRANSDUCTION GENES

Recognition between a parasite and its host is an essential step for successful continuation of the parasitic process and like other organisms, fungi use signaling cascades to recognize suitable hosts, penetrate and invade the host tissue, overcome host defenses, and optimize growth in the host by altering their transcripts abundance and secreting specific proteins and metabolites leading to morphological changes in the host (Zeilinger and Omann 2007). The signal transduction pathways involved in these mechanisms are conserved in most of the eukaryotes and are composed of three components: heterotrimeric G proteins, cyclic AMP-dependent protein kinase and Mitogen Activated Protein Kinase (MAPK) (Bolker 1998; Kronstad et al. 1998; Lee and Dean 1993; Mitchell and Dean 1995; Xu 2000; Xu and Hamer 1996).

2.1.8.1. G-PROTEIN

Heterotrimeric G proteins are composed of α, β, and γ subunits. Upon binding of a ligand molecule to the receptor in the cell wall, G-proteins are activated leading to the formation of GTP bound on the Gα subunit followed by the dissociation of Gα subunit from the Gβγ dimer. In filamentous fungi, Gα subunits

play crucial roles in the recognition process, and in the regulation of different functions such as sexual and asexual reproduction, and pathogenicity in which fungi sense the presence of mating partners by pheromones and pathogenic fungi respond to signals from their hosts (Gronover et al. 2001; Jain et al. 2002).

Fungal Gα subunits are highly conserved and can be divided into three major subgroups (I, II, and III) with subgroup I and III involved in the mycoparasitic process and fungal development respectively (Bolker 1998). Loss-of-function mutants of two different Gα proteins (TgaA and TgaB) in *T. virens* belonging to subgroup I have showed different functions in mycoparasitism (Mukherjee et al. 2004). TgaB mutants did not manifest any difference from the wild type concerning its mycoparasitic ability towards *R. solani* and *S. rolfsii* whereas TgaA has manifested a host specific selectivity during mycoparasitism by being essential for the antagonism against *S. rolfsii* but not against *R. solani*.

2.1.8.2. Cyclic Adenosine Monophosphate (cAMP)

cAMP signaling is involved in a variety of processes in fungi including the control of differentiation, mating processes, virulence, and stress (Kronstad et al. 1998). Following the activation of G proteins, signal transition to the cytoplasm and nucleus takes place through Gα or Gγ protein subunits via stimulation of adenylyl cyclase which synthesizes the messenger cAMP (Clapham and Neer 1993; Gilman 1984). Although the cAMP signaling cascade is conserved in fungi, cAMP-dependent protein kinases (PKA) can have different functions by either activating or inhibiting transcriptional factors or repressors to achieve specific control of downstream events (Kim et al. 2011; Schumacher et al. 2008; Yamagishi et al. 2005).

Evidence on the role of PKA in the development and pathogenicity of plant pathogenic fungi was demonstrated in *Magnoporthe grisea*. A delay in appressorium formation and host tissue penetration were observed when the *cpkA* gene was disrupted (Mitchell and Dean 1995). Similar findings on the involvement of a PKA signaling gene in the biocontrol process of *Trichoderma virens* has been reported (Mukherjee et al. 2007). The importance of *tac1* was

manifested in growth reduction and in confrontation assays between a mutant type of *T. virens* (Δ*tac1*) and several hosts (*S. rolfsii*, *R. solani* and *Pythium* sp.) where no overgrowth of the Δ*tac1* mutant on the hosts was observed. Additionally, it was shown that many factors could be involved in a synchronized signaling mechanism where a pheromone response transcription factor activity was regulated by both cAMP and MAP kinase pathways in *M. grisea* (D'Souza and Heitman 2001; Kahmann et al. 1999).

2.1.8.3. MAP kinase

Mitogen-activated protein (MAP) kinases are a family of serine/threonine protein kinases involved in transducing a variety of extracellular signals that will have an impact on regulating the growth and differentiation processes of the organism (Dickman and Yarden 1999; Nishida and Gotoh 1993; Schaeffer and Weber 1999; Zhao et al. 2007).

MAPK cascades are conserved in all eukaryotes and are organized in a three-kinase architecture consisting of a MAPK kinase kinase (MAPKKK), a MAPK kinase (MAPKK), and a MAPK. After ligand binding to the G protein coupled receptors (GPCR), the signal is transmitted to the nucleus via sequential activation of these kinases by phosphorylation (Banuett 1998; Schaeffer and Weber 1999).

Phylogenetically, MAPKs are divided into three phylogenetically related subgroups, ERKs, SAPKs (JNK, and HOG/p38), and MAPK3 (Kültz 1998) based on the conserved sequences in the catalytic domain. Two fundamental differences are the basics of the separation between these subgroups: the nature of the external stimuli, and the TXY consensus sequence present in the activation loop of the catalytic domain. ERKs are known to be activated by pheromones, cytokinins, growth factors, and pathogen's presence and are critical for cell proliferation whereas the SAPKs are stimulated by starvation conditions, temperature, UV, and osmotic stress and they mediate growth arrest and apoptosis (Pearson et al. 2001). The remaining subgroup MAPK3 remains poorly understood. MAP kinases are activated by dual phosphorylation on the Thr and Tyr within the motif Thr-Glu-Tyr (ERKs), Thr-Pro-Tyr (JNK), and Thr-Gly-Tyr

(HOG/p38) in the subdomain VIII of the catalytic domain (Strnisková et al. 2002).

Although genes in signaling pathways are highly conserved at the amino acid level, the pathways and their interconnections are distinct in different fungi. Accordingly, disruption of these genes may result in different effects. MAP kinases belonging to the yeast extracellular signal-regulated kinase (YERK1) subfamily (Kültz 1998) have been shown to play key roles in the formation of infection structures and in invasive growth of several phytopathogenic fungi including *M. grisea* (Xu and Hamer 1996), *Ustilago maydis* (Andrews et al. 2000; Kahmann et al. 1999; Müller et al. 1999), *B. cinerea* (Zheng et al. 2000), *Colletotrichum lagenarium* (Takano et al. 2000), and *Fusarium oxysporum* (Di Pietro et al. 2001).

Different functions for MAP kinases have been highlighted in biocontrol studies. The deletion of the MAPK *tmkA* in *T. virens* reduced its ability to induce resistance in cucumber seedlings, along with a decrease in sclerotial parasitism of *S. rolfsii* and *R. solani*, whereas hyphal parasitism remained unaffected and similar to the wild type (Mukherjee et al. 2003; Viterbo et al. 2005). Contrary to the role of *tmkA*, an increase in the antagonism and the biocontrol ability of *T. virens* was observed when another MAP kinase gene, *tvk1*, was deleted in *T. virens* (Mendoza-Mendoza et al. 2003). While the disruption of *pmk1* in *M. grisea* resulted in the formation of normal mycelia and conidia and had no effect on mating, disruption of its homologue in *C. heterostrophus chk1* resulted in strains with reduced pathogenicity (Lev et al. 1999; Xu and Hamer 1996).

Collectively, these observations indicate that the roles of MAPK/ERK homologues in plant protection, biocontrol and mycoparasitism can be more diverse and require further investigation. Chapter 4 will address the expression of MAPK/ERK of *Stachybotrys elegans* grown under different conditions.

2.1.9. METABOLISM

Among the most important mechanisms that fungi employ to induce the defense response in host plants, termed "induced systemic resistance", is antibiosis (Van Loon et al. 1998). The antagonists produce an array of metabolites that help in limiting and controlling the development of plant pathogens (Gao et al. 2010; Zabalgogeazcoa 2008).

The metabolism is defined as the sum of all the biochemical reactions carried out by an organism. These biochemical pathways are divided into two categories. Primary metabolism is responsible for the formation of essential metabolites (e.g., proteins, polysaccharides, and lipids) associated with the growth and cellular activity of an organism. By contrast, secondary metabolism involves the synthesis under extreme or stressful conditions of a wide array of complex and low molecular-weight compounds that are implicated and involved in signaling, development and interaction with other organisms and are considered species-specific or strain-specific, and sensitive to environmental and nutritional cues (Hoffmeister and Keller 2007; Osbourn 2010).

Considered not essential for growth and development, several researchers have concluded that the production of secondary metabolites might have been an evolution in organisms for communication with, or as a defense reaction against, other microbes or multicellular organisms (Brakhage and Schroeckh 2011; O'Brien and Wright 2011). Any application for fungal strains as biocontrol agents should be preceded by a thorough investigation of their secondary metabolites repertoire and their mode of actions.

Many biocontrol strains are known to produce a wide array of secondary metabolites: polyketides (i.e. 2,4-diacetylphloroglucinol), non-ribosomal peptides (gliotoxin, gliovirin and peptaibols), and terpenes (i.e. trichothecenes, viridin) (Anitha and Murugesan 2005; Frisvad et al. 2007; Gardiner et al. 2009; Howell 1999; Reddy et al. 2009; Rowan 1993).

2.1.9.1. Classes of secondary metabolites

2.1.9.1.1. Terpenes

Fungi synthesize several bioactive classes of terpenes via terpene cyclases enzymes, (Lee and Chappell 2008). Present in *Trichoderma* and *Stachybotrys* genera, the trichothecenes along with their hydrolysis products (trichodermol and verrucarol) have been reported to be potent inhibitors of protein and DNA synthesis (Bloom et al. 2007; Cundliffe and Davies 1977; Hinkley and Jarvis 2001; McCormick et al. 2011). Another trichothecene-type toxin named trichodermin, which is secreted by *S. chartarum* and *Trichoderma* sp. has been shown to be effective against the soil-borne pathogen *R. solani* (Bertagnolli et al. 1998; Jarvis 2003). The presence of these mycotoxins in the *Stachybotrys* genus is not limited to the species *chartarum*. Morissette and colleagues (2008) identified genes in *S. elegans* with putative functions related to toxin production. Cytochrome P450 and *O*-methyltransferase genes are part of several mycotoxin biosynthetic pathways and complex bioconversion processes related to detoxification and production of secondary metabolites in fungi (Gershater and Edwards 2007; Guengerich 2001).

The efficacy of terpenes such as viridin in controlling phytopathogens has been demonstrated in biocontrol studies using *Trichoderma viride* against *Verticillium dahlia* in cotton (Hao et al. 1999).

2.1.9.1.2. Polyketides

Polyketides are synthesized by polyketide synthases (PKSs) and include the 2,4-diacetylphloroglucinol (2,4-DAPG) metabolite that is secreted by fluorescent *Pseudomonas* spp. to suppress the fungal pathogen *Gaeumannomyces graminis* var. *tritici* (Bangera and Thomashow 1999). Generally, polyketides are known for their antibiotic and antifungal properties. Additionally, they play a role in communication establishment between organisms (Khosla 2009; Staunton and Weissman 2001).

2.1.9.1.3. Non-ribosomal peptides (NRP)

NRP are derived from both proteinogenic and non-proteinogenic amino acids by multidomain, multi modular enzymes named non-ribosomal peptide synthetases (NRPSs) (Finking and Marahiel 2004; von Döhren 2009). Examples of NRP are gliotoxin, gliovirin, siderophores and peptaibols that are known for their anti-microbial activities (Mukherjee et al. 2011; Wei et al. 2005).

2.1.9.1.3.1. Gliotoxin and gliovirin

They were discovered in *T. virens* based on their antibiotic/antifungal properties against different fungi (Howell 2006). Gliotoxin is produced by the "Q" strains of *T. virens* and is active against *Botrytis allii* when applied at a concentration of 3.75 µg/mL in the growth media (Brian and Hemming 1945; Wilhite and Straney 1996) whereas the "P" strains produce gliovirin which causes coagulation and disintegration of the protoplasm of *Pythium* spp. (Howell and Stipanovic 1983).

2.1.9.1.3.2. Peptaibols

Peptaibols are peptides, produced by *Trichoderma* sp. containing α-aminoisobutyric acid, a C-terminal 1,2-amino alcohol and an acetylated N-terminus (Degenkolb et al. 2008). Their antimicrobial properties reside in their ability to form ion-channels in lipid membranes that help them in controlling plant pathogens (Goulard et al. 1995). Tex1 peptaibol synthetase, one of the two peptaibol synthetases that have been identified in *Trichoderma*, is responsible for the production of trichovirin II that can trigger and induce resistance in plants (Viterbo et al. 2007).

Evidence on the induction of resistance in cucumber plants infected with *Pseudomonas syringae* pv. *lachrymans* has been attributed to the secretion of two peptaibols, alamethicin and trichovirin II, by *T. virens* strain Gv29-8 (Leitgeb et al. 2007; Viterbo et al. 2007). Following plant root colonization, higher transcript levels of *tex1* were observed in *T. virens* as compared when the fungus was grown

alone. A decrease in phenols production and also in the biocontrol efficacy in *T. virens* mutants lacking the *tex1* gene was observed in cucumber plants in response to foliar pathogen attack (Viterbo et al. 2007). Responses similar to hypersensitive reaction to pathogen attack were observed in *Arabidopsis* after alamethicin application (Rippa et al. 2010). Additionally, the Trichokonins (VI, VII, VIII) from *Trichoderma koningii* SMF2 have showed a broad-spectrum of action against many bacteria and phytopathogens such as *R. solani*, *F. oxysporum*, *B. cinerea* and *Colletotrichum* sp. (Xiao-Yan et al. 2006).

2.1.9.2. Metabolic profiling of pathosystems

Metabolome analysis seeks to identify and quantify the entire collection of intracellular and extracellular metabolites. Conceptually, there are two basic approaches used in metabolomics: metabolite profiling strategy that investigates qualitatively all the detectable metabolites through metabolic fingerprinting, covering the endometabolome (intracellular metabolites), and metabolic footprinting, which deals with the exometabolome (metabolites released from the cells). The second approach is considered target analysis where quantification of predefined metabolites is achieved (Allwood et al. 2008; Nielsen et al. 2004).

Most of the fungal metabolites that have been studied so far are the result of plant-pathogen interactions. Their identification and quantification was achieved using different analytical platforms (Allwood et al. 2012; van der Werf et al. 2007) Although most quantitative strategies couple a separation technique (e.g. liquid chromatography (LC) or gas chromatography (GC) with mass sprectrometry (MS) or nuclear magnetic resonance (NMR) based detection, it is not uncommon to make use only of direct infusion MS for metabolite profiling (Sauer and Kliem 2010; Villas-Bôas et al. 2005). From a practical standpoint, it is impossible to extract and detect the complete set of all the metabolites using a single or even limited set of analytical techniques (Dettmer et al. 2007).

A pathosystem relationship is governed by an intimate crosstalk between the two partners where the pathogen secretes secondary metabolites to colonize the

plant host, which in turn activates its metabolism to counteract and defend the attack. This crosstalk has been shown to be specific in the sense that each pathosystem possesses its own metabolome (Abdel-Farid et al. 2009; Aliferis and Jabaji 2012; Hong et al. 2012; López Gresa et al. 2010). When *Brassica rapa* was infected with three different fungi; *Leptosphaeria maculans, Aspergillus niger,* and *Fusarium oxysporum,* the levels of phenylpropanoids (sinapoyl-, feruloyl- and 5-hydroxyferuloyl malate), flavonoids (kaempferol and quercetin) and fumaric acid were detected by ^{1}H NMR and found to be higher in plants infected with *Fusarium* compared to plants infected with other fungi (Abdel-Farid et al. 2009). Coupling LC-MS and ^{1}H NMR analysis, López Gresa et al. (2010) studied the changes in the metabolome of tomato leaflets infected with *citrus exocortis viroid CEVd,* and *Pseudomonas syringae* pv. *tomato.* The glycosylated gentisic acid was the most induced metabolite in the viroid infection, whereas phenylpropanoids and the flavonoid rutin were found to be associated with bacterial infection only.

Compared to the wealth of studies conducted on the metabolome of plant-pathogen systems, only few studies have investigated the secretion of metabolites during antagonism (Jonkers et al. 2012; McQuilken et al. 2003; Morris et al. 1995; Rodriguez Estrada et al. 2011). Isolated from the mycoparasite *Coniothyrium minitans* by thin layer chromatography (TLC) and identified using NMR, the compound macrosphelide A exhibited an antifungal ability against the mycelia growth of *Sclerotinia sclerotiorum*, and *Sclerotium cepivorum* when it was amended in the growth media (McQuilken et al. 2003). Morris and co-workers (1995) combined different analytical platforms (TLC/GC-MS/NMR) with the aim to isolate and identify potential antifungal compounds from the mycoparasite *Verticillium bigutattum*. Two metabolites, named bigutol and methylbigutol, were purified from culture filtrate of *V. bigutattum* and manifested an inhibitory ability against a range of plant pathogenic fungi (*B. cinerea, R. solani, Fusarium oxysporum f.* sp. *narcissi, Fulvia fulva, Pyrenochaeta lycopersici)* when amended in the culture media. The relationship between the antagonist *Fusarium verticillioides* and *Ustillago maydis* was investigated at the

metabolomic level using LC-TOF-MS (Jonkers et al. 2012; Rodriguez Estrada et al. 2011). Reduced growth of *U. maydis* during co-cultivation with the biocontrol agent was attributed to the combined presence of the antifungal compound fusaric acid and cell wall degrading enzymes that were secreted by *F. verticillioides.* These studies have tested the efficacy of few compounds on the growth of pathogens or explored the whole metabolome at one specific time point (i.e. after 10 days of co-cultivation).

Collectively, these observations indicate that in-depth studies are required to understand the metabolic changes occurring during fungal-fungal interactions. This will be dealt in Chapter 6.

2.1.10. CONCLUSION

Despite intensive research on mycoparasitism in the last two decades, the mechanism is still poorly understood and little is known about the genetic regulation occurring during the mycoparasite/host interaction. In fact, the majority of the reports focus on the mycoparasitic action towards its host by studying the production of CWDEs, the expression of their encoding genes and the effect of certain metabolites on the host. Although mycoparasites have been widely applied as biocontrol agents but their efficacy in controlling pathogens is not consistent and stable due to the defense reaction of the pathogen that is still not investigated. Thus, a better understanding of the modes of action and genetic regulation of mycoparasites and their hosts and their corresponding metabolites will improve our understanding on this mechanism.

CONNECTING STATEMENT BETWEEN CHAPTERS 2 AND 3

Chapter 3 highlights the temporal transcripts abundance between the Ascomycete *Stachybotrys elegans* and its host, the plant pathogen *Rhizoctonia solani*. Using two different host structures, hyphae and sclerotia, the expression of several mycoparasitic and host genes belonging to different functional categories was monitored over 5 days of interaction. This study revealed the involvement of multiple regulator mechanisms employed by both partners and manifested by differential expression patterns of some genes in parasitized sclerotia and mycelia of *R. solani.* To the best of our knowledge, we are the first to report on the host response to attack by the mycoparasite. Elevated levels of pyridoxal reductase-encoding gene that is known to contribute to ROS quenching as in response to stress conditions was documented. This finding can help in understanding the genetic regulation mechanisms exploited by *R. solani* during the mycoparasitic process. The results of this section are published in Mycologia (2011, Vol 103, pp.483-493).

I have contributed to the following chapter by designing the experimental set-up, conducting all the experiments and writing the manuscript. Professor S. Jabaji provided supervision, funding throughout the study, made suggestions to the experimental set-up and corrected the manuscript.

CHAPTER 3

Expression of genes of *Rhizoctonia solani* and the biocontrol *Stachybotrys elegans* during mycoparasitism of hyphae and sclerotia

Rony Chamoun and Suha Jabaji*

*Corresponding author: Suha Jabaji

McGill University, Macdonald Campus, Department of Plant Science, 21,111 Lakeshore Road, Montreal, Qc, H9X 3V9

Phone: (514) 398-7561 Fax: (514) 398-7897

E-mail: suha.jabaji@mcgill.ca

"Reprinted from Mycologia, Vol 103, Chamoun, R. and Jabaji, S. Expression of genes of *Rhizoctonia solani* and the biocontrol *Stachybotrys elegans* during mycoparasitism of hyphae and sclerotia. Pages 483-493, Copyright (2011), with permission from Mycological Society of America".

3.1. ABSTRACT

Knowledge of mycoparasitism has been focused on how antagonists affect pathogens in relation to mechanisms, metabolites and transcripts abundance. Just as microbial antagonists use a diverse arsenal of mechanisms to dominate interactions with hosts, hosts also have diverse responses to counteract antagonism. In this study differential transcripts abundance of eight mycoparasitism-induced genes and eight host-response genes was monitored during in vivo interactions between the mycoparasite *Stachybotrys elegans* and hyphae and sclerotia of the host, *Rhizoctonia solani* over 5 d of interaction. Using real time reverse transcription polymerase chain reaction, comparative analyses demonstrated that hyphal and sclerotial structures triggered different expression patterns. These results indicated that multiple regulatory mechanisms might be involved. The high elevated expression of some genes belonging to the mycoparasite and the host suggest that these genes play an important role during the mycoparasitic process and host defense respectively.

Keywords: Host-response genes, Mycoparasitism, Quantitative Real time RT-PCR

3.2. INTRODUCTION

The cellular interaction between a mycoparasite and its host that begins with a molecular interaction and the expressions of some of the genes involved in mycoparasitism require direct contact with a live host. Direct confrontation studies between a mycoparasite and its living host may comprise factors, excluded during simulated mycoparasitism, that affect gene regulation. Global transcripts abundance studies on mycoparasites other than Trichoderma strains and involving direct contact with the hosts have been limited to a few (Morissette et al. 2008; Muthumeenakshi et al. 2007; Seidl et al. 2009). The availability of inducible genes not only permit us to study their expression during the mycoparasitic process between the partners but also allows comparison of their induction to that of similar genes from other sources (i.e. *T. harzianum*).

Stachybotrys elegans is a filamentous soilborne fungus that displays biocontrol capabilities against several anastomosis groups (AGs) of *Rhizoctonia solani* (Benyagoub et al. 1994). The mycoparasitic properties of *S. elegans* let it colonize its host by accomplishing several successive steps: production of fimbrial extracellular matrix that surrounds the host cell, coiling of the hyphae and the formation of appressoria-like structures that aid in penetrating the host cell wall followed by intracellular colonization leading to destruction of hyphae and sclerotia of *R. solani*. This process is accompanied by the secretion of cell wall-degrading enzymes (Archambault et al. 1998; Taylor et al. 2002). A total of 94 identified unique genes of *S. elegans* associated with several functional categories, including pathogeneic processes, toxin metabolism, translation, transcription and DNA repair, were expressed preferentially during mycoparasitism (Morissette et al. 2008). Based on our findings, some of these genes were not identified or reported previously to be involved in mycoparasitism thus making them potential targets for gene regulation studies during this process.

To date knowledge on mycoparasitism has focused on how antagonists affect pathogens in relation to mechanisms, metabolites and transcripts abundance. Just as microbial antagonists use a diverse arsenal of mechanisms to dominate interactions with hosts, hosts also have diverse responses to counteract

antagonism (Duffy et al. 2003). Information is lacking on how pathogens respond to attack and what mechanisms dominate to counteract mycoparasitism. Understanding the pathogen's reaction mechanisms provides an innovative approach to improving the durability of biologically based disease control strategies. ESTs previously identified 81 sequences associated with cellular respiration, metabolism, transcription, thiamin synthesis and pathogenesis. None of these putative genes have been investigated under conditions of R. solani mycoparasitism.

Based on the EST analysis of both the pathogen and the mycoparasite, the objective of this study was to monitor the expression patterns of selective novel mycoparasitism-induced and host genes during the beginning of contact and associate the transcriptional changes with the formation of different mycoparasitic structures. In addition we examined whether transcriptional changes in both the host and the mycoparasite markedly differed under different mycoparasitism situations (i.e. parasitized host's hyphae and sclerotia).

3.3. MATERIALS AND METHODS

3.3.1. Organisms and cultures conditions

Cultures of *Stachybotrys elegans* (ATCC 18825) and *Rhizoctonia solani* AG-3 (ATCC 10183) were revived from pre-colonized oat kernels on 1% potato dextrose agar (PDA; Difco Laboratories, Michigan, USA). They were incubated at 24^{o}C for 7 and 5 d respectively. To induce conidiation of *S. elegans*, cultures were homogenized in a blender (Model 31BL92, Waring) for 4 x 2s pulses with sterile double-distilled water. One milliliter of homogenate was spread on a permeable cellophane membrane (500 PUT; UCB, North Augusta, USA) that was placed on 1% PDA culture plates and incubated at 24^{o}C. After 7 d mycelia were harvested by scraping the surface of the membrane and gently shaken in sterile water to dislodge conidia. The mycelia were removed from suspension by filtering through a sterile nylon cloth. The filtrate was centrifuged at 9000 rpm for

10 min, and the conidial pellet was resuspended in sterile water and kept on ice until further use. The concentration was adjusted to 10^6 conidia/mL with a haemocytometer (s/p ULTRALANE Spot lite counting chamber; Improved Neubauer 1/4000 sq. mm, 1/10 mm deep). Conidia were applied to the respective treatments immediately after the concentration was adjusted.

To harvest sclerotia of *R. solani* agar plugs (5 mm) from 5 d old *R. solani* starter cultures were placed on cellophane-covered PDA. Cultures were incubated at 24^{o}C for 25 d, allowing sufficient development of sclerotia. Uniform-size mature sclerotia (5 x 5 mm) were selected and air dried.

3.3.2. Confrontation assays

Assays between the pathogen (i.e. *S. elegans*) and morphologically different structures of the host (i.e. *R. solani*) were established to evaluate whether changes in target transcript abundance are attributable to the mycoparasitic activity of *S. elegans* and/or to the defense reaction of *R. solani*. Plate confrontation assays were carried out in the dark on culture plates containing minimal synthetic medium (Tweddell et al. 1995) supplemented with 1% gellan gum (MSMA; Phytagel, Sigma, St Louis, Missouri) and covered with a permeable cellophane membrane.

3.3.3. Dual culture of *S. elegans* with hyphae of *R. solani*

The experimental set-up consisted of agar plugs (5 mm) of *R. solani* placed on the surface of the cellophane-covered solid MSMA plates. The plates were incubated at 24^{o}C letting *R. solani* cultures grow for 3 d. Cultures were sprayed with 100 µL suspension containing 10^6 conidia/mL with a Badger 350 air brush and MC-80 mini air compressor at 1 kg/cm^2 and incubated at 24^{o}C. The control treatment consisted of spraying 100 µL of *S. elegans* conidia on cellophane-covered MSMA plates. Transcripts abundance was monitored during hyphae-

hyphae interaction at 3 d and every 24 h for 5 d. There were six replicates for each treatment and harvesting time.

3.3.4. Dual culture of *S. elegans* with the sclerotia of *R. solani*

To investigate whether the expressions of *S. elegans* target genes are altered in the presence of a morphologically different host structure, transcript abundance was monitored at 3, 4, 5, 6 and 7 d after inoculation of host sclerotia with *S. elegans* conidia. Each treatment consisted of five sclerotia (0.2 g fresh wt) placed on a cellophane membrane on solid MSMA in Petri plate (100 x 15 mm). Each sclerotium was inoculated with 30 µL 10^6 conidia/mL for a total of 150 000 conidia/plate. The control treatment consisted of sclerotia inoculated with 30 µL sterile distilled water. There were six replicates for each treatment and harvesting time. All plates were incubated at 24^{o}C.

Mycelia from both fungi as well as from *R. solani* sclerotia from dual cultures and controls were collected at each time point from four replicates and immediately immersed in liquid nitrogen and stored at -80^{o}C for total RNA extraction. The remaining two replicates at each time point were used for microscopic observations.

3.3.5. Light microscope observation of the mycoparasitic process

To associate the transcriptional changes with the development of biological steps of the mycoparasitic process membrane pieces (5 x 5 mm) from the conidia-hyphae interaction plates as well as from the control cultures were excised while individually infected and control sclerotia were sectioned (10 µM) with a cryotome (Thermo Scientific, Ontario). All sections were stained with lactophenol blue or water and viewed under a light microscope at 40X and 100X magnifications respectively. Conidial germination, presence of hyphal coiling and penetration pegs and colonization of the host were digitally documented with the Moticam 2300 digital camera (GENEQ In. Montreal, Quebec).

3.3.6. RNA extraction and retrotranscription (RT)

All fungal samples were ground into powder with a mortar and pestle. Total RNA was extracted from 100 mg powdered tissue with RNeasy Plant Mini KitTM (QIAGEN, Mississauga, Ontario) following manufacturer's recommendations. RNA integrity and concentration were assessed by spectrophotometry with NC1000 (NanoDrop, Wilmington, Delaware) and 1.2% folmaldehyde-agarose gel electrophoresis. A total of 500 ng RNA was reverse transcribed with QuantiTect reverse transcription kit (QIAGEN) following the manufacturer's recommendations, and DNA present in the samples was destroyed with the DNase wipeout buffer included in the kit. cDNA integrity was verified by conventional RT-PCR with the universal primers ITS-1F and ITS4 (Gardes and Bruns 1993, White et al. 1990; Table 3.1) followed by electrophoresis on a 1 % agarose gel. The transcribed cDNA was diluted one-fifth in sterile distilled water to reduce effects of interference by RT reaction components in downstream PCR applications. The transcribed diluted cDNA was used in further PCR reactions.

3.3.7. Primer design

Primer pair sets for eight *S. elegans* target genes and eight *R. solani* genes were designed with the software Primer 3 (Rozen and Skaletsky 2000). Primers were checked to avoid hairpins or primer-dimer formations and submitted to Nucleotide blast at NCBI (http://www.ncbi.nlm.nih.gov/) to confirm specificity (Table 3.1) and were custom synthesized by AlphaDNA (Montreal, Quebec). These primers were constructed from EST sequences generated from different SSH libraries (Morissette et al. 2008).

For normalization purposes of quantification of fungal target transcript abundance in the mycoparasite and the host, reference genes whose expressions remain stable irrespective of the treatment are necessary as is their specificity. For dual cultures of *S. elegans* with *R. solani* the primer pair H4-1a and H4-1b (Glass and Donaldson 1995) was used to amplify HISTONE-4 encoding gene from *S. elegans* only, whereas the glyceraldehydes-3-phosphate dehydrogenase gene

(*gpd11*) (Cubeta et al. 1996) was used to normalize the transcript abundance of *R. solani* target genes (Table 3.1).

To confirm that the designed primers amplify only the target and reference genes in their respective organism, they were tested on cDNA of each organism, and the amplified products were sequenced and blasted for specificity. This was necessary to ensure that primers did not amplify a putative product in the wrong organism.

3.3.8. Transcripts abundance by real time quantitative RT-PCR

QRT-PCR assays were conducted on 16 target genes (Table 3.1). Four biological replicates and two technical replicates were performed for each template and two negative controls were included in each run. QRT-PCR was conducted in Mx3000 (Stratagene, Cedar Creek, USA) with SYBR Green II master mix (Stratagene) following the manufacturer's recommendations. Amplification was performed in a 25 µL reaction mixture containing 160 nmol each primer, 2X SYBR Green II master mix, 15 mM reference dye ROX and 2 µL cDNA template (one-fifth dilution). The amplification conditions were 95^{o}C for 10 min (hot start), followed by different cycles and annealing temperatures (Table 3.1) and then an extension at 72^{o}C for 30 s. the fluorescence reading was 72^{o}C at the end of the elongation cycles. Data generated by QRT-PCR were estimated with Stratagene analysis software.

3.3.9. Data quantification

Data from technical replicates were averaged before normalization. The relative transcript abundance ratios of the target genes versus reference genes were calculated with the equation [1] developed by Zhao and Fernald (2005), based on crossing point (CP) and efficiency obtained for each sample amplified with the reference genes (*histone-4* and *gpd11*) and the different target genes.

$$R0: 1 / (1+E)^{\wedge} CT$$

R0 is the initial template concentration, E is the efficiency in the exponential phase and CT is the cycle number at threshold.

The relative transcript abundance of each target gene was tested for significant difference between harvesting time point and treatments by two-way analysis of variance (ANOVA) with the software SPSS statistical package (release 17.0.0, 2008). Comparison between means at each time point was made with least significant differences (LSD) at $P < 0.05$.

3.4. RESULTS

3.4.1. Light microscopy

In pure and in dual cultures, *S. elegans* hyphae are easily recognized and distinguished from those of *R. solani* (Fig. 3.1A) by the small diameter and the profuse production of conidia arising from phialides (Fig. 3.1B). Germination of *S. elegans* conidia and hyphal growth toward the hyphae of *R. solani* was observed 2 d after inoculation (data not shown). The first apparent contact between *S. elegans* and *R. solani* occurred at 3 d of interaction with limited intracellular colonization of host hyphae (Fig. 3.1C). Coiling and appearance of penetration peg-like structures was observed 4 d after inoculation (Fig. 3.1D) followed by rapid and excessive coiling at 5 d (Fig. 3.1E). Hyphal overgrown and sporulation of the mycoparasite was observed respectively at 6 and 7 d. Substantial intracellular growth and colonization of *S. elegans* inside *R. solani* was observed by day 4 and onward. Several hyphae of *R. solani* were degraded and the cytoplasm appeared empty compared to control hyphae. The first signs of *S. elegans* growth over the surface of infected sclerotia were observed after 3 d of inoculation with complete coverage with white mycelia by day 7. This sections of infected sclerotia confirmed that intercellular and intracellular colonization of cells began 3-4 d (Fig. 3.1F-G) and continued thereafter. Colonized cells appeared empty (Fig. 3.1H).

3.4.2. Quantification of target and reference genes transcripts

The primer sets designed for each of the target genes of *S. elegans* and *R. solani* as well as for the reference genes (*histone-4* and *gpd11*) (Table 3.1) successfully amplified a single product with the expected putative size in all experiments. The identity of each product was confirmed by sequencing. In addition the QRT-PCR melting-curve analysis resulted in a single peak with specified melting temperatures for each primer set and the amplification plots were highly reproducible between technical replicates (data not shown) and fluorescence data from negative controls containing no template always remained below the detection threshold.

3.4.3. *S. elegans* transcript abundance during interaction with the host's hyphae and sclerotia

In the presence of the host's hyphae and sclerotia relative expression of *S. elegans* target genes was significantly altered ($P < 0.05$) compared to the control treatment. Depending on the gene and in situations where *S. elegans* has parasitized the host hyphae, four of eight genes were highly induced, two were down-regulated (Fig. 3.2), and two were not affected (data not shown). Compared to *S. elegans* alone substantially high transcript abundance of oxidoreductase was observed with an increase of 696-fold at 5 d after inoculation at which excessive coiling of host hyphae was observed and then diminishing to 49-fold at 6 d (Fig. 3.2A). All three genes belonging to the toxin metabolism functional category were highly induced, peaking at 4 d for carboxylesterase (16-fold increase) and at 5 d for cytochrome P450 monoxygenase and *O*-methyltransferase with an increase of 35 and 4.5-fold respectively (Fig. 3.2D-F). In contrast xylanolytic transcriptional activator (Fig. 3.2B) and ankyrin repeat domain encoding genes were significantly down-regulated in the presence of the host's hyphae with a highest decrease of 11 and 3.7-fold at day 6, a period at which the host hyphae was overgrown by the mycoparasite respectively (Fig. 3.2B-C). In sclerotial mycoparasitism the relative transcript abundance of all except two target genes of

S. elegans were not affected. Similar to colonized hyphae, a 109-fold increase in oxidoreductase encoding gene transcription was detected at 6 d (Fig. 3.2G). On the other hand expression of 60S ribosomal protein encoding gene decreased significantly fourfold and ninefold at 4 and 5 d (Fig. 3.2H).

3.4.5. *R. solani* transcript abundance during interaction with the mycoparasite

In response to infection of only one out of eight genes the pyridoxal reductase was highly up-regulated in both infected hyphae and sclerotia (Fig. 3.3A-B), four were highly down-regulated (Fig. 3.3C-J) and the remaining genes were not affected (data not shown). Compared to uninfected hyphal and sclerotial cells transcription of pyridoxal reductase peaked by 369 and 388-fold increase in infected hyphae and sclerotia respectively at which time excessive coiling and appearance of infection-like pegs (day 5) and overgrowth and sporulation (day 6) of the mycoparasite occurred (Fig. 3.1). Of interest all genes whose transcript abundance was significantly down-regulated showed a similar expression trend with the highest decrease peaking at 7 d for infected sclerotia and at 5 d for infected hyphae (Fig. 3.3).

Table 3.1. Primers used in QRT- PCR assays to amplify target genes of *S. elegans* (mycoparasite) and *R. solani* (pathogen) belonging to different functional categories

Functional Category	Target genes	Sequence (5' ⟶ 3')	Accession number	Annealing temperature (°C)	Amplicon size (bp)
		S. elegans target genes			
Pathogenic processes	Ankyrin repeat domain protein [a]	(F) TACTCTCAACACTCAGGACCGCTT (R) TCACTGGACTCATCGTTGTCGCAT	DW520683	64	138
	Xylanolytic transcriptional activator [a]	(F) CGACCTTGTATAGCGTGCGAAGTT (R) TTCTACAATGCTAGGCCCTTTGCG	DW520684	61	118
	Oxireductase [a]	(F) GAAGACTTTGCCAAGAAGCTGG (R) TAACTGATCATCCTGACCGTGC	EU008743	60	243
Toxin metabolism	Cytochrome P450 monooxygenase [a]	(F)AGATGCGAGTGGCGCAAGTTCTTT (R) TTCGCAGCGACTCGAGAACCATTA	DW520689	64	137

	O-methyltransferase [a]	(F) CAAAGTCCTTATTTCGGAGCGG (R) CTCATCACCGAAGTTGACGAAG	DW520859	60	265
	Carboxylesterase [a]	(F) GAAATCGCATAGCGGCTCTTAC (R) CAGGCGTATCATTCCCAAACTC	EU008749	60	303
Translation	60S ribosomal protein L 12 [a]	(F) GTTCGATCCCAATGAGGTCAAG (R) CCAAGCTAACAGACTTGGTGTG	DQ369842	60	308
Replication, transcription & DNA repair	Histone H2A [a]	(F) CGTATCATTCCTCGTCATCTGC (R) CAAGCAACCGTGAACCCTTAAC	DW520724	60	255
		R. solani target genes			
Apoptosis	Proteasome subunit alpha [a]	(F) GTTAAAGACGGAGTCGTTCTCG (R) CTTATACCGAATGGTCGAACGG	DW520861	57	281
Lipid metabolism	Esterase/lipase [a]	(F) CTACTCGACCGGGATATCAACA (R) CAATCAGAGCTGTAGGGAATGG	DW520718	57	400

Vitamin metabolism	Pyridoxal reductase AKR8 [a]	(F)GAAAGCCTCCTCTTGGAATCTG (R) GGGTAAGATTGGATCGATTGGG	DW520695	58	277
Energy & Cellular respiration	Cytochrome C oxidase subunit [b]	(F) TCAACCCTTGCTTGTCAGTCCTCT (R) AACGATAAATACCGCCTTGCCTTT	EG026321	63	214
Pathogenesis	Metallo peptidase putative protein [b]	(F) TGCTGAGGTTTTTGCCAATCACG (R) CCCAAGGTAGTCTGCTGGCTTCG	EG026298	64	236
Biosynthesis protein	Thiamine [b]	(F) CATGGGCTGCTTTCTGCGATTTC (R) TCTCAATGGGATCGGCGATA	EG026296	66	234
Stress-responsive gene product	Thiazole [b]	(F) ATTGTTAGCGCGACTGGTCACGAC (R) TGGCACCATCATGTTCGGAGAGT	EG026342	66	202
Metabolism	MMS2 putative protein [b]	(F) CTTTGAGGAAGCGATGAAGTTTGC (R) CCGCACCCGGTCCACCTTCTGG	EG026327	58	140

Table 3.1 Primers used in QRT- PCR assays to amplify target genes of *S. elegans* (mycoparasite) and *R. solani* (pathogen) belonging to different functional categories (continued)

Functional Category	Target genes	Sequence (5' ⟶ 3')	Accession number	Annealing temperature (°C)	Amplicon size (bp)
		Reference genes			
	Histone H4 [c]	(F) GCTATCCGCCGTCTCGCT (R) GGTACGGCCCTGGCGCTT	AY062173	57	260
	Glyceraldehyde-3-phosphate dehydrogenase [d]	(F) GGTATTATTGGATACACTGA (R) TTAAGCCTCAGCGTCTTTCT	AF339929	55	204

[a] Genes generated from SSH library between *S. elegans* and *R. solani* (Morissette et al. 2008)

[b] Genes generated from SSH library between *R. solani* and *S. tuberosum*

[c] Reference gene used for normalizing *S. elegans* QRT-PCR target genes (Glass and Donaldson 1995)

[d]Reference gene used for normalizing *R. solani* QRT-PCR target genes (Cubeta et al. 1996)

Figure 3.1. Microscopic images of mycoparasitism between *S. elegans* and *R. solani*. A. *R. solani* hyphae in pure culture at 3 d. B. *S. elegans* hyphae growing in pure culture at 3 d. Note the production of conidia (c) and their phialides (ph). C-E. Interaction between *S. elegans* and *R. solani* hyphae at 3, 4 and 5 d respectively. Note the formation of *S. elegans* pegs (P) on *R. solani* hyphae. F-H. Interaction between *S. elegans* and *R. solani* sclerotia at 3 d and onward. Note the empty cells of *R. solani*. Bar = 1 µm.

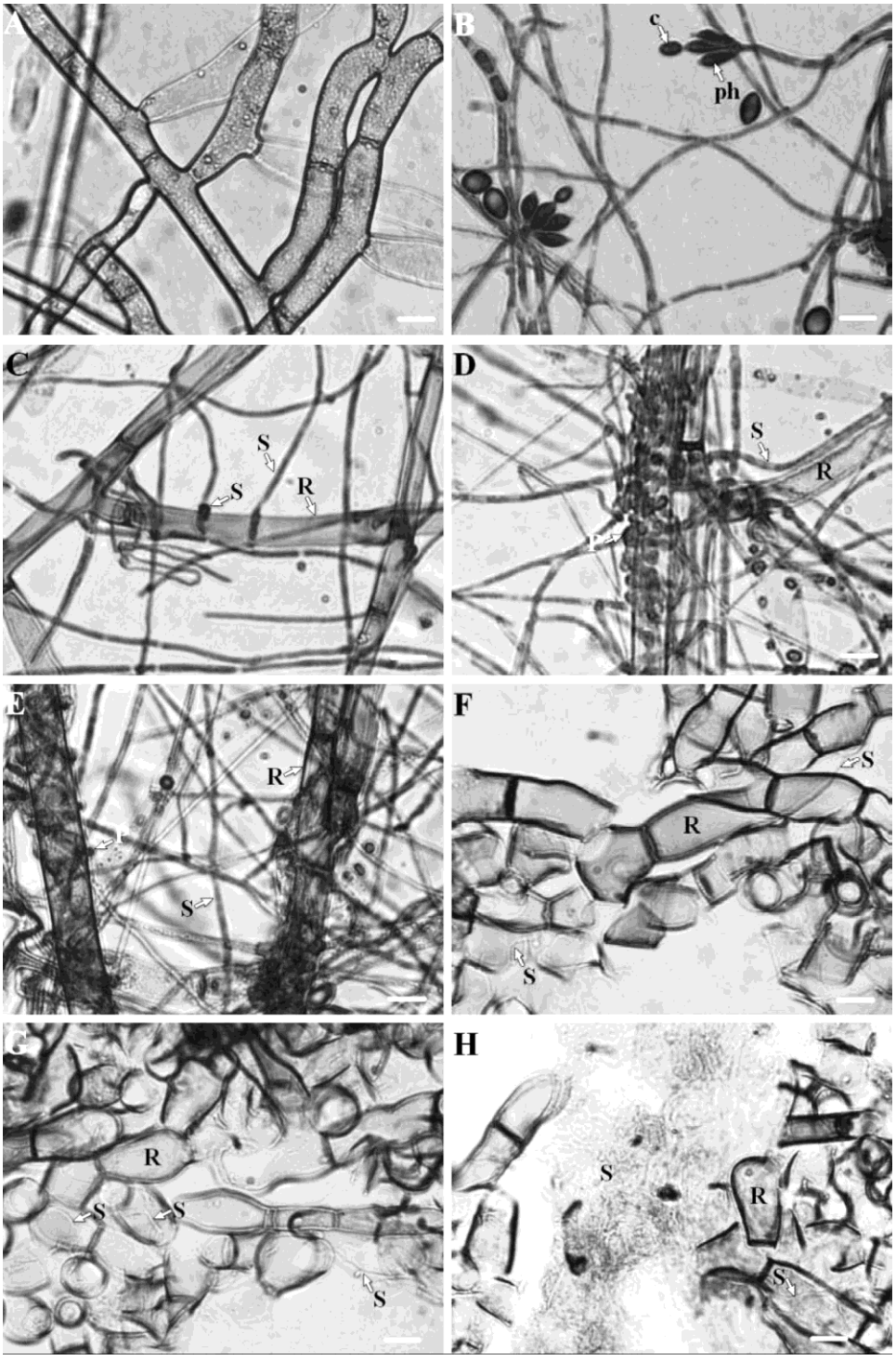

A
B
c
ph
C
S
S
R
D
S
R
E
R
S
F
S
R
S
G
R
S
S
S
H
S
R
S

Figure 3.2. Relative abundance of *S. elegans* trancripts during mycoparasitism of *R. solani* hyphae and sclerotia over 5 d of inoculation normalized by the *histone-4* encoding gene. A-F. *S. elegans* transcript abundance on *R. solani* hyphae. G, H. *S. elegans* transcript abundance on *R. solani* sclerotia. A. Oxidoreductase. B. Xylanolytic transcription factor. C. Ankyrin. D. Cytochrome P450 monoxygenase. E. Methyltransferase. F. Carboxylesterase. G. Oxidoreductase. H. 60S ribosomal protein. * indicates a significant transcript abundance between the control and the interaction ($P < 0.05$). ● = Interaction. ○ = *S. elegans* control.

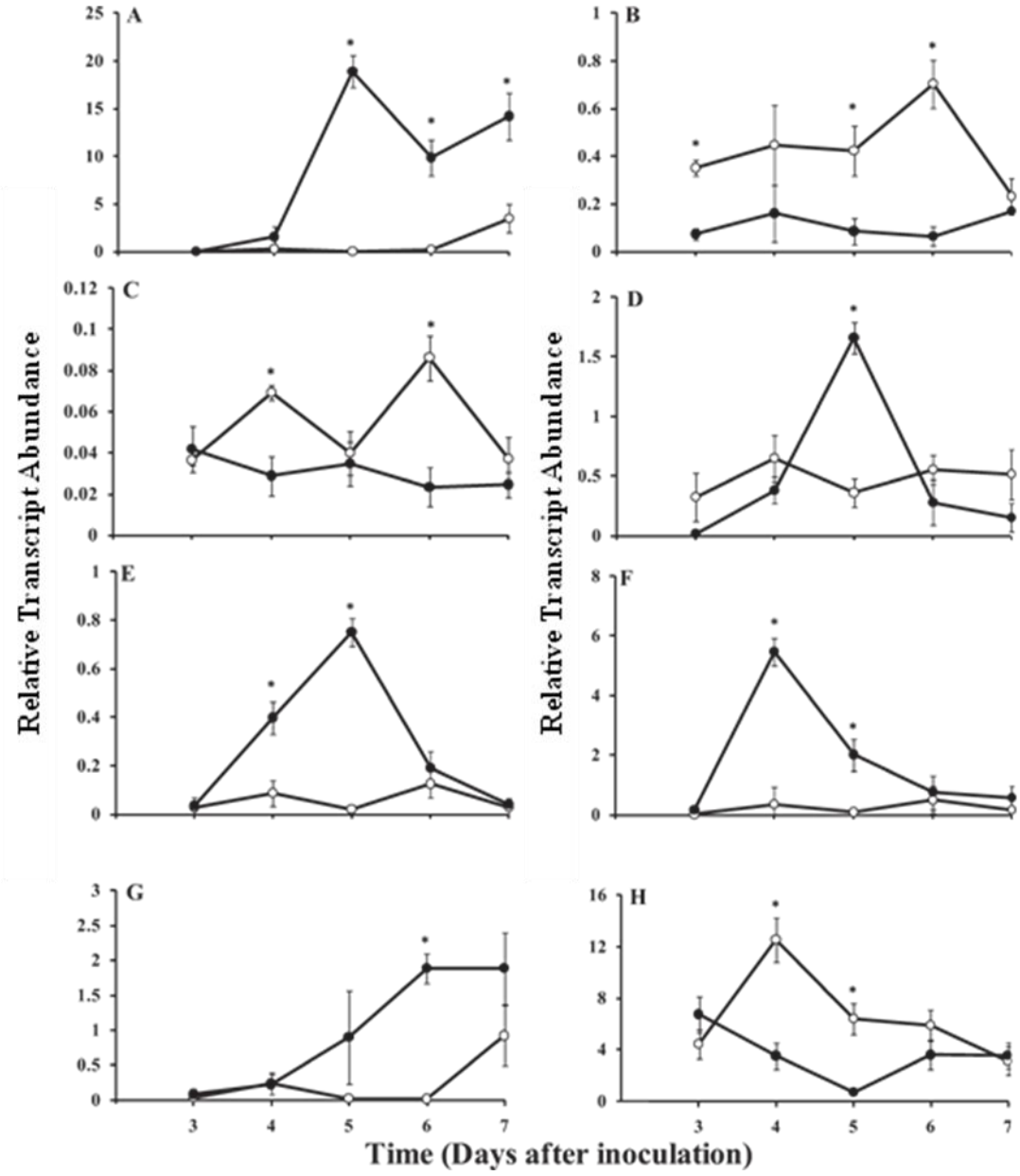
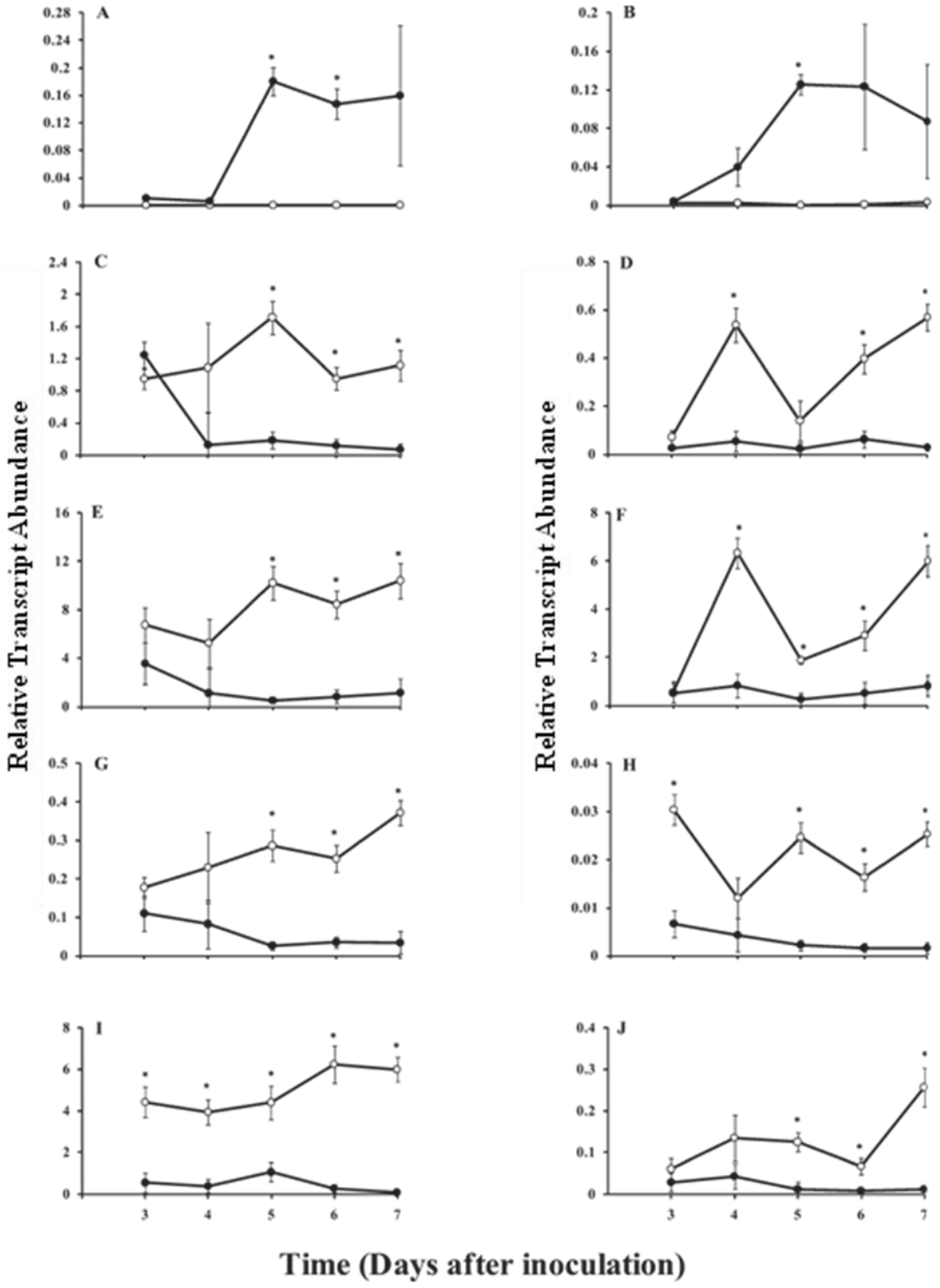

A
B
C
D
E
F
G
H
Relative Transcript Abundance
Relative Transcript Abundance
Time (Days after inoculation)

Figure 3.3. Relative abundance of *R. solani* transcripts during mycoparasitism of *R. solani* hyphae and sclerotia by *S. elegans* during 5 d inoculation normalized by the *gpd11* encoding gene. A, C, E, G, I. *R. solani* hyphae transcript abundance. B, D, F, H, J. *R. solani* sclerotia transcript abundance. A, B. Pyridoxal reductase. C, D. Metallopeptidase. E, F. Cytochrome c oxidase. G, H. Thiamin. I. J. Thiazole. * Indicates a significant transcript abundance between the control and the interaction ($P < 0.05$). ● = Interaction. ○ = *R. solani* control.


A
B
C
D
E
F
G
H
I
J
Relative Transcript Abundance
Relative Transcript Abundance
Time (Days after inoculation)

3.5. DISCUSSION

3.5.1. Mycoparasitism-associated genes

In Morissette et al. (2008), 90 ESTs were identified to encode mycoparasitism-induced genes via an SSH library established between *S. elegans* and *R. solani*. The preferential transcript abundance of these genes was based on pooled RNA samples from different time points, and their abundance was attributed to the mycoparasitism process in general and could not be ascribed to a specific time point. Therefore in a extension to our work we undertook this comprehensive study to highlight the kinetics of some of these genes that were not previously reported to be involved in mycoparasitism and studied their transcript abundance over a period in which the different biological stages of mycoparasitism (i.e. germination, contact, coiling and appearance of penetration pegs and colonization) occurred.

The results of this study demonstrated that the temporal expression of oxidoreductase encoding gene for 5 d after inoculation under different mycoparasitic situations was substantially over-expressed when excessive coiling, peg-like formation around the host hyphae and heavy colonization of sclerotial cells had occurred. Consistent with the findings of other mycoparasite genomic approach studies on *Trichoderma harzianum*, *T. hamatum* and *Coniothyrium minitans*, high abundance of oxidoreductase encoding genes also was reported (Carpenter et al. 2005; Liu and Yang 2005; Muthmeenakshi et al. 2007). Induction of oxidoreductase-encoding genes in plant pathogens had been attributed to appressorium formation in *Magnaporthe oryzae* and *M. grisea* (Oh et al. 2008). Furthermore, due to their additional role in catalyzing a wide array of chemical reactions, stressful conditions encountered by *S. elegans* during mycoparasitism of *R. solani* sclerotia are likely to occur. It is well established that sclerotia of *R. solani* produce toxic phenolic, fatty acid compounds and reactive oxygen species (Aliferis and Jabaji 2010; Georgiou et al. 2000). The high expression of oxidoreductase in *S. elegans* under sclerotia mycoparasitism could play a role in ROS scavenging and oxidative stress as also reported in the

mycoparasitic interaction *C. minitans*-*S. sclerotiorum* (Muthumeenakshi et al. 2007). Cytochrome P450 and *O*-methyltransferase-encoding genes in fungi are organized in clusters and are part of several mycotoxin biosynthetic pathways (Bhatnagar et al. 2003; Ehrlich et al. 1999; Mukherjee et al. 2006; Yu et al. 2004). In this study Cytochrome P450, *O*-methyltransferase and carboxylesterase showed a high transcript abundance compared to the control under hyphal mycoparasitic conditions only. These findings were similar to those reported for the biocontrol *T. harzianum* (Seidl et al. 2009) and suggest the importance of these genes in hyphal mycoparasitic mechanisms of *S. elegans*. In addition the involvement of these genes in many complex bioconversion processes such as detoxification and production of secondary metabolites in fungi (Gershater and Edwards 2007; Guengerich 2001) strengthens the assumption that their highly elevated expression during *S. elegans* interaction with host hyphae could be related to detoxifying compounds emitted from the host that could affect *S. elegans* in a dreadful way.

It is difficult to explain why the toxin-encoding genes did not show a high transcript abundance during sclerotia mycoparasitism. Similar relative transcript abundance of these genes in *S. elegans* growing alone or in confrontation with sclerotia lead us to entertain the possibility that multiple regulatory mechanisms might be required when *S. elegans* is in confrontation with different host structures or it could be related to the presence of inhibitor molecules produced by the host sclerotial cells. How these molecules trigger lower transcript abundance is not known and deserves further investigation. Clearly much remains to be discovered for our understanding of the relationship between these two organisms.

Of interest the expression of 60S ribosomal protein L12 exhibited a pronounced down-regulation under sclerotia mycoparasitism. Mycoparasitism is generally associated with stress in which the freely available carbon and nitrogen sources become limited especially in fungal resistant vegetative structures such as the sclerotia. Genes encoding ribosomal protein in yeasts were down-regulated during carbon and nitrogen limitation or starvation (DeRisi et al. 1997; Rautio et

al. 2007). In line with the above finding the down-regulation of 60S ribosomal protein L12 encoding gene in our study could very well be in response to unavailable carbon and nitrogen sources.

3.5.2. Host response genes

To understand how fungal hosts respond to attacks by mycoparasites the expression of several *R. solani* genes belonging to different categories were monitored. Our findings showed that only pyridoxal reductase was highly expressed during sclerotial and hyphal mycoparasitism, while the majority of the genes were significantly down-regulated compared to control.

Pyridoxal reductase is an upstream enzyme in the vitamin B6 biosynthesis pathway catalyzing the conversion of pyridoxal (PL) to pyridoxine (PN), a product that will generate at the end of its pathway the pyridoxal 5'-phosphate (PLP) (Morita et al. 2004; Sang et al. 2007). The three products (PL, PN and PLP) collectively are known to form vitamin B6, a cofactor essential for a wide array of chemical reactions in cells (Benabdellah et al. 2009; Bilsky et al. 2000). A role as antioxidant and quencher of reactive oxygen species recently had been attributed to vitamin B6 in stressed fungi and during host defense responses against abiotic and biotic stress (Bilski et al. 2000; Denslow et al. 2005; Havaux et al. 2009; Sang et al. 2007). Based on these findings we could safely interpret the over-expression of pyridoxal reductase as a result of *R. solani* defense response to *S. elegans*.

Thiamin and thiazole-encoding genes showed significant low transcript abundance in parasitized hyphal and sclerotial host cells during mycoparasitism. In fungi thiamin or vitamin B1 is a cofactor required for the activity of several enzymes of carbon metabolism (Sohn et al. 2000) and its biosynthesis occurs via two precursors, pyrimidine and thiazole (Chatterjee et al. 2006). These compounds are known to have antifungal activity against ergosterol biosynthesis that is mediated by the activity of cytochrome P450 monoxygenases (Tsuruoka et al. 1998; Wagle et al. 2008). Of note the substantial over-expression of cytochrome P450 monoxygenase-encoding gene in *S. elegans* during

mycoparasitism coincides with the low transcript abundance of thiamin and thiazole-encoding genes in *R. solani*. This observation might be an indication of the inability of thiazole-encoding gene in *R. solani* to counteract *S. elegans* attack.

In response to attack, *R. solani* cytochrome c oxidase-encoding gene was consistently down-regulated to almost negligible levels. Cytochrome c oxidase is the terminal enzyme in the energy transducing respiratory chain of eukaryotes and is known to contribute to ATP synthesis and therefore providing energy to the different cellular functions (Joseph-Horne and Hollomon 2000). Clearly *R. solani* tissue death would provide a hostile environment for *S. elegans* and probably a reduction in nutrients and free oxygen. Thus it is to the advantage of *S. elegans* to substantially suppress the host's cytochrome oxidase expression, which will affect the ability of mitochondria to synthesize ATP. In our study the relative transcript abundance of metallopeptidase encoding gene is negligible during interaction with *S. elegans*. Metallopeptidases act on a wide range of host proteins and are activated through the binding of divalent cations such as Fe^{2+}, Cu^{2+} and Zn^{2+} (Miyoshi and Shinoda 2000; Rao et al. 1998). Morissette and coworkers (2008) reported on the up-regultion of *S. elegans* pathogenic genes such as the Ctr copper transporter and ferric-chelate reductases during interaction with *R. solani*. Both genes are reported to mediate mineral (copper and iron) uptakes and sequestration during growth of the host (Zarnowski and Woods 2005), which in turn will have an effect on the nutrient availability for *R. solani*. Consequently the shortage of these cations may affect the transcription and translation of metallopeptidase.

In conclusion for the first time the temporal transcript abundance of mycoparasitism-related genes and host-response genes was monitored under different mycoparasitism situations and for 5 d after inoculation. This study also demonstrated that colonized sclerotia and mycelia trigger different transcriptional patterns of some genes, which points to the involvement of multiple regulatory mechanisms. Of significance was the finding that during mycoparasitism the host's response to attack is characterized by elevated levels of transcript for the pyridoxal reductase-encoding gene whose role in ROS quenching as a result to

stress conditions is established. This finding can serve as basis for a broader exploitation of *R. solani* genetic regulation during this process.

3.6. ACKNOWLEDGMENTS

This work was supported by a research grant to S. Jabaji from the Natural Sciences and Engineering Research Council of Canada (NSERC-Discovery). We thank Dr. H. Chen for technical help in real time PCR.

CONNECTING STATEMENT BETWEEN CHAPTERS 3 AND 4

The mycoparasitism process takes place through binding of external ligands to receptors coupled to G-proteins and embedded in the membrane of the mycoparasite. Following activation of G-proteins, the signal is transmitted to the nucleus via Mitogen Activated Protein Kinases (MAPK) pathways that will activate transcription factors leading to the regulation of genes expression. In chapter 4, we have completely characterized one MAPK gene, *smkA*, from *S. elegans* and showed that it is a homologue of MAPK/ERK subfamily and it is a member of a small gene family. We then conducted proteomic and transcriptomic studies to understand the regulation and activation of this gene when the mycoparasite is in confrontation with different structures of the host (i.e., a biotic stress) and when the mycoparasite is grown under carbon starvation conditions (i.e. an abiotic stress). Results clearly show that the differential transcript abundance of *smkA* in *S. elegans* was influenced by the type of stress over time. Our study suggests that *smkA* seems to be implicated in multifunction pathways. Future experiments are aimed at construction of disruptants that will help in elucidating *smkA* functional role in mycoparasitism and growth and how it perceives different cues from its environment.

The results of this chapter are the subject of a manuscript that is published in Current Genetics (2013, Vol. 59, pp. 43-54). I have designed the experimental set-up, conducted all the experiments and wrote the manuscript. Dr. K. A. Aliferis has contributed to the targeted proteomics analyses, and revised the manuscript. Dr. S. Jabaji provided supervision, funding throughout the study and corrected the manuscript.

CHAPTER 4

Characterization and transcriptional regulation of *Stachybotrys elegans* mitogen-activated-protein kinase gene s*mkA* following mycoparasitism and starvation conditions

Rony Chamoun, Konstantinos A. Aliferis and Suha H. Jabaji*

*Corresponding author: Suha Jabaji

McGill University, Macdonald Campus, Department of Plant Science, 21,111 Lakeshore Road, Montreal, Qc, H9X 3V9
Phone: (514) 398-7561 Fax: (514) 398-7897
E-mail: suha.jabaji@mcgill.ca

"Reprinted from Current Genetics, Vol 59, Chamoun R, Aliferis A. K., and Jabaji S., Characterization and transcriptional regulation of *Stachybotrys elegans* mitogen-activated-protein kinase gene s*mkA* following mycoparasitism and starvation conditions. Pages 43-54, Copyright (2013), with permission from Springer".

4.1. ABSTRACT

Mitogen-activated protein kinase (MAPK) signaling pathways play an important role in the development and conidiation of fungal pathogens on their hosts and the sensing of host-derived cues. Mycoparasitism is a fungus–fungus interaction comprising host-pathogen cross talk. Until now, only little information is available on the role of the MAPK signaling pathway during this interaction. Here, we report on the differential expression of a MAPK/ERK gene in the mycoparasite *Stachybotrys elegans* in response to direct parasitism of different vegetative structures of the plant pathogen *Rhizoctonia solani* (i.e., carbon-rich condition) and to nutrient starvation (i.e., carbon-poor condition). Western blot analysis against ERK1/2 highlighted an increase in their phosphorylated forms when *S. elegans* was grown under starvation condition compared to that detected in response to mycoparasitism. A higher abundance of phosphorylated ERK1/2 at the third day of interaction compared to that estimated under starvation condition was detected applying LC–MS/MS. At the transcriptional level, *smkA*, a YERK1 class member, was significantly induced in response to hyphal parasitism compared to parasitized sclerotia at 3, 4, and 5 days of interaction. However, under starvation condition, *smkA* levels were significantly induced after 7 days of growth. Southern blot analysis revealed that *smkA* is member of a small gene family. Collectively, these results suggest that *smkA* could be implicated in the mycoparasitic process in *S. elegans* as well as in stress-activated pathways. These results may be of wider significance in other fungus–fungus interactions.

Keywords: Mycoparasitism, MAP kinase, *Rhizoctonia solani*, QRT-PCR.

4.2. INTRODUCTION

A successful fungal pathogen must overcome the physical and chemical barriers set up by the host to block infection. Conserved eukaryotic signal transduction proteins participate in a number of steps that lead to infection and disease development. Fungal mitogen-activated protein kinases (MAPK) are serine/threonine proteins involved in transducing a variety of extracellular signals responsible for cell growth and differentiation processes, pathogenicity, and physical and chemical stresses (Banuett 1998; Xue et al. 2000). These can promote transcript abundance via phosphorylation of many transcription factors (Banuett 1998; Xue et al. 2000; Zeilinger and Omann 2007). The MAP kinase modules are organized into three subfamilies: extracellular signal-regulated kinase (ERK 1/2), high-osmolarity glycerol (p38/HOG), and c-jun N-terminal kinase (JNK). Their role in virulence and development, in regulating fungal cell physiology in response to nutritional stress (i.e., nitrogen and carbon starvation) as well as environmental stresses has been addressed in many plant pathogenic fungi (Chuang et al. 2000; Jain et al. 2011; Xu 2000; Xue et al. 2004; Zeilinger 2004; Zhao et al. 2007). Nevertheless, little information is available on the role of MAPK in mycoparasitism.

Mycoparasitism is a fungus-fungus interaction involving a cross talk between the host and the mycoparasite. Until now, most of the information on the signaling pathways during the mycoparasitic interaction has been reported on the model mycoparasite genus Trichoderma (Zeilinger 2004; Zeilinger and Omann 2007). There is a general phenomenon that among fungal pathogens, MAP kinases play key roles in virulence, plant infection, stress tolerance and cell wall integrity and that gene disruption compromises pathogenicity (Xu 2000; Zeilinger 2004). Their involvement in the regulation of mycoparasitism-related processes that are essential in fungal–fungal disease development remains unclear. *Trichoderma* constructed mutants (*tmkA* and *tvk1*) with MAPK/ERK1 loss of function produced contradictory results concerning their role in the production of mycoparasitism-related enzymes that were influenced by the growth media and the confronting fungal host (Mendoza-Mendoza et al. 2003;

Mukherjee et al. 2003). In addition, *lf pmk1* disruption transformants of *Verticillium fungicola*, a mycoparasite of the cultivated mushroom *Agaricus bisporus* showed unaltered virulence and secreted enzyme profiles compared to the wild type (Collopy et al. 2010). Collectively, these observations indicate that the roles of MAPK/ERK homologs in mycoparasitism can be more diverse and require further investigation.

Stachybotrys elegans is a necrotrophic mycoparasite that colonizes the hyphae and sclerotia of its host *Rhizoctonia solani* by accomplishing a series of consecutive steps: recognition and production of an extramatrical fibrillar material that surrounds the host cell, coiling and formation of infection pegs and appressoria-like structures followed by cell wall penetration and intracellular colonization (Benyagoub et al. 1994; Chamoun and Jabaji 2011). This process is partly accompanied by the production of chitinases, and b-1,3-glucanases (Archambault et al. 1998; Morissette et al. 2003; Taylor et al. 2002). Based on ESTs previously identified from suppression subtractive library (SSH), a total of 94 identified unique genes of *S. elegans* associated with several functional categories including pathogenic processes, toxin metabolism translocation, transcription and DNA repair were over expressed during extended periods of mycoparasitism (Chamoun and Jabaji 2011; Morissette et al. 2008). Among these unique genes, an EST encoding a MAP kinase was identified. To the best of our knowledge, differential expression studies of MAPK/ERK kinases in mycoparasites involved in different mycoparasitic situations (i.e. different parasitized host's structures) or when the mycoparasite is grown under nutrient limiting growth conditions have not been reported.

As a first step toward understanding the molecular basis of MAP kinases in *S. elegans*, we monitored MAPK/ERK kinases protein expression and applied LC–MS/MS to determine the relative abundance of phosphorylated MAP kinase (ERK1/2) during the mycoparasitic interaction between *S. elegans* and the host *R. solani*, and also when *S. elegans* is grown on nutrient-poor medium. As a second step, we fully cloned and characterized the first MAPK gene *smkA* from *S. elegans* and confirmed that it is homolog of the MAPK/ERK1 subfamily

of protein kinases (Kültz 1998). We then conducted comparative expression studies of *smkA* during extended periods of mycoparasitism of two different morphological structures (i.e. hyphae and sclerotia) of *R. solani* and also in response to nutritional stress.

4.3. MATERIALS AND METHODS

4.3.1. Fungal strains, media and culture conditions

Starter cultures of the mycoparasite *Stachybotrys elegans* (Pidoplichko) W. Gams (anamorph; ATCC 18825), an Ascomycete and the pathogen *Rhizoctonia solani* Kühn AG-3 (ATCC 10183), a Basidiomycete, were grown on potato dextrose agar (PDA; Difco Laboratories, Detroit, USA) at room temperature (24°C) for 7 and 5 days, respectively. From each of the corresponding starter culture, 8 mm agar plugs were grown on fresh PDA on different Petri plates (100 mm) for 7 days.

Expression of *S. elegans* MAPK gene (*smkA*) and ERK1/2 protein in response to nutritional stress was monitored when the fungus was grown on minimal synthetic medium (MSMA) with no carbon source (carbon-poor medium). The medium is composed (in g/liter) of: $MgSO_4 \cdot 7H_2O$, 0.2; K_2HPO_4, 0.9; KCl, 0.2; $FeSO_4.7H_2O$, 0.002; $MnSO_4$, 0.002; $ZnSO_4$, 0.002; $NaNO_3$, 1.0; biotin, 10 mg; gellan gum, 1 % (Phytagel, Sigma, St. Louis, USA) and covered with a permeable cellophane membrane (500 PUT; UCB, North Augusta, USA) (Chamoun and Jabaji 2011). Gene and protein expression was also monitored when the fungus was grown on MSMA in plate confrontation with live vegetative structures of *R. solani* (carbon-rich condition).

4.3.2. Experimental set up

The expression of *S. elegans* MAPK gene (*smkA*) and ERK1/2 protein under carbon starvation condition was monitored over time. *S. elegans* conidia

(100 µL) adjusted at 10^6 conidia/mL were sprayed on MSMA plates using a Badger 350 air brush and MC-80 mini air compressor at 1 kg/cm^2.

Confrontation assays (carbon-rich condition) with *R. solani* hyphae were performed by placing hyphal plugs (8 mm) of actively growing culture of *R. solani* on the surface of the cellophane-covered MSMA plates and allowed to grow at 24°C for 3 days. Cultures were sprayed with 100 µL of *S. elegans* suspension containing 10^6 conidia/mL. Confrontation assays with *R. solani* sclerotia were conducted by placing five sclerotia (0.2 g fresh wt) on cellophane-covered MSMA Petri plate (100 x 15 mm) and each sclerotium was inoculated with 30 µL of *S. elegans* spore suspension (10^6 conidia/mL). All plates were incubated at 24°C in the dark.

Protein analysis by Western blot and transcript abundance was monitored in response to nutritional starvation conditions and during dual cultures of hyphae and sclerotia starting from the second or the third day of interaction, respectively for the duration of the experiment. There were three replicates for each treatment and harvesting time point. The abundance of ERK1/2 phosphorylation performing LC-MS/MS analysis was conducted on hyphae of *S. elegans* grown under starvation conditions, and also under carbon-enriched conditions but only in response to parasitized hyphae of *R. solani*. In all cases, mycelia from *S. elegans* grown under starvation condition and parasitized host's mycelia and sclerotia by *S. elegans* were collected at each time point, immediately immersed in liquid nitrogen and stored at -80°C for total RNA and protein extraction.

4.3.3. Protein extraction

The level of phosphorylation of ERK1/2 during mycoparasitism of *R. solani* by *S. elegans* was examined by LC-MS/MS and Western blot analysis. For both analyses, total proteins were isolated following the protocols of the total protein extraction kit (Sigma-Aldrich, St. Louis, MO, USA). At the corresponding time point, fungal material from *S. elegans* grown on carbon-poor medium and from

parasitized fungal structures (carbon-rich condition) was pulverized to a fine powder under liquid nitrogen. Following the manufacturer recommendations, total protein was extracted from 200 mg of powder material and the supernatant was transferred to a new tube and stored at -80°C. The concentration of protein extracts was determined using a Bio-Rad protein assay kit (Bio-Rad, Mississauga, ON, Canada) with bovine serum albumin (Sigma) as the standard. Fifty micrograms of total protein (per lane) was resolved on a 10 % sodium dodecyl sulfate (SDS)-polyacrylamide gel electrophoresis (PAGE).

4.3.4. Western blot

Following SDS-PAGE, proteins were transferred onto polyvinylidene fluoride (PVDF) membranes by wet electroblotting (Bio-Rad). Blocking of membranes was per- formed for 2 h in Tris-buffered saline (50 mM Tris [pH 7.5], 150 mM NaCl), 0.2 % Tween 20, and 5 % non-fat dried milk at room temperature. The membranes were subsequently incubated with either anti-p44/42 MAP kinase (1:1,000 dilution) or anti-phospho-p44/42 MAPK (Thr^{202}/Tyr^{204}andThr^{185}/Tyr^{187}) antibody (1:1,000 dilution) that specifically detects endogenous levels of p44 (ERK1) and p42 (ERK2) MAP kinases when dually phosphorylated using the Phos- phoPlus antibody kit (Cell Signaling Technology; Danvers, MA, USA) in Tris-buffered saline (50 mM Tris [pH 7.5], 150 mM NaCl), 0.1 % Tween 20, and 1 % non-fat dried milk overnight at 4°C. Following hybridization, blots were washed three times for 10 min each in Tris-buffered saline and 0.2 % Tween 20 and subsequently incubated with horseradish peroxidase-conjugated secondary antibody (Abcam 6721; 1:2,500 dilution) (Cambridge, MA, USA) for 1.5 h at room temperature, followed by washing for 2 h in Tris-buffered saline and 0.2 % Tween 20 with changing the buffer every 10 min. Antibody binding was visualized using an enhanced chemiluminescence kit (ThermoFisher Scientific, Canada) according to the manufacturer's instructions. Equal protein loading was verified by Coomassie brilliant blue (CBB), and also

blots were probed with a polyclonal anti-Histone H3 (Abcam 1791; 1:5,000 dilution).

4.3.5. Targeted proteomics analyses

4.3.5.1. Sample preparation for proteomics

Protein bands located in the region of 37-50 kDa on the Coomassie 1D gel were excised, cut into small pieces, and placed in 2 mL Eppendorf tubes. Samples were subjected to TCA precipitation and protein extracts were re-solubilized in 10 µL of urea buffer (6 M). An aliquot of 2.5 µL of the reduction buffer (45 mM DTT and 100 mM NH_4HCO_3) was added to reduce the proteins for 30 min at 37 °C, and then alkylated by adding 2.5 µL of the alkylation buffer (100 mM iodoacetamide and 100 mM NH_4HCO_3) for 20 min at 24 °C in the dark. Following alkylation, the urea concentration was diluted with 20 µL of HPLC grade water and then 50 ng of trypsin (Promega, Madison, USA) were added. Protein digestion by trypsin was performed at 37 °C for 18 h and stopped by adding 5 µL of 5 % (v/v) formic acid Optima® (Fisher Scientific). Protein digests were dried using a Lab-conco CentriVap refrigerated vacuum concentrator equipped with a cold trap (Labconco, Kansas City, MO, USA) and stored at -20°C until further analysis.

4.3.5.2. Liquid chromatography-MS/MS

To determine the amount of phosphorylated relative to the non-phosphorylated MAP kinases at the amino acid threonine (T) and tyrosine (Y), LC-MS/MS analysis was performed using an LTQ Orbitrap Velos (Thermo Scientific, San Jose, CA, USA) equipped with a Proxeon nanoelectrospray ion source (nESI, Proxeon Biosystems, Odense, Denmark). For chromatographic separation, a Self-Pack PicoFrit fused silica capillary column (New Objective, Woburn, MA, USA) packed with the C18 Jupiter reverse-phase material (75 µm x 15 cm x 5 µm, 300 Å) (Phenomenex, Torrance, CA, USA) was installed on the

Easy-nLC II system (Proxeon Biosystems). The buffers used were 0.2% (v/v) formic acid (buffer A) and 100% acetonitrile/formic acid 0.2% (v/v, buffer B). For more details on LC-MS/MS analytical conditions see Appendix I.

4.3.5.3. Protein identification

Data were analysed using the Proteome Discoverer v1.3 (Thermo Scientific) applying the SEQUEST search algorithm for searches against a target in-house-built protein library in FASTA format composed of 293 entries of MAP kinases (See Appendix II). Searches for phosphorylation (S, T, and Y) were performed for the detection of phosphorylated forms of the MAPK/ERK protein. In addition, the Percolator algorithm was applied performing semi-supervised machine learning since it improves the discrimination between incorrect and correct peptide-spectrum matches (PSMs) (Käll et al. 2007). Proteome Discoverer report files were exported to SIEVE v1.3 (Thermo Scientific) for the calculation of normalized intensities of identified peptides of MAPK/ERK in the analyzed samples. Peptides with cross correlation value Xcorr < 0.9 (z=1), Xcorr < 1.0 (z=2), Xcorr < 1.2 (z=3), and Xcorr < 2.0 (z>3) were removed during import. The software SIEVE aligns the MS spectra over time from different experimental conditions and then determines features in the data (*m/z* vs retention time pairs), the so-called frames. Based on the created frames, normalized intensities of the identified peptides are calculated. For more details on SIEVE proteomics analysis consult Appendix III.

4.3.6. Protein sequence alignment and primers design

To obtain the entire sequence of the MAP kinase gene (*smkA*) from *S. elegans*, several primer sets were designed for different stages of this study (Table 4.1). All primers were tested for self-complementarity, complementarity between both primers, and theoretical melting temperature was determined using the software DNAman v.4.13. Primers: DegF and DegR were designed from the

alignment of 13 protein sequences of MAP kinase (ERK1/2) belonging to different ascomycetes (Fig. 4.1) and were used in PCR reactions to amplify putative product from genomic DNA with a 300 bp size. For Genome-walking PCR reactions, a set of gene-specific primers (GSP: 5'GSP1, 5'GSP2, 3'GSP1, and 3'GSP2) were designed based on the genomic DNA sequence of the 300 bp putative product.

4.3.7. Nucleic acid extraction and manipulation

Total genomic DNA was isolated from frozen mycelia of *S. elegans* according to Lee and Taylor (1990) with the following modifications: the genomic DNA was RNase treated and subjected to two rounds of phenol-chloroform, washed with 70% ethanol, air dried and dissolved in TE (10 mM Tris, 1 mM EDTA).

For the construction of Genome-walking libraries, four blunt-end cutting restriction enzymes (EcoRV, DraI, PvuII, and StuI) were used individually to digest *S. elegans* genomic DNA completely. Each batch of digested genomic DNA was purified and ligated to the adaptors provided in the GenomeWalker^{TM} Universal kit (Clontech, CA, USA) according to the manufacturer's protocol. The ligated products were used as templates to perform primary PCR reactions using gene specific primers (GSP1, Table 4.1) and the Ap1 primer (GenomeWalker^{TM} Universal kit). The secondary PCR reaction was performed using the internal primers (GSP2, Table 4.1) and Ap2 (GenomeWalker^{TM} Universal kit) and the diluted primary PCR product as the template, to selectively amplify the desired product in the subsequent nested PCR. The PCR conditions for both PCR reactions were done according to the manufacturer's recommendations. The PCR fragments were then purified using the QIAquick gel extraction kit (Qiagen, Mississauga, ON, Canada), subcloned in plasmid pCR-TOPO (Life Technologies Inc**.,** Burlington, ON, Canada) sequenced, and assembled in a contig using DNAman v.4.13, and then blasted on NCBI for homology and identity confirmation. The full sequence of *smkA* gene was deposited in the GenBank database under the accession number JX094498.

4.3.8. Southern blot analysis

To construct the probe for Southern blotting, a 709 bp cDNA fragment of the *smkA* gene was amplified by PCR using the two primers; probe forward and reverse (Table 4.1). The amplified product was purified and DIG labeled via random priming according to the manufacturer's recommendation (Roche Applied Science, QC, Canada). The genomic DNA of *S. elegans* was digested with BamHI, EcoRI, and HindIII, electrophoresed on a 0.8% agarose gel, transferred onto Nylon Hybond N+ membrane (Roche Applied Science) and UV cross-linked. DIG-labeled probe was heat-denatured at 95^{o}C for 10 min and added to the hybridization solution. Hybridization was performed according to the manufacturer's instructions. Detection of chemiluminescent signals was performed using the BioRad chemiDoc^{TM} XRS^{+} imaging system (Mississauga, ON, Canada) for 30 min.

4.3.9. Phylogenetic analysis

The phylogenetic relationship of *S. elegans* (*smkA*) to other members of MAPK/ERK1/2 of selected fungi (Ascomycetes and Basidiomycetes) and plants was generated from multiple sequence alignments using ClustalW. Dendrogram construction was made using MEGA 5.05 (Tamura et al. 2011) applying the maximum likelihood method. The MAPK subfamily HOG was used as an out-group.

4.3.10. Isolation of RNA and reverse transcription

RNA for RT-PCR assays was extracted from parasitized hyphae and sclerotia of *R. solani* at each time point of interaction, and also from *S. elegans* hyphae grown on MSMA (carbon-poor medium) and harvested at the same time periods. Fungal material was ground to a fine powder in liquid nitrogen using a mortar and a pestle. Total RNA from 100 mg of powder was isolated using the RNeasy Plant Mini Kit^{TM} and treated with RNase-free DNase I^{TM} (QIAGEN) according to the

manufacturer's recommendations. Contamination of RNA with DNA was verified by PCR amplification of total RNA with the ITS 1-F and ITS 4 primer set which amplifies a 650 bp product of filamentous fungi (White et al. 1990). The concentration and purity of RNA was checked by absorbance on 260 nm and 280 nm, while the quality of RNA was checked on 1.2 % (w/v) formaldehyde agarose gel. Total RNA amounts of 500 ng from the different treatments were reverse transcribed using the Quantitect Reverse transcriptase kit^{TM} (QIAGEN) following the manufacturer's recommendations and each cDNA was diluted to 1/5th.

4.3.11. Quantitative RT-PCR conditions

QRT-PCR assays were conducted on the target gene MAP kinase (*smkA*) and two reference genes (*histone-4* and *β-tubulin*) (Table 4.1). Three biological replicates and two technical replicates were performed for each template and two negative controls were included in each run. QRT-PCR using SYBR Green II master mix (Stratagene, Cedar Creek, USA) was conducted according to previously published conditions (Chamoun and Jabaji 2011) except that the annealing temperature was 57°C for 30 s.

The relative transcript abundance ratios of *S. elegans smkA* during interaction with *R. solani* and in response to carbon starvation were normalized against the geometric mean of the two reference genes: *histone-4* and *β-tubulin.* The statistical software tool Bestkeeper (http://www.gene-quantification.info) was applied to select the best reference gene exhibiting minimal variation across treatments. The transcript abundance levels of *histone-4* and *β-tubulin* encoding genes had the lowest variation with a standard variation (SD) less than 1 and a coefficient of variation (CV) of 2.32-2.46 respectively. Because of their low variation in transcript abundance, both genes were chosen as the appropriate reference genes.

Data from technical replicates were averaged before normalization. QRT-PCR data were calculated as a normalized transcript abundance of gene using the equation (1) developed by Zhao and Fernald (2005) based on crossing point (CP)

and efficiencies obtained for the samples amplified with the reference genes (*histone-4* and *β-tubulin*) and the target gene *smkA*. The relative transcript abundance of the target gene was tested for significance between harvesting time point and treatments by two-way analysis of variance (ANOVA) using the SPSS statistical package v.17.0.0 (IBM Corporation, Armonk, NY, USA). Comparison between means at each time point was made using least significant differences (LSD) at $P < 0.05$.

$$R0 = 1 / (1+E)^{\wedge} CT \qquad (1)$$

R0 is the initial template concentration, E is the efficiency in the exponential phase, and CT is the cycle number at threshold.

4.4. RESULTS

4.4.1. Activation of ERK1/2 during interaction with *R. solani* and in response to starvation condition

The activation of the MAP kinase proteins is done by phosphorylation that occurs at the amino acid positions threonine (T) and tyrosine (Y) of the conserved site TXY of ERK1/2 subfamily (Kültz 1998). Using specific anti-phospho-p44/42 MAPK (Thr^{202}/Tyr^{204}andThr^{185}/Tyr^{187}) antibodies that detect endogenous levels of p44 (ERK1) and p42 (ERK2) MAP kinase, the phosphorylation levels around 44 and 42 kDa were detected during interaction, and in *S. elegans* alone grown on carbon-poor culture medium (Fig. 4.2A). Highest expression levels were observed in the phosphorylation of two MAPK proteins at around 42 and 44 kDa in *S. elegans* in response to carbon starvation condition compared to the mycoparasitism where there was no difference in expression between parasitized hyphae and sclerotia over time. No significant increase in the protein level was observed under all conditions (Fig. 4.2B).

4.4.2. A phosphoproteomic approach identified one phosphopeptide with a TXY motif, which is activated during mycoparasitism and in response to nutrient starvation

Targeted searches against the in-house built library using the Proteome Discoverer and applying the SEQUEST search algorithm, and Percolator for the detection of target and decoy PSMs returned 527 peptides which were either phosphorylated at the threonine (T) or tyrosine (Y) or both amino acids, and 7301 peptides that were not phosphorylated at any of the two amino acids. Blastp on NCBI identified fifty-nine identical peptide sequences in both phosphorylated and non-phosphorylated forms as MAP kinase fragments. Among them, a single peptide with the TXY motif, the signature sequence for MAP kinases, was identified. Using the SIEVE software, the normalized intensities of the frame corresponding to this peptide were calculated. In general, under both conditions (i.e., starvation and mycoparasitism) there was an induction in the phosphorylation sites of MAP kinases. At 48 h, there was a 1.5-fold increase in phosphorylation in response to nutrient starvation as compared to mycoparasitism. The highest increase in the abundance of phosphorylation (2.5-fold) was observed at 72 h compared to 48 h of mycoparasitic interaction (Table 4.2).

4.4.3. *smkA* is a homologue of the ERK1 subfamily

The designed primer pair DegF and DegR successfully amplified a PCR product of 300 bp in size that was confirmed via sequencing to be MAP kinase. Four different primers were designed from that sequence and used in the Genome-walking with the aim to obtain the whole sequence of the *smkA* gene. Following the second PCR amplification of the first round PCR product with nested GSP2 and adaptor primers, two PCR products (500 and 1.500 bp) were obtained and assembled into a contig. The sequence analysis using NCBI led to the identification of the first MAP kinase named *S. elegans* MAP kinase A (*smkA* accession no JX094498). The organization of the gene and its features

are shown in Fig. 4. 3. The full length of *smkA* gene is 1631 bp and consists of an open reading frame (ORF) of 993 bp. The coding sequence of *smkA* is interrupted by 3 introns (42-112, 309-361 and 744-838 bp), and is shown in italic letters in the gene sequence. The predicted protein sequence of 331 amino acids has a molecular weight of 38.4 kDa with a calculated isoelectric point (pI) of 6.49. The different subdomains of the ERK catalytic domain are identified in italic letters in the protein sequence and designated by Roman letters. The phosphorylation lip of the protein contains two important sites for the function of the protein. First, the ATP binding site that is recognized by the conserved sequence "dfg" and second the activation site represented by the motif "tey". We were able to highlight the presence of the Kinase Interaction Motif (KIM) "mltfkeytkaidv" underlined in the protein sequence and located after the active site of the protein. This motif appears to be conserved in all MAPKs with the consensus sequences $X\text{-}\emptyset_H\text{-}X_2\text{-}(Arg/Lys)_{1\text{-}2}\text{-}(X)_{2\text{-}6}\text{-}\emptyset_A\text{-}X\text{-}\emptyset_B$ (where $\emptyset_A$, $\emptyset_B$ and $\emptyset_H$ are hydrophobic residues Leu, Ile, or Val).

To confirm the relatedness between SMKA and members of the subfamily of protein kinases, a phylogenetic tree of protein kinases belonging to selected Ascomycetes, Basidiomycetes, as well to *Arabidopsis thaliana* was constructed using the protein sequences (Fig. 4.4). A complete separation between the major groups of MAP kinases belonging to ERKs and HOG pathways was observed. *S. elegans* MAP kinase SMKA belongs to the large group of ERK1/2 subfamily in which the Ascomycetes, Basidio-mycetes and Arabidopsis are each clustered in a separate clade. Within this group, SMKA was closely clustered to the MAP kinase of the *F. oxysporum* f.sp. *lycopersici* (Fmk1 AAG01162). In addition, all the MAP kinases that belong to the HOG/OSM pathway were clustered together in a separate clade.

4.4.4. *smkA* is member of a small gene family

The number of genes that encode the MAPK/ERK1 *smkA* in the genome of *S. elegans* was estimated by Southern blot analysis (Fig. 4.5). Genomic DNA was

digested with BamHI, EcoRI, and HindIII, and probed with a DIG-labeled cDNA segment (709 bp) of the *smkA* gene (Table 4.1). Under high-stringency conditions of hybridization, the probe hybridized one high-molecular-weight EcoRI fragment, two BamHI and two HindIII fragments. The size and the intensity of the fragments suggest that at least one additional member closely related to *smkA* is present in *S. elegans* genome.

4.4.5. Differential induction of *smkA* transcripts during mycoparasitism and carbon starvation

The *S. elegans* MAPK/ERK1 *smkA* showed distinct temporal kinetic patterns and transcript abundance levels under different mycoparasitic and nutritional starvation situations (Fig. 4.6). In the presence of host hyphae and sclerotia, relative expression of *smkA* was significantly altered ($P < 0.05$). When *S. elegans* has parasitized the hyphae of *R. solani*, an up-regulation of *smkA* with 3.6- and 1.8-fold increases at 3 and 7 days, respectively was observed. No difference in transcript levels was noted at 4, 5, and 6 days of interaction. In the case of parasitized sclerotia, *smkA* expression was significantly different from that expressed under carbon starvation with a fold increase of 2.2, 1.5 and 1.9 at 4, 5 and 7 days of interaction, respectively. Transcript levels of *smkA* were substantially higher in parasitized hyphae than in sclerotia at 3, 4 and 5 days of interaction with a significant fold increase of 2.0, 2.6 and 1.9, respectively. No difference in *smkA* transcript abundance was observed between parasitized hyphae and sclerotia at 6 and 7 days after interaction. In response to carbon starvation, *smkA* transcript abundance levels did not significantly vary compared to those expressed in parasitized structures except at 7 days of growth. The specificity of the primers tested on gDNA/cDNA of *R. solani* showed no amplification (data not shown).

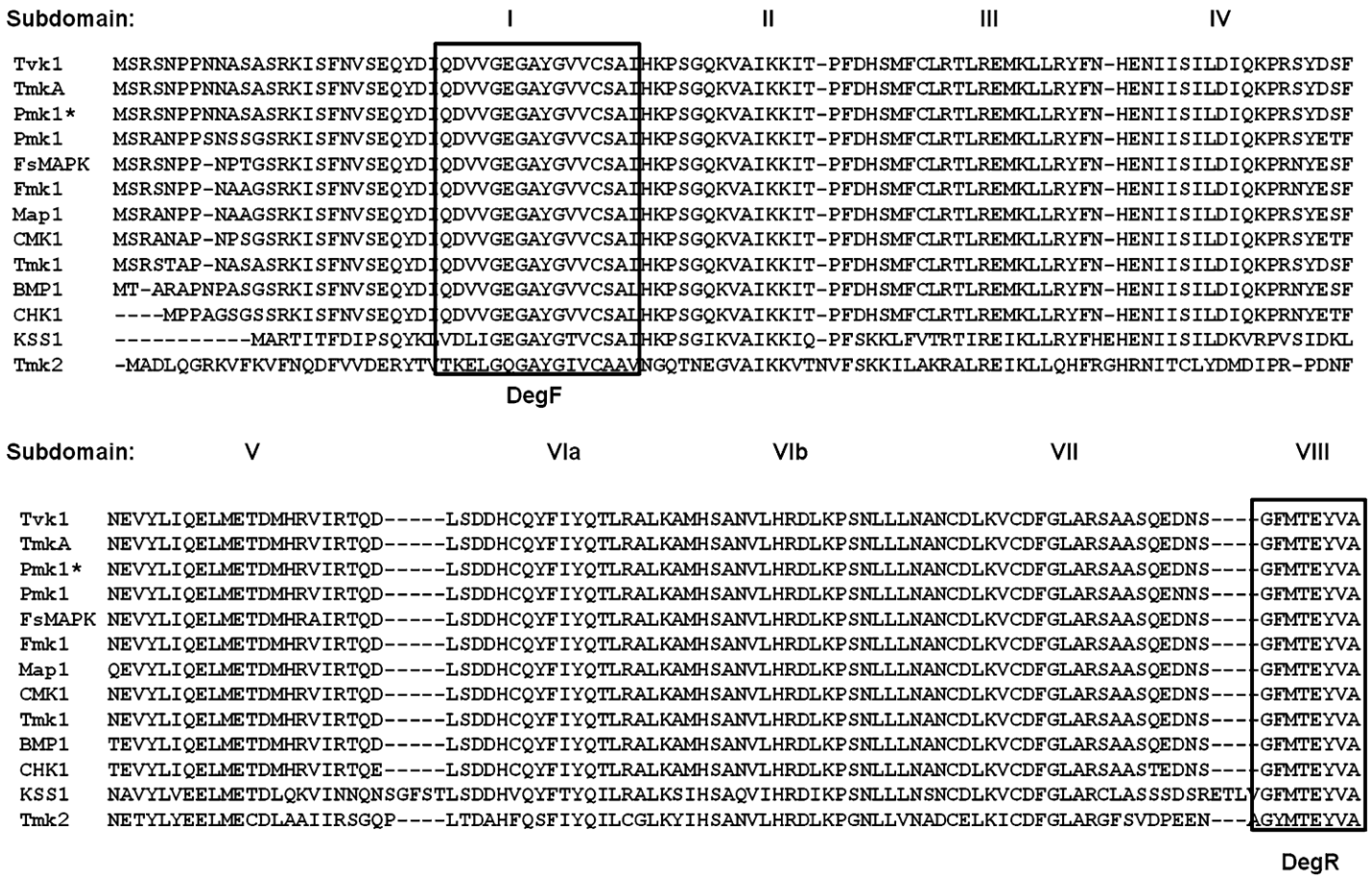
Table 4.1. Primers used in this study

Primer name	Sequence (5' ⟶ 3')	Strategy
DegF	GATGTNGTDGGHGARGG	Degenerate PCR
DegR	GCVACRTATTCNGTCATGAA	Degenerate PCR
5'GSP1	TGAAGCTGCTGCGCTACTTCAACCACG	Genome-walking
5'GSP2	GACCTTTCCGACGACCACTGCCAGTAC	Genome-walking
3'GSP1	ACAGTTGGCGTTGAGGAGGAGGTTGGA	Genome-walking
3'GSP2	GACGTTGGCTGAGTGCATGGCCTTGAG	Genome-walking
Probe	F: CTACTTCAACCACGAGAACATCAT R: GTATGGGTGCTTGAGGGCCT	Probe construction for Southern blot with a probe size of 857 bp
β-tubulin	F: GGTAACCAAATCGGTGCTGCTTTC R: ACCCTCAGTGTAGTGACCCTTGGC	Realtime – PCR with an amplicon size of 300 bp
Histone 4	F: GGTGTCAAAGCGTATCTCTGCCAT R: ACATCAAGCGACGTGACAGTCTTG	Realtime – PCR with an amplicon size of 136 bp
SmkA	F: ATGGAGACGGATATGCACAGAG R: ACTCCTTGAACGTCAACATGATC	Realtime – PCR with an amplicon size of 292 bp

Table 4.2. Normalized intensities of MAP kinase in *S. elegans* in response to nutrient starvation and mycoparasitism of *R. solani*

Organism	Total (T) MAP kinase	Phosphorylated (P) MAP kinase	Non-Phosphorylated (NP) MAP kinase	Ratio of P/NP	Ratio of P/T	Fold of Phosphorylation
S.elegans	2.12E+06	1.95E+06	1.77E+05	1.10E+01	9.17E-01	Control vs 48 h: 1.58
48 h of interaction	1.31E+06	1.22E+06	8.85E+04	1.38E+01	9.33E-01	72 h vs 48 h: 2.5
72 h of interaction	3.26E+06	3.09E+06	1.74E+05	1.78E+01	9.47E-01	72 h vs control: 1.58

Figure 4.1. Alignment of 13 MAP kinase protein sequences belonging to different Ascomycetes. *Trichoderma virens* (Tvk1 AY162318; TmkA AY141978), *T. harzianum* (Pmk1* AB195835), *T. atroviride* (Tmk1 AF452096; Tmk2 AY279002), *Colletotrichum* lagenarium (Cmk1 AF174649), *Magnaporthe grisea* (Pmk1 U70134), *Fusarium solani* (FsMAPK U52963), *F. oxysporum* f.sp *lycopersici* (Fmk1 AF286533), *Botrytis cinerea* (Bmp1 AF205375), *Blumeria graminis* (Map1 AF301165), *Saccharomyces cerevisiae* (Kss1 M26398), and *Cochliobolus heterostrophus* (Chk1 AF178977). DegF Degenerate forward primer. DegR Degenerate reverse primer. Boxes represent the location of degenerate primers used in PCR. The multiple sequence alignment was done using ClustalW on the Biology Workbench server (http:// workbench.sdsc.edu/). Roman letters indicate the different sub-domains of the catalytic domain of MAP kinases.


Subdomain: I II III IV
Tvk1 MSRSNPPNNASASRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKIT-PFDHSMFCLRTLREMKLLRYFN-HENIISILDIQKPRSYDSF
TmkA MSRSNPPNNASASRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKIT-PFDHSMFCLRTLREMKLLRYFN-HENIISILDIQKPRSYDSF
Pmk1* MSRSNPPNNASASRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKIT-PFDHSMFCLRTLREMKLLRYFN-HENIISILDIQKPRSYDSF
Pmk1 MSRANPPSNSSGSRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKIT-PFDHSMFCLRTLREMKLLRYFN-HENIISILDIQKPRSYETF
FsMAPK MSRSNPP-NPTGSRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKIT-PFDHSMFCLRTLREMKLLRYFN-HENIISILDIQKPRNYESF
Fmk1 MSRSNPP-NAAGSRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKIT-PFDHSMFCLRTLREMKLLRYFN-HENIISILDIQKPRNYESF
Map1 MSRANPP-NAAGSRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKIT-PFDHSMFCLRTLREMKLLRYFN-HENIISILDIQKPRSYESF
CMK1 MSRANAP-NPSGSRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKIT-PFDHSMFCLRTLREMKLLRYFN-HENIISILDIQKPRSYETF
Tmk1 MSRSTAP-NASASRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKIT-PFDHSMFCLRTLREMKLLRYFN-HENIISILDIQKPRSYDSF
BMP1 MT-ARAPNPASGSRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKIT-PFDHSMFCLRTLREMKLLRYFN-HENIISILDIQKPRNYESF
CHK1 ----MPPAGSGSSRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKIT-PFDHSMFCLRTLREMKLLRYFN-HENIISILDIQKPRNYETF
KSS1 ----------MARTITFDIPSQYKLVDLIGEGAYGTVCSAIHKPSGIKVAIKKIQ-PFSKKLFVTRTIREIKLLRYFHEHENIISILDKVRPVSIDKL
Tmk2 -MADLQGRKVFKVFNQDFVVDERYTVTKELGQGAYGIVCAAVNGQTNEGVAIKKVTNVFSKKILAKRALREIKLLQHFRGHRNITCLYDMDIPR-PDNF
DegF
Subdomain: V VIa VIb VII VIII
Tvk1 NEVYLIQELMETDMHRVIRTQD-----LSDDHCQYFIYQTLRALKAMHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNS----GFMTEYVA
TmkA NEVYLIQELMETDMHRVIRTQD-----LSDDHCQYFIYQTLRALKAMHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNS----GFMTEYVA
Pmk1* NEVYLIQELMETDMHRVIRTQD-----LSDDHCQYFIYQTLRALKAMHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNS----GFMTEYVA
Pmk1 NEVYLIQELMETDMHRVIRTQD-----LSDDHCQYFIYQTLRALKAMHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQENNS----GFMTEYVA
FsMAPK NEVYLIQELMETDMHRAIRTQD-----LSDDHCQYFIYQTLRALKAMHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNS----GFMTEYVA
Fmk1 NEVYLIQELMETDMHRVIRTQD-----LSDDHCQYFIYQTLRALKAMHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNS----GFMTEYVA
Map1 QEVYLIQELMETDMHRVIRTQD-----LSDDHCQYFIYQTLRALKAMHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNS----GFMTEYVA
CMK1 NEVYLIQELMETDMHRVIRTQD-----LSDDHCQYFIYQTLRALKAMHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNS----GFMTEYVA
Tmk1 NEVYLIQELMETDMHRVIRTQD-----LSDDHCQYFIYQTLRALKAMHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNS----GFMTEYVA
BMP1 TEVYLIQELMETDMHRVIRTQD-----LSDDHCQYFIYQTLRALKAMHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNS----GFMTEYVA
CHK1 TEVYLIQELMETDMHRVIRTQE-----LSDDHCQYFIYQTLRALKAMHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASTEDNS----GFMTEYVA
KSS1 NAVYLVEELMETDLQKVINNQNSGFSTLSDDHVQYFTYQILRALKSIHSAQVIHRDIKPSNLLLNSNCDLKVCDFGLARCLASSSDSRETLVGFMTEYVA
Tmk2 NETYLYEELMECDLAAIIRSGQP----LTDAHFQSFIYQILCGLKYIHSANVLHRDLKPGNLLVNADCELKICDFGLARGFSVDPEEN---AGYMTEYVA
DegR

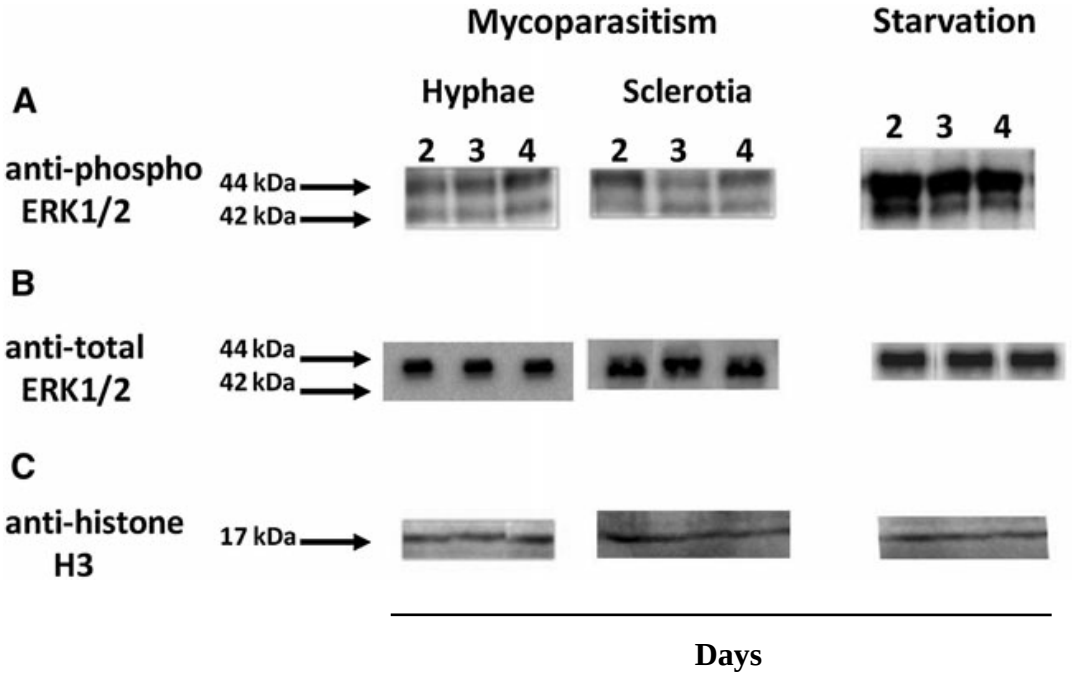
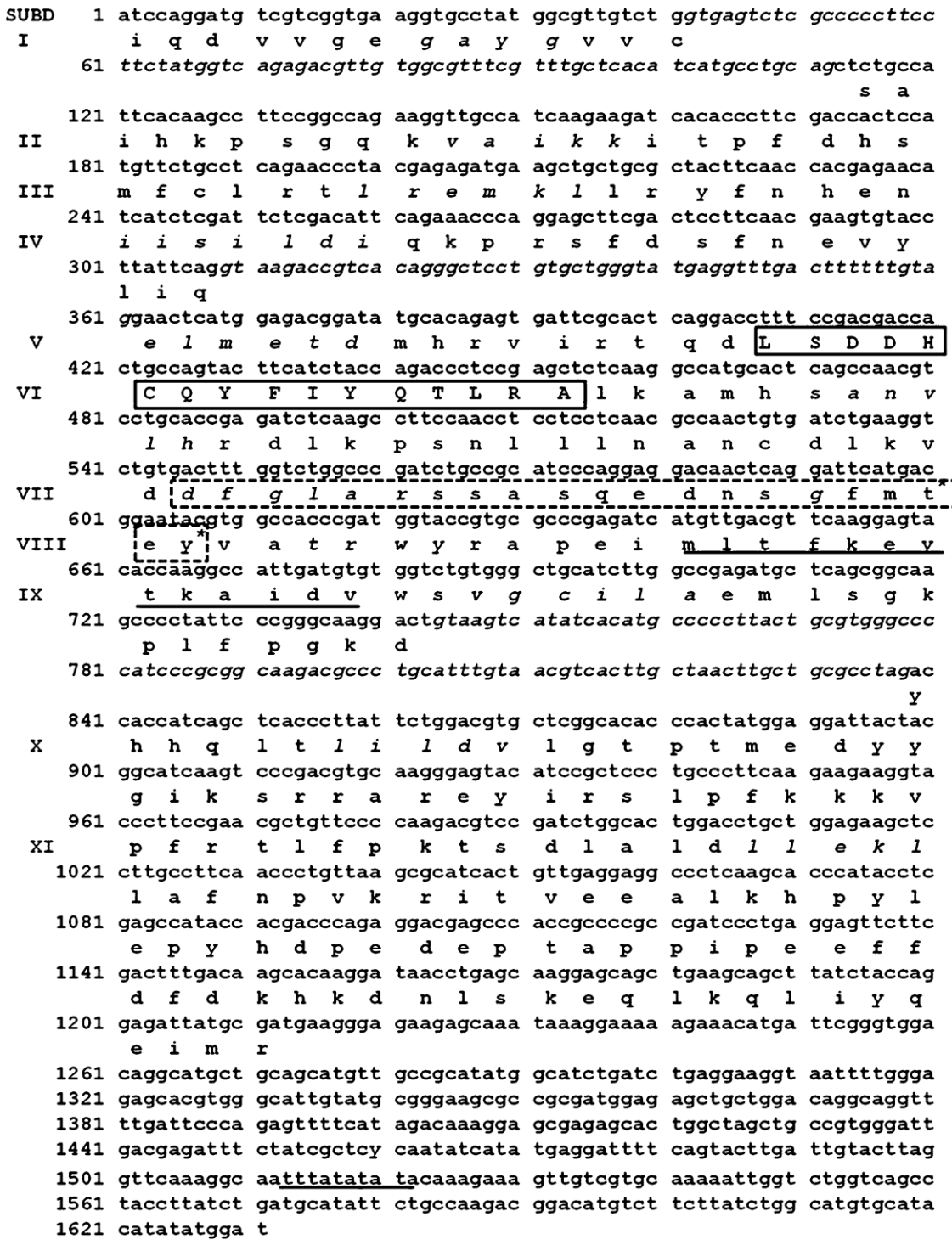


Figure 4.2. Western analysis of ERK1/2 protein at different time points. A. Samples from mycoparasitic interaction of different vegetative structures of *R. solani* and carbon starvation condition probed with anti- phospho-p44/42 antibodies. B. Total MAP kinase ERK1/2 probed with anti-p44/42 antibodies. C. Normalization by anti-Histone H3 antibody. 2, 3, and 4 indicate the sampling days after mycoparasitism interaction or starvation.

Figure 4.3. Sequence of *smkA*. Introns are written in italic in the gene sequence. A Putative polyadenylation site is underlined in the gene sequence. Conserved signature of YERK1 fungal MAPK class is in capital letters and boxed in the amino acid sequence. Dashed line box represents the phosphorylation lip. *Designs the phosphorylation sites of the protein. KIM motif site is underlined in the protein sequence. The different subdomains of the proteins are indicated in italic in the protein sequence and designated by Roman letters on the left margin.


SUBD 1 atccaggatg tcgtcggtga aggtgcctat ggcgttgtct ggtgagtctc gccccttccc
I i q d v v g e g a y g v v c
61 ttctatggtc agagacgttg tggcgtttcg tttgctcaca tcatgcctgc agctctgcca
s a
121 ttcacaagcc ttccggccag aaggttgcca tcaagaagat cacacccttc gaccactcca
II i h k p s g q k v a i k k i t p f d h s
181 tgttctgcct cagaacccta cgagagatga agctgctgcg ctacttcaac cacgagaaca
III m f c l r t l r e m k l l r y f n h e n
241 tcatctcgat tctcgacatt cagaaaccca ggagcttcga ctccttcaac gaagtgtacc
IV i i s i l d i q k p r s f d s f n e v y
301 ttattcaggt aagaccgtca cagggctcct gtgctgggta tgaggtttga ctttttttgta
l i q
361 ggaactcatg gagacggata tgcacagagt gattcgcact caggaccttt ccgacgacca
V e l m e t d m h r v i r t q d L S D D H
421 ctgccagtac ttcatctacc agaccctccg agctctcaag gccatgcact cagccaacgt
VI C Q Y F I Y Q T L R A l k a m h s a n v
481 cctgcaccga gatctcaagc cttccaacct cctcctcaac gccaactgtg atctgaaggt
l h r d l k p s n l l l n a n c d l k v
541 ctgtgacttt ggtctggccc gatctgccgc atcccaggag gacaactcag gattcatgac
VII d d f g l a r s s a s q e d n s g f m t*
601 ggaatacgtg gccacccgat ggtaccgtgc gcccgagatc atgttgacgt tcaaggagta
VIII e y* v a t r w y r a p e i m l t f k e v
661 caccaaggcc attgatgtgt ggtctgtggg ctgcatcttg gccgagatgc tcagcggcaa
IX t k a i d v w s v g c i l a e m l s g k
721 gcccctattc ccgggcaagg actgtaagtc atatcacatg ccccttact gcgtgggccc
p l f p g k d
781 catcccgcgg caagacgccc tgcatttgta acgtcacttg ctaacttgct gcgcctagac
y
841 caccatcagc tcacccttat tctggacgtg ctcggcacac ccactatgga ggattactac
X h h q l t l i l d v l g t p t m e d y y
901 ggcatcaagt cccgacgtgc aagggagtac atccgctccc tgcccttcaa gaagaaggta
g i k s r r a r e y i r s l p f k k k v
961 ccttccgaa cgctgttccc caagacgtcc gatctggcac tggacctgct ggagaagctc
XI p f r t l f p k t s d l a l d l l e k l
1021 cttgccttca accctgttaa gcgcatcact gttgaggagg ccctcaagca cccatacctc
l a f n p v k r i t v e e a l k h p y l
1081 gagccatacc acgacccaga ggacgagccc accgccccgc cgatccctga ggagttcttc
e p y h d p e d e p t a p p i p e e f f
1141 gactttgaca agcacaagga taacctgagc aaggagcagc tgaagcagct tatctaccag
d f d k h k d n l s k e q l k q l i y q
1201 gagattatgc gatgaaggga gaagagcaaa taaaggaaaa agaaacatga ttcgggtgga
e i m r
1261 caggcatgct gcagcatgtt gccgcatatg gcatctgatc tgaggaaggt aattttggga
1321 gagcacgtgg gcattgtatg cgggaagcgc cgcgatggag agctgctgga caggcaggtt
1381 ttgattccca gagttttcat agacaaagga gcgagagcac tggctagctg ccgtgggatt
1441 gacgagattt ctatcgctcy caatatcata tgaggatttt cagtacttga ttgtacttag
1501 gttcaaaggc aatttatata tacaaagaaa gttgtcgtgc aaaaattggt ctggtcagcc
1561 taccttatct gatgcatatt ctgccaagac ggacatgtct tcttatctgg catgtgcata
1621 catatatgga t

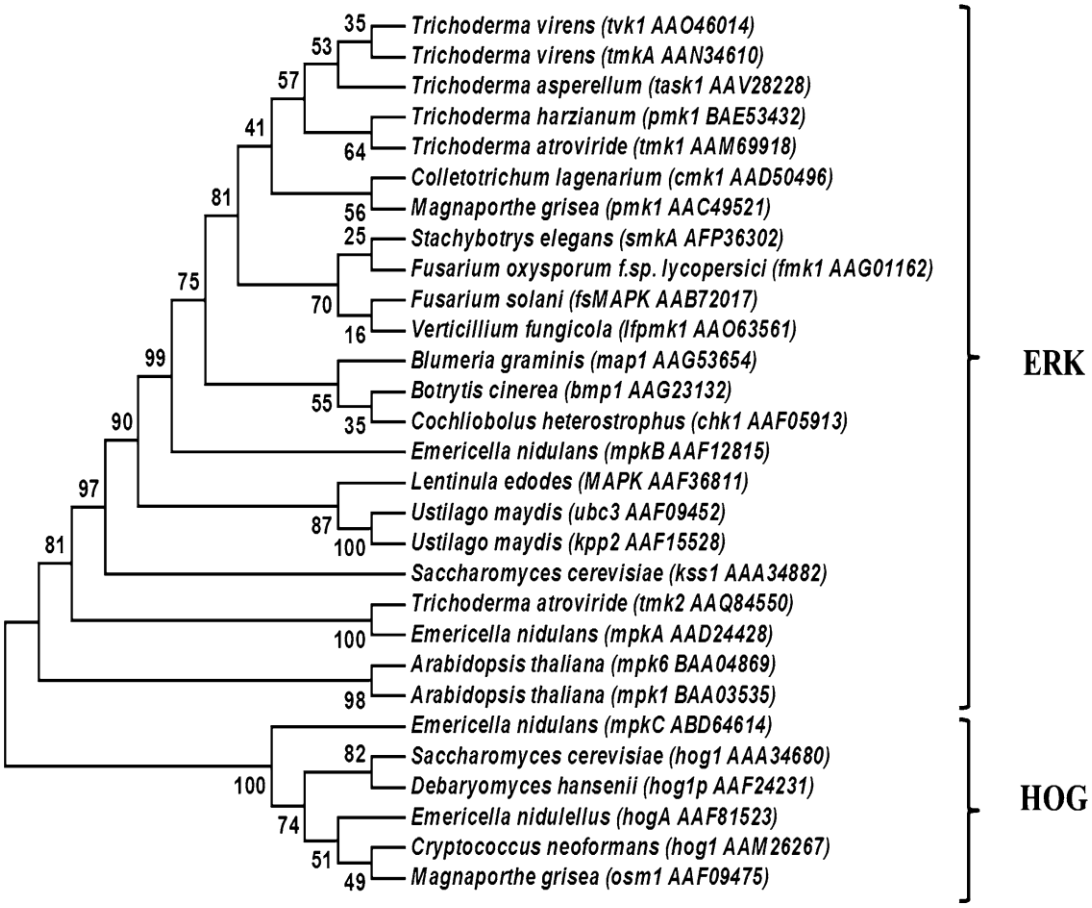


Figure 4.4. A rooted phylogenetic tree based on the distance among protein sequences of MAP kinases from various Ascomycetes, Basidiomycetes and *Arabidopsis* calculated using the maximum likelihood method. NCBI accession numbers are listed next to the species names. ERK extracellular regulated kinase. HOG high-osmolarity glycerol. The percentage of replicate trees in which the associated taxa clustered together in the bootstrap test (1,000 replicates) is shown next to the branches.

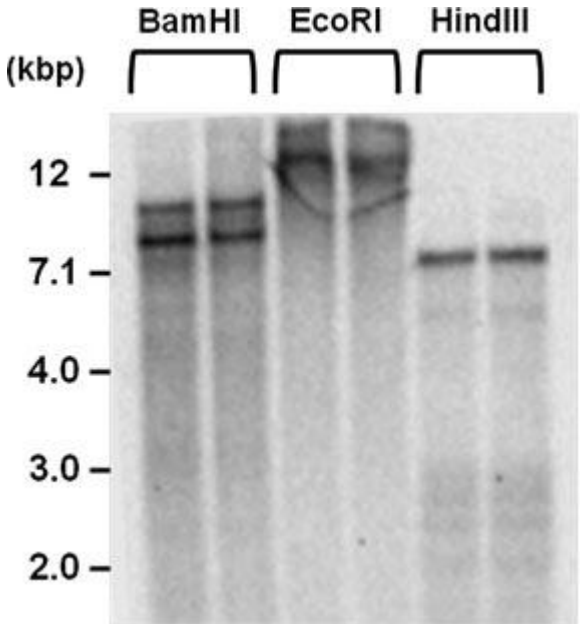


Figure 4.5. Southern blot analysis showing the *smkA* gene copy number in *S. elegans.*

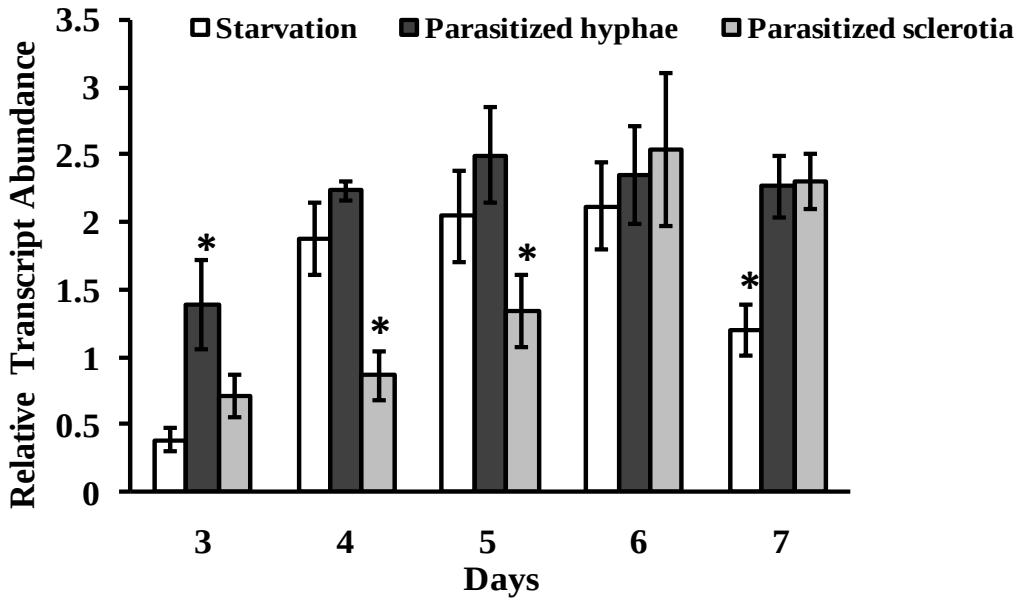


Figure 4.6. Relative transcript abundance of *smkA* in response to mycoparasitism of *R. solani* and starvation conditions. Transcript abundance was normalized by the geometric mean of two housekeeping genes: *Histone-4* and *β-tubulin.* Asteriks indicate significant transcript abundance between the different treatments ($P < 0.05$).

4.5. DISCUSSION

The morphological and molecular responses (Benyagoub et al. 1994; Chamoun and Jabaji 2011; Morissette et al. 2008) observed in *S. elegans* when confronted by a host depend on its capacity to sense and respond to external stimuli and to adjust its intracellular activities accordingly. In this study, we isolated and characterized the first MAPK-encoding gene *smkA* from *S. elegans*. The deduced protein sequence of SMKA showed high similarity (99 %) with other MAPK/ERK1/2 subfamily members reported for mycoparasitic and phytopathogenic fungi. Interestingly, the similarity of deduced protein sequences of SMKA and FMK1 from *F. oxysporum* f.sp. *lycopersici* (Di Pietro et al. 2001) at the protein level is also extended to the genomic level where both were found as several copies in their corresponding genomes using Southern blot analysis. We conclude that *smkA* contains additional structurally related MAPK genes. This finding raises the possibility that *S. elegans* implicates parallel modules of the kinase cascade to activate distinct downstream effectors and to elicit specific cellular responses (Cook et al. 1996; Kahmann and Kämper 2004). The signature sequence present in the SmkA protein indicates that it belongs to the YERK1 family (i.e. yeast and fungal ERK1) (Kültz 1998). SMKA contains the entire key motifs conserved in the subdomains of the serine/threonine protein kinases (Takano et al. 2000; Xu and Hamer 1996), the ATP binding site (Huang et al. 2010) and the invariant motif TXY required for the activation by phosphorylation of MAPK/ERK protein kinases (Müller et al. 2003). It is known that signaling specificity in eukaryotic cells is maintained by several mechanisms (Xu 2000). One mechanism by which MAP kinases confer their specificity is through docking domains known as KIM. The importance of these domains comes from the fact that they recruit the kinases to their interaction partners including activating kinases, inactivating phosphatases, scaffolding proteins, and substrates, which enhance their fidelity and efficiency of action (Akella et al. 2008; Liu et al. 2006). A closer look at SMKA protein, the consensus sequence for KIM was identified. Although we did not attempt to identify the interacting partner in this study, it is intriguing to note that the LC-MS/MS

analysis of the excised MAP kinase fragment pointed to the high presence of ubiquitin (data not shown). Accumulating evidence indicates that one of the mechanisms employed by the cell to down regulate the MAP kinases levels is via the ubiquitin/ proteasome pathway (Lu and Hunter 2009). Clearly, much remains to be discovered for our understanding on deregulation of MAP kinases by ubiquitination in fungi.

In phytopathogenic fungi, signal transduction via MAPK modules is among other processes involved in the parasitic interaction (Takano et al. 2000; Xu 2000). As would be expected from a gene that might potentially play a role in mycoparasitism, *smkA* transcripts were substantially upregulated during infection of *R. solani*. However, differential and temporal transcript abundance patterns of *smkA* were observed under different mycoparasitic situations when compared to that of *S. elegans* growing on minimal medium (carbon starvation). Transcript abundance was elevated 3 and 4 days and onwards after confrontation with hyphae and sclerotia of *R. solani*, respectively. Later activation of *smkA* transcripts in parasitized sclerotia may well be attributed to the difference in their architectural structure and composition as compared to hyphae (Coley-Smith and Cooke 1971; Insell et al. 1985). Irrespective, *smkA* transcript abundance trend coincided with the formation of various mycoparasitic structures (i.e. coiling, and infectious pegs), and also with the transcript abundance of several *S. elegans* mycoparasitic-induced genes such as DNA methyltransferase (DNMT), oxidoreductase and cytochrome P450 during confrontation with *R. solani* under different mycoparasitic situations (Chamoun and Jabaji 2011). This is not surprising since there is clear evidence that activation of DNMT and oxidoreductases and deregulation of cytochrome P450 in diseased or mechanically stressed mammalian cells is directly regulated by MAPK/ERK1/2 kinases pathways (Abdulnour et al. 2006; Jiang et al. 2011; Murray et al. 2010; Samudio-Ruiz and Hudson 2012; Sontag and Weber 2012).

Under nutrient starvation conditions, *smkA* transcript abundance was maintained at similar levels during the course of the study, but was significantly induced at later stages of vegetative growth (7 days) coinciding with heavy

sporulation (Chamoun and Jabaji 2011). Evidence on MAP kinase transcript abundance under nutrient limiting conditions including the induction of sporulation has been reported for several fungi (Jain et al. 2011; Kays et al. 2000; May et al. 2005; Reyes et al. 2006; Solomon et al. 2005; Xue et al. 2004). When mycelia of *Aspergillus fumigatus* were transferred from rich to minimal media lacking carbon and nitrogen sources, an increase of *sakA* MAP kinase transcript was observed (May et al. 2005; Xue et al. 2004).

When fungal protein extracts responding to selective anti-phospho-p42/p44 MAPK (thr202/tyr204) were analyzed, we observed an increase in the phosphorylation levels around 44 and 42 kDa in response to carbon starvation conditions compared to levels detected in response to mycoparasitism. The influence of nutrient starvation and mycoparasitism conditions on the phosphorylation levels of ERK1/2 was also observed in LC-MS/MS analysis but with higher phosphorylation abundance at the third day of interaction compared to that detected under starvation conditions. Collectively, these results provide evidence that MAPK/ERK1/2 kinases respond to different chemical and physical cues (Jiang et al. 2011). Therefore, the induction in the MAP kinase protein phosphorylation levels could not be attributed to the mycoparasitic process alone but also to stressful growth conditions. This dual function could be attributed to the presence of structurally related genes in the same subfamily of MAPK as has been detected in *S. elegans* (this study) and in other fungi, such as *Saccharomyces cerevisiae* and *F. oxysporum* f.sp. *lycopersici* (Cherkasova et al. 1999; Di Pietro et al. 2001; Gartner et al. 1992).

The discrepancy in the abundance profile of *smkA* transcripts and levels of phosphorylated MAPK/ERK1/2 protein during mycoparasitic interaction can be easily explained by the fact that SMKA protein sequence has the YERK1 signature sequence (Kültz 1998; Mukherjee et al. 2003) and therefore the transcript abundance levels are a reflection of ERK1 mRNA transcripts only and not ERK1 and ERK2 combined. Furthermore, since the monoclonal anti-phospho-p42/p44 MAPK antibody is not specific to a particular organism,

phosphorylated protein levels in both fungi are expected to highlight, as is the case in this study.

In summary, this study reports on the MAPK/ERK1/2 expression in response to different types of stress: direct mycoparasitism with its host (carbon-rich condition) and poor nutritional conditions (carbon-poor medium), using a proteomic and transcriptomic approach. Applying mass spectrometry, a higher abundance in phosphorylation of MAPK/ERK1/2 protein was detected in response to mycoparasitism compared to stressful growth conditions. In addition, the differential transcript abundance of *smkA*, the first isolated and characterized MAP kinase gene in *S. elegans* was influenced by the type of stress over time. Our study suggests that *smkA* seems to be implicated in multifunction pathways and this could be supported by the fact that it belongs to a small gene family. Future experiments are aimed at construction of disruptants that will help in elucidating *smkA* functional role in mycoparasitism and growth and how it perceives different cues from its environment.

4.6. ACKNOWLEDGMENTS

This work was supported by a research grant to S. Jabaji from the Natural Sciences and Engineering Research Council of Canada (NSERC-Discovery). We would like to thank Dr. J-B. Charron for the use of the BioRad chemiDoc^{TM} XRS^{+} imaging system.

CONNECTING STATEMENT BETWEEN CHAPTERS 4 AND 5

In chapter 4, I have characterized the first MAPK gene, *smkA*, from the mycoparasite *S. elegans* and highlighted its transcript abundance under biotic and abiotic stresses. In order to reveal its function and role, two different plasmids were constructed to over-express or to silence *smkA* in *S. elegans* and study its contribution in the mycoparasitism process and its efficacy in biocontrol against *R. solani*. In both plasmids, the *smkA* gene was driven by promoters ensuring its constitutive expression once it is introduced inside the mycoparasite cells. To that end, two fungal transformation methods (polyethylene glycol and *Agrobacterium tumefaciens*) were applied.

I have designed the experimental set-up, designed the plasmids, implemented the transformation protocols, conducted all the experiments and wrote the section. The RNAi silencing plasmid was constructed with help of Professor Neena Mitter (The University of Queensland, Australia). Dr. S. Jabaji provided supervision, funding throughout the study and corrected the chapter.

CHAPTER 5

Transformation of *Stachybotrys elegans* by polyethylene glycol and *Agrobacterium tumefaciens*

Rony Chamoun, Suha Jabaji*

Department of Plant Science, Macdonald Campus of McGill University, 21,111 Lakeshore Road, Saint-Anne-de-Bellevue, Quebec, H9X 3V9, Canada

*Corresponding author: Suha Jabaji

McGill University, Macdonald Campus, Department of Plant Science, 21,111 Lakeshore Road, Montreal, Qc, H9X 3V9
Phone: (514) 398-7561 Fax: (514) 398-7897
E-mail: suha.jabaji@mcgill.ca

5.1. ABSTRACT

An attempt to investigate the role and biological function of the signal transduction gene *smkA* during mycoparasitism of *R. solani* through the construction of *S. elegans* transgenic lines was made. Two different plasmids were constructed: pSMKA an over-expression plasmid in which *smkA* is driven by the constitutive promoter (*gpdA*) of *Aspergillus nidulans,* and pSMKAi, a silencing vector harboring an inverted repeat sequence of *smkA* driven by the CaMV 35S promoter. We used two different approaches for fungal transformation, the protoplast transformation (PEG-CaCl2) and the *Agrobacterium-tumefaciens* mediated transformation methods. No successful transformants were obtained and factors that could contribute to the lack of transformants production are discussed.

Keywords: RNAi, Fungal transformation, *Agrobacterium tumefaciens,* Protoplasts

5.2. INTRODUCTION

The implication of signal transduction MAPK pathways in virulence and development has been addressed in many plant pathogenic fungi and different roles were attributed to each pathway through the generation of knock-out mutant strains with loss of function (Guo et al. 2011; Mendoza-Mendoza et al. 2003; Xu 2000; Zhao et al. 2007). The Fus3/Kss1MAPK pathway is involved in appressorium formation, virulence of the plant pathogens, and in plant infection processes in several fungi including *Magnaporthe oryzae*, *Colletotrichum lagenarium*, *Alternaria brassicicola*, *Fusarium oxysporum*, *Botrytis cinerea*, *Ustilago maydis*, *Verticillium dahliae*, and *Puccinia striiformis* f. sp. *tritici* (Cho et al. 2007; Gao et al. 2012; Guo et al. 2011; Mehrabi et al. 2009; Müller et al. 1999; Xu 2000; Zhao et al. 2007). Deletion of Fus3/Kss1 MAPK genes, (*tmkA, tmkB* and *tvk1*) in the biocontrol fungus *Trichoderma virens* has revealed some similarity in the functions of these genes, but also were distinct in other aspects as well. While retaining their ability to overgrow *R. solani* and *Pythium* spp., *tmkB* mutants exhibited sensitivity to cell wall degrading enzymes compared to *tmkA* that showed a reduction in resistance induction in cucumber (Kumar et al. 2010; Mendoza-Mendoza et al. 2003). Alternatively, under simulated mycoparasitic conditions and in confrontation assays with the plant pathogen *R. solani*, *tvk1* mutants showed an increase in disease control through the activation of the expression of genes coding for cell wall degrading enzymes.

Due to the low rate of homologous recombination (0.1-5%) in many knock-out mutant strains of fungi, the regulatory effects of fungal MAPK genes on development, growth, and survival can be studied with other effective approaches such as applying fungal transformation with overexpressing or RNAi silencing plasmids (Chaveroche et al. 2000; Colot et al. 2006; Lee et al. 2011; Limón et al. 1999; Liu et al. 2001; Ma et al. 2006; Montero-Barrientos et al. 2008; Pöggeler and Kück 2006; Yamagishi et al. 2005). In the fungal Kingdom, RNAi-silencing pathway is highly conserved throughout the fungal kingdom and studies over the past decade have demonstrated that RNAi pathways use small noncoding RNAs

(sRNAs) to regulate diverse cellular, developmental, and physiological processes (Cogoni and Macino 1999; Gheinani et al. 2011; Kadotani et al. 2003). This approach is based on the introduction of sense and anti-sense sequences that are complementary to the targeted gene into the organism where they will trigger RNA cleavage or post-transcriptional silencing mediated by the Argonaute proteins (Chang et al. 2012). Alternatively, the overexpression of a gene of interest (GOI) requires the presence of a strong promoter. Among the impressive set of promoters available for fungi, are the inducible carbon or nitrogen dependent promoters (i.e. the *Aspergillus oryzae* thiamine biosynthesis promoter, *thiA*) (Shoji et al. 2006); and the constitutive growth related promoters (i.e. the *Aspergillus nidulans* glyceraldehyde-3-phosphate dehydrogenase promoter, *gpdA*) (Meyer et al. 2011; Punt et al. 1987).

The most common methods of fungal transformation are polyethylene glycol (PEG-CaCl2)-mediated transformation and *Agrobacterium tumefaciens*-mediated transformation (ATMT) methods. PEG-$CaCl_2$ is based on using protoplasts as starting target material for transformation (Kuo and Huang 2008; Ruiz-Diez 2002), whereas the fundamental basis of the ATMT method does not require protoplast isolation and relies on the co-cultivation of the target organism with the *Agrobacterium tumefacien*s bacterium harbouring the manipulated plasmid (de Groot et al. 1998; Michielse et al. 2005).

We previously reported on *smkA,* a mitogen activated protein kinase (MAPK) encoding gene that was fully characterized from *S. elegans*. We have shown that *smkA* could be implicated in mycoparasitism of *R. solani* as well as in stress-activated pathways (Chamoun et al. 2013). In this study, we aimed to investigate the biological function of *smkA* by attempting to create two transgenic *S. elegans* strains: those that overexpress *smkA,* and those silencing *smkA*.

5.3. MATERIALS AND METHODS

5.3.1. Strain and culture conditions

Starter cultures of the mycoparasite *Stachybotrys elegans* were grown on

potato dextrose agar (PDA; Difco Laboratories, Detroit, USA) at room temperature (24^{o}C) for 7 days or until sporulation had occurred. Conidia were harvested from the surface of the cultures as previously described (Chamoun and Jabaji 2011) and used as protoplasting starting material or as starting material for *Agrobacterium tumefaciens*-mediated transformation (ATMT).

5.3.2. Protoplast formation

S. elegans conidia (10^6 spores/mL) were used to inoculate Erlenmeyer flasks containing 100 mL of potato dextrose broth (PDB). The cultures were shaken at 200 rpm for 22 h at room temperature. Germlings were collected by centrifugation at 9000 rpm for 10 min and washed once with ultrapure water and twice with the osmotic stabilizer (OS: 0.6 M manitol). Fungal protoplasts were obtained by digesting the germlings in digestion buffer (OS + β-mercapthoethanol) containing 10 mg/mL of *Trichoderma harzianum* lysing enzyme (Sigma, St. Louis) for 4h at 100 rpm at 30°C. The digested protoplasts were laid over a sucrose cushion (35%) and spinned for 10 min at 3000 rpm. The protoplasts, formed at the interface of the two phases, were collected using a Pasteur pipette and transferred to a new tube containing 10 mL of OS. After one round of centrifugation at 3000 rpm for 5 min, and washing, they were resuspended in the osmotic stabilizer and ready for transformation with the desired plasmid.

5.3.3. Protoplast transformation

Fungal transformation was carried out by mixing 100 µl of competent protoplasts with10 µg of plasmid DNA of pSMKAi or pSMKA and incubated on ice for 30 min. Following incubation, 1 mL of PEG solution (20% PEG 6,000, 1 M sorbitol, 50 mM Tris-HCl, pH 7.5, 50 mM $CaCl_2$) was added and suspensions were incubated for 10 min at room temperature followed by the addition of 2 mL of the osmotic stabilizer. An aliquot of 200 µl from each transformation were

plated on selective regeneration media (PDA supplemented with 0.6 M sorbitol and containing 50 μg of hygromycin B). After incubation at 25°C for 7 days, antibiotic resistant transformants appearing on the plates were transferred to new PDA media containing antibiotics for a second round of screening.

5.3.4. Transformation by *Agrobacterium tumefaciens* AGL-1

Transformation with *Agrobacterium tumefaciens* strain AGL-1 was carried out as described previously (Michielse et al. 2008). Briefly, different ratios (1:1; 1:2; 1:3; 2:1; and 3:1) of *S. elegans* conidia (10^7 spores/mL) and *Agrobacterium* cells were co-cultivated at 24°C for 5 days on cellophane membrane (500 PUT; UCB, North Augusta, USA) overlaid on solid induction media that is supplemented with 0.2 μM of acetosyringone. Following co-cultivation, transformants were selected by placing the membranes over PDA supplemented with 25μg ml^{-1} hygromycin B (Gold Biotechnology, St. Louis) and with cefotaxim (200 μM) (Gold Biotechnology) to reduce the bacterial background. After 1 week, well-separated growing fungal transformants were randomly picked and subjected to a second round of selection on a gradient concentration of hygromycin B (50, 75, 100, 150 and 200 μg ml^{-1}).

5.3.5. Assessment of protoplast viability and transformation efficiency

Microscopic analysis was performed using a Zeiss SteREO Discovery V20 stereomicroscope equipped for epifluorescence microscopy with a Leitz Ploemopak 2.2 illuminator (Carl Zeiss Microscopy, LLC**,** NY, USA**)**. The fluorescent dye fluorescein diacetate (FDA) was used to test the viability of the protoplasts, and Green Fluorescent Protein (GFP) expression was checked during fungal growth. FDA and GFP were visualized using the filter set 09 (BP 450–490 excitation filter, RKP 510 nm dichroic and LP 515 suppression filter).

5.3.6. Primers design

Several primer sets were designed for different stages of this study (Table 5.1). All primers were tested for self-complementarity, complementarity between both primers, and theoretical melting temperature was determined using the software DNAman v. 4.13. Primer pair RNAi F and RNAi R was designed from the *smkA* gene sequence of *S. elegans* (Accession No. JX 094498), and HYG F and HYG R were obtained from the hygromycin gene sequence (Accession No. AF 234298).

5.3.7. Generation of *S. elegans* MAP kinase overexpression mutant lines: pSMKA

Based on the full-length DNA sequence of the *smkA* gene (JX094498), a 851 bp sequence of the coding region was designed and inserted between the *PgpdA* promoter and the *TtrpC* terminator of *Aspergillus nidulans*. The whole sequence *PgpdA-smkA* gene product-*TtrpC* was synthetized by BioBasic Inc. (Ontario, Canada) and digested with EcoRI and HindIII to be inserted into the *lacZ* region of the pCambia 1302 plasmid (Fig. 5.1). The plasmid construct was transformed into *E. coli and A. tumefaciens* using a standard electroporation protocol (Sambrook et al. 1989).

5.3.8. RNAi vector construction: pSMKAi

Throughout the construction of pSMKAi, and after many attempts to ligate the anti-sense sequence in its corresponding place in the plasmid, a silencing vector containing an inverted repeat (IR) sequence was constructed with the help of Professor Neena Mitter (The University of Queensland, Australia). IR sequence was amplified using the primers RNAi F and RNAi R (Table 5.1) from *smkA* DNA (Accession No. JX094498) and then ligated in the opposite orientation in the *A. tumefaciens* binary vector pART27 (Gleave 1992) to be driven by the CaMV 35S promoter and followed by the octopinne synthase (OCS) terminator

(Fig. 5.2). The sense and anti-sense sequences of the IR are separated by an intron derived from the endochitinase gene *sechi44* of *S. elegans*.

5.3.9. Analysis of transformants

To confirm the integration of the T-DNA section of the pSMKA plasmid inside *S. elegans* genome, transformed mycelia of *S. elegans* lines grown on PDA overlaid with cellophane membrane and amended with antibiotics were harvested and total genomic DNA was extracted using the DNeasy Plant Mini Kit (QIAGEN, Ont, Canada). Primers were designed to amplify the hygromycin gene from transformants (Table 5.1). The PCR reaction was performed in a BioRad T100^{TM} thermal Cycler in a 25 µL mixture [0.20 mM of each dNTP, 1.5mM of MgCl2, 0.2 µM of each primer, 1x of PCR buffer and 1U of Taq DNA polymerase (Fermentas, Ont, Canada)] and 10 ng of DNA. The PCR conditions consisted of an initial denaturation at 95^{o}C for 5 min, 35 cycles of amplification consisted of denaturation at 95^{o}C for 1 min, annealing at 56^{o}C for 1 min, and extension at 72^{o}C for 2 min, followed by another extension at 72^{o}C for 7 min.

5.4. RESULTS

5.4.1. Sensitivity to hygromycin B

Growth of *S. elegans* was completely inhibited at concentrations of hygB higher than 150 µg/mL and spontaneous resistance was low. Based on these observations, resistance to hygB provided by the *E. coli* hygromycin B phosphotransferase gene was considered a valuable dominant marker to select transformed *S. elegans* lines.

5.4.2. Protoplasts isolation, transformation and regeneration

Initial attempts to obtain protoplasts after digestion of intact conidia were unsuccessful and their abundance was not high enough for developing a gene

transfer system. Germinated conidia were found to be more appropriate for the production of protoplasts. Approximately 1 $x10^6$ protoplasts were typically obtained from a 22-h-old culture after 4 h of digestion. Viable protoplasts were determined by staining with fluorescein diacetate (FDA). In the presence of FDA, protoplasts with an intact plasma membrane appeared green whereas those with a damaged plasma membrane appeared red (Fig. 5.3).

Following transformation with plasmids pSMKAi or pSMKA, protoplasts were plated on regeneration media amended with osmotic stabilizer and kept for two weeks for stabilization and cell wall restoration. No spheroplasts were able to grow and form colonies after transformation with either plasmid.

5.4.3. *Agrobacterium tumefaciens*-mediated transformation (ATMT)

Agrobacterium tumefaciens-mediated transformation (ATMT) of *S. elegans* conidia was conducted with the binary vector pSMKA containing the coding region of bacterial hygromycin B phosphotransferase gene (*hph*) under the control of CAMV 35S promoter as a selectable marker. Co-cultivation of *S. elegans* conidia with *A. Tumefaciens* AGL-1 cells carrying pSMKA led to the formation of hygromycin-resistant colonies in the presence of acetosyringone (AS), a compound inducing the expression of virulence genes in *A. tumefaciens* (Fig. 5.4).

To inhibit false-positive transformants, hyphal tips of the transformants were transferred and plated on PDA amended with gradient concentrations of hygromycin B ranging from 50 to 200 μg/mL. Control plates containing wild *S. elegans* plugs were plated on the corresponding concentrations of the antibiotic (Fig. 5.5).

The integration of the T-DNA into *S. elegans* genome was tested by PCR amplification of the hygromycin gene from randomly selected transformants. The amplification did not produce any DNA amplicon of the expected size. Also no fluorescence was detected for the GFP when fungal mycelia of the transformants were examined under the epifluorescence microscope (Fig. 5.6).

Table 5.1. Primers used in this study

Name	Primer (5' ⟶ 3')	Comments	Amplicon size (bp)
RNAi	F: CTACTTCAACCACGAGAACATCAT R: GTATGGGTGCTTGAGGGCCT	Used to amplify the sense/anti-sense sequences for *smkA* silencing.	857
HYG	F: CTTGTCGATCGAACAGATCCG R: CTTTCGCAGATCCCGGG	Used to amplify the hygromycin gene from putative transformants.	1,088

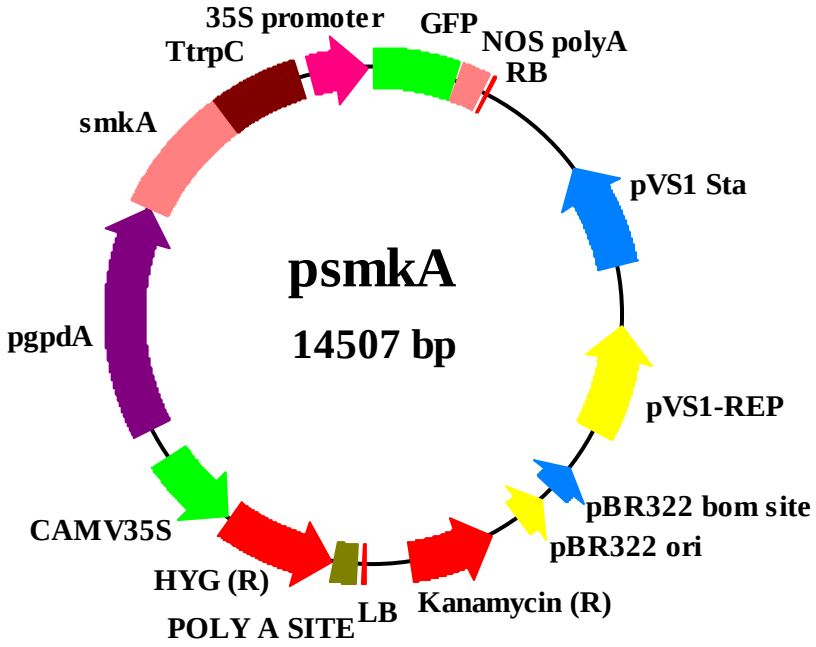


Figure 5.1. Overexpression vector for *smkA* MAP kinase in *S. elegans*. The right border (RB) and left border (LB) are indicated by the red fine lines. The coding sequence of *smkA* is represented by the orange box and driven by the *PgpdA* promoter from *Aspergillus nidulans*. The hygromycin (HYG) gene responsible for the fungal selection after transformation is designated by a red arrowed box localized between RB and LB.

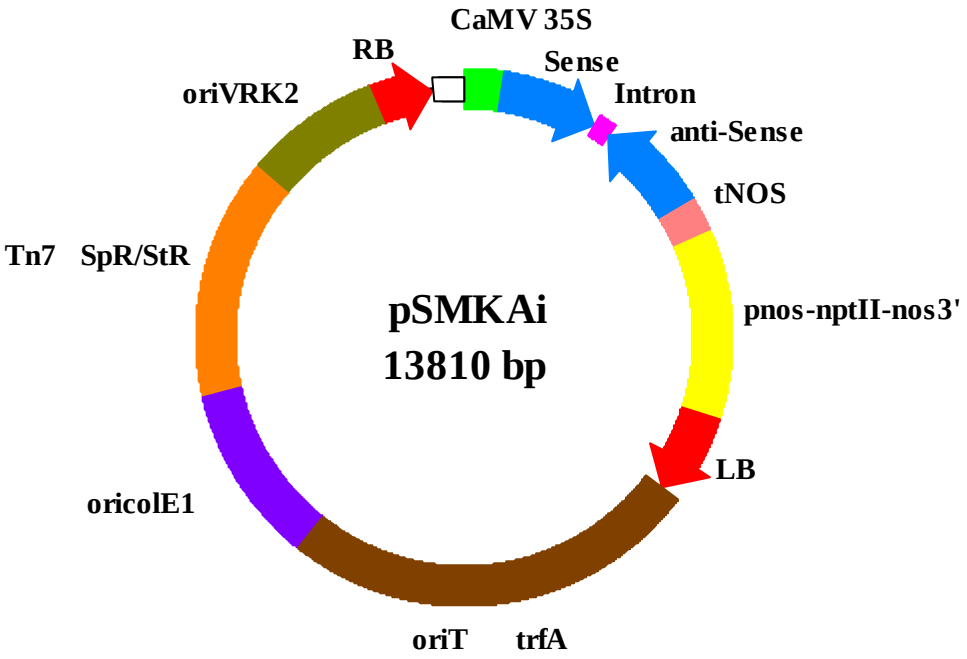


Figure 5.2. RNAi silencing vector for *smkA* MAP kinase in *S. elegans*. The right border (RB) and left border (LB) are indicated by the red boxes. The sense and anti-sense sequences of the IR are represented by the blue arrowed boxes. The neomycin phosphotransferase (nptII) gene responsible for the fungal selection after transformation is designated as yellow box.

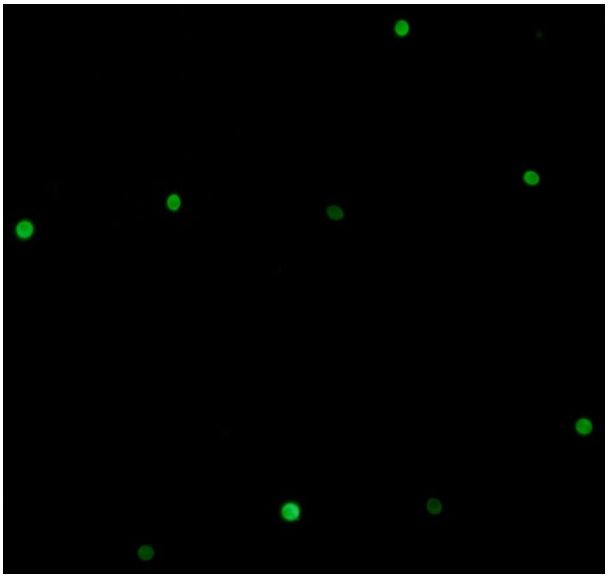


Figure 5.3. *S. elegans* protoplasts labelled with FDA and observed under UV light (epifluorescence)

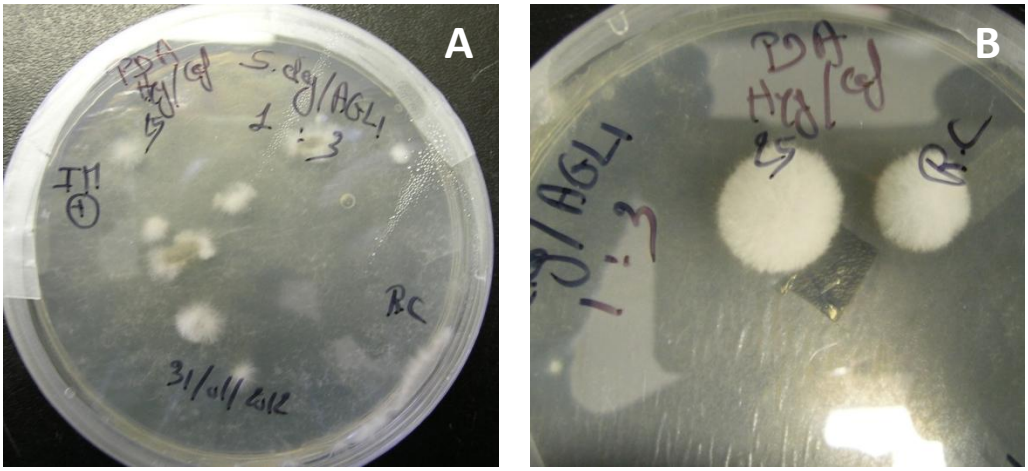


Figure 5.4. *Agrobacterium tumefaciens*-mediated transformation (ATMT) of *S. elegans* conidia. (A) and (B): Formation of putative transformants on solid induction media amended with 25 µg of hygromycin B and 0.2 µM of acetosyringone.

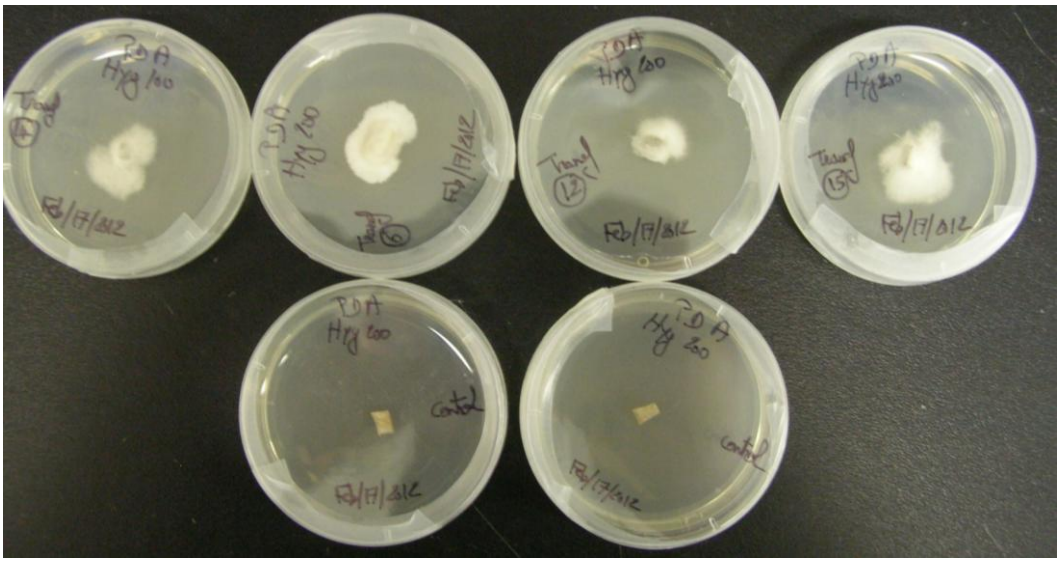


Figure 5.5. *S. elegans* transformation. Upper panel: Putative *S. elegans* transformants plated on PDA media amended with 200 µg of hygromycin. **Lower panel: Control *S. elegans*** plugs growing on PDA media amended with 200 µg of hygromycin.

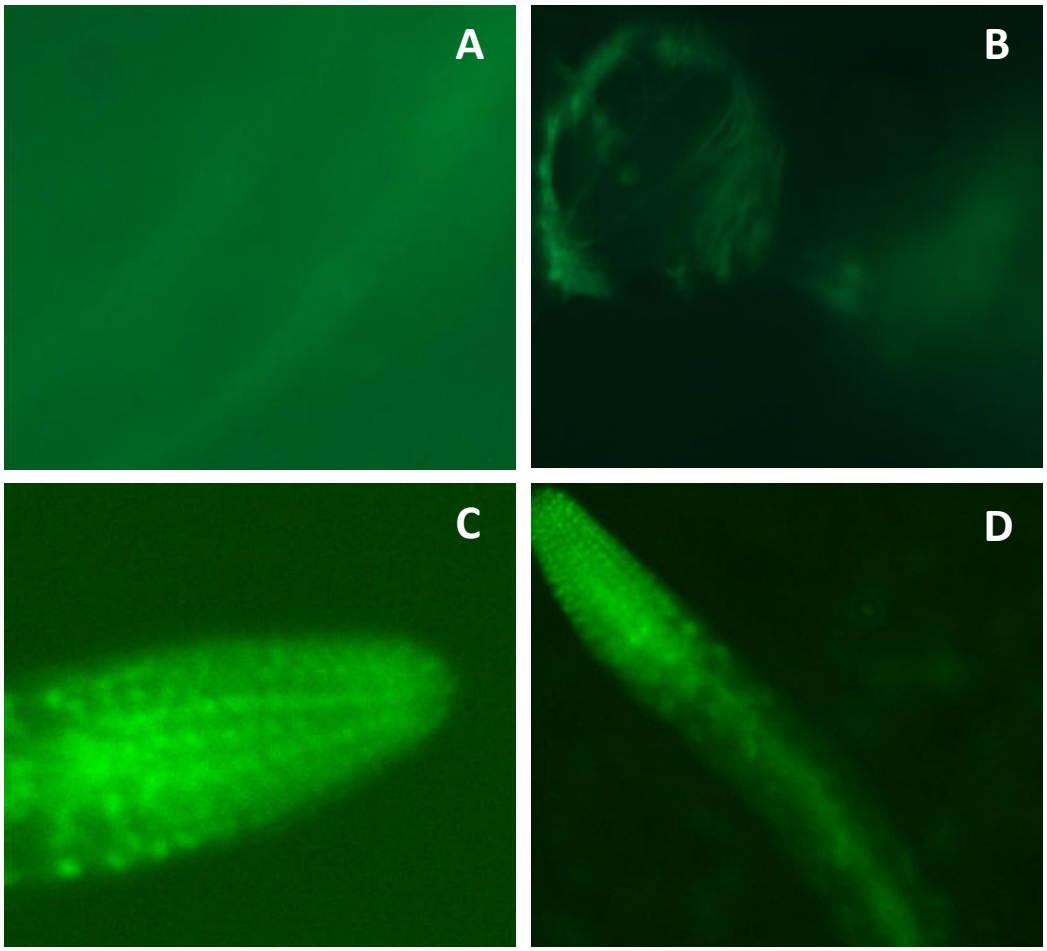


Figure 5.6. Epifluorescence microscopic visualisation for GFP expression. (A) *S. elegans* putative transformant. (B) Wild *S. elegans* serving as a negative control. (C) and (D) Tips of *Arabidopsis* roots serving as a positive control.

5.5. DISCUSSION

Genetic and metabolic engineering approaches to both natural and recombinant metabolite producing strains are powerful tools for improving production levels, producing novel tailored compounds or directing the synthesis of desired products (Meyer 2008). However, this will only become feasible with the development of efficient methods to introduce and control transcript abundance in filamentous fungi (Ruiz-Diez 2002).

To generate a holistic knowledge of the *smkA* gene function during mycoparasitism of *R. solani*, we attempted to transform *S. elegans* with two vectors (pSMKA and pSMKAi). pSMKA (an overexpression plasmid) had a sequence of the *smkA* gene driven by the constitutive promoter *PgpdA* from *A. nidulans* to permanently express the *smkA* gene in *S. elegans*, whereas pSMKAi (a RNAi plasmid) carried sense and antisense strands of the *smkA* gene driven by the 35S promoter.

In an effort to enhance transformation efficiency for *S. elegans*, for which no transformation protocols exist, two transformation methods were conducted: PEG-$CaCl_2$ using protoplasts and *Agrobacterium tumefaciens*-mediated transformation (ATMT) method. Fungal protoplasts have been obtained from strains belonging to all the major taxonomic groups for physiological and genetic studies and their application for molecular studies depends on their successful reversion and regeneration to normal mycelia. Our goal was to integrate our target plasmids inside the fungal genome using the most common factors established for the transformation of fungi belonging to the Ascomycetes (Balasubramanian et al. 2003; Beri and Turner 1987; Shi-Wang et al. 2004; Shishido et al. 2001; Skory et al. 1990; Tamova et al. 1993; Tanguay et al. 2003; Wei et al. 2004; Wnendt et al. 1990).

Applying identical conditions to other studies, protoplasts from the *S. elegans* germlings were successfully obtained and the percentage of their viability was in the range of other fungal species (3×10^3 - 5.75×10^7). When used as a starting material for transformation, protoplasts failed to grow on media supplemented

with hygromycin B as antibiotic. Among the factors that could have possibly affected the efficiency of protoplast formation and regeneration are the type of cell-wall lysis cocktail mixture and the chemical nature (i.e. inorganic or organic) of the osmotic stabilizers (OS) used (Tamova et al. 1993; Varavallo et al. 2004; Zhou et al. 2008). In our study we have used mannitol for protoplast formation, and sorbitol for their regeneration. These organic stabilizers have been reported to favour cell wall regeneration but negatively affect the enzymatic digestion of the cell wall that could be due to the role of sugars in favouring the osmotic stability for protoplast viability (Varavallo et al. 2004). Inorganic stabilizers (NaCl, MgSO4, or KCl) have been shown to be more effective than sugar alcohols in releasing protoplasts from filamentous fungi (Peberdy 1979). Future experiments aiming at protoplast formation of *S. elegans* should take into consideration the use of inorganic stabilizers.

Similar to the PEG-CaCl2 transformation, no positive transformants were obtained when *S. elegans* trasnformation by the ATMT method was attempted. Taking into consideration the numerous parameters that might influence the efficiency of ATMT, several factors could account for the results obtained in our study. These include the fungal starting material, the co-cultivation conditions, and acetosyringone concentration. The fungal starting material seems to play a major role in the *Agrobacterium* transformation. Although we followed similar conditions reported in other studies by using spores as starting material (Meyer et al. 2003; Michielse et al. 2005; Mullins et al. 2001; Rho et al. 2001; Tsuji et al. 2003; Zeilinger 2004), others have achieved successful transformation using only protoplasts or mycelium (Michielse et al. 2004; Zhang et al. 2003; Zwiers and De Waard 2001). During the co-cultivation step, two factors (conidia:bacteria ratio, and co-cultivation period) can influence the transformation efficiency. In our study, no difference in the transformation efficiency was observed when we tested different ratios of conidia to bacteria cells (1:1; 1:2: 1:3). Covert et al. (2001) have found that an increase in the conidia concentration of *F. circinatum* from 10^4 to 10^7 per plate will make the identification of resistant colonies harder due to excessive fungal growth; whereas Meyer et al. (2003) have found that an increase

in the number of bacteria cells can result in a decrease in the efficiency of transforming *Aspergillus giganteus.* This could be attributed to the competition for nutrients and space between Agrobacterium cells and fungal spores. The co-cultivation period has also a role in influencing the transformation efficiency. Due to the slow growth of *S. elegans*, the co-cultivation period between *S. elegans* and *Agrobacterium* cells was prolonged for 5 days until putative transformants began to appear. However, it has been reported in the case of the entomopathogenic biocontrol fungus, *Beauveria bassiana* that the transformation frequency was lower when the co-cultivation period was prolonged (Leclerque et al. 2004). Additionally, the absence of acetosyringone (AS) from the liquid induction media (IM) during the pre-culture step could have affected our transformation efficiency (Leclerque et al. 2004; Michielse et al. 2005).

In conclusion, although many transformation systems are available for filamentous fungi, not all are suitable for a given organism and appropriate systems have to be optimized for each individual strain. Several factors could attribute to the lack of success in transforming *S. elegans* (i.e. enzyme mixtures, osmotic stabilizers, ratio of conidia to bacteria, co-cultivation time). An alternate method, but costly would be the application of biolistics (Chaves Barreto et al. 2006) to transform *S. elegans*. This method consists of coating tungsten or gold microshperes of 1 µm diameter with the plasmid and introducing it into the target cells via bombardment where it will be integrated into the host's genome. This transformation takes place inside an acceleration chamber that operates under a partial vacuum and a high pressure maintained by the helium gas, which allows for improved microsphere movement (Djulic et al. 2011; Meyer et al. 2003). The introduction of a reproducible and effective method for transforming *S. elegans* is of great advantage to complete our understanding on the role of *smkA* under different stresses.

5.6. ACKNOWLEDGMENTS

This study is supported by a Natural Science and Engineering Research Council of Canada (NSERC) grant to S. Jabaji. The authors would like to thank Professor Neena Mitter for her help in constructing the RNAi silencing plasmid and Katia Colton-Gagnon for her assistance in the Epifluorscence microscope visualization.

CONNECTING STATEMENT BETWEEN CHAPTERS 5 AND 6

This chapter focuses on the application of metabolomics to understand the mechanisms of interactions between *Stachybotrys elegans* and *Rhizoctonia solani*. Here, we developed methods (direct-infusion mass spectrometry) to differentially evaluate changes in the relative concentration of secondary metabolites produced in pure cultures and in confrontation zones during fungal-fungal interaction over a period of 96 and 120 hours of interaction.

Putative identification of key metabolites during mycoparasitism was made possible through public databases (KEGG, YMDB, PlantCyc, LIPID MAPS, KNApSAcK), an in-house built library of 409 fungal metabolites and MS/MS spectra whenever available.

The results of this chapter will be submitted for publication in Metabolomics. I have designed the experimental set-up, harvested the material, helped in the metabolite identification process and wrote the manuscript. The contributions of the co-authors were as follows: Dr. K. Aliferis has conducted the metabolites extraction and identification and Dr. S. Jabaji provided supervision, funding throughout the study, made suggestions and corrected the manuscript.

CHAPTER 6

Metabolic biomarkers associated with the mycoparasitic process between the plant pathogen *Rhizoctonia solani* and the mycoparasite *Stachybotrys elegans*

Rony Chamoun, Konstantinos A. Aliferis and Suha H. Jabaji*

*Corresponding author: Suha Jabaji

McGill University, Macdonald Campus, Department of Plant Science, 21,111 Lakeshore Road, Montreal, Qc, H9X 3V9

Phone: (514) 398-7561 Fax: (514) 398-7897

E-mail: suha.jabaji@mcgill.ca

6.1. ABSTRACT

The mycoparasite *Stachybotrys elegans* possesses the ability to limit the growth of the plant pathogen *Rhizoctonia solani* AG3 through production of cell wall degrading enzymes and expression of pathogenic process encoding genes. In response to this infection, *R. solani* express genes encoding antioxidants. Here, we applied direct-infusion mass spectrometry to assess and detect metabolic changes in single and co-cultures of *R. solani* following five days of interaction with *S. elegans*. Multivariate analysis highlighted 486 compounds identified as biomarkers in both types of cultures. Searches against five public databases (KEGG, YMDB, PlantCyc, LIPID MAPS, KNApSAcK), and an in-house built library of 409 fungal metabolites, provided putative identification of 42 metabolites with assigned molecular formula. Carboxylic acids (23%), heterocyclic compounds (20%), terpenoids (11%), and fatty acids (8%) were the most predominant chemical groups in *R. solani* monoculture. Surprisingly, only carboxylic acids, alkaloids and indoles remained present during the mycoparasitic interaction. These results highlight the role of secondary metabolites in the mycoparasitic process. In response to infection, the secondary metabolite camptothecin, known for its antifungal activity was detected. Notably, was the significant increase in the relative level of the pathogen-derived metabolite alkaloid, 11-hydroxycanthin-6-one in parasitized hyphal cells of *R. solani*. This finding represents the first report on the production of canthin-6-one alkaloid derivative in fungi. Collectively the findings present evidence that the pathogen produces secondary metabolites some of which are known for their antifungal activities. Studying plant pathogen metabolome will help in implementing novel strategies for biological control and plant disease tolerance.

Keywords: *Rhizoctonia solani*, Mycoparasitism, Direct-Infusion Mass Spectrometry, Metabolomics

6.2. INTRODUCTION

Metabolomics is a functional genomics technology of vital importance for understanding cellular functioning because the metabolome is a direct reflection of the physical status of a cell (van der Werf et al. 2007). Another key feature of this technology is that it analyses all metabolites, allowing an unbiased approach towards identifying those biomolecules that are important for a specific biological question (Dettmer et al. 2007).

Interactions among microbes encompass antagonistic, mycoparasitic or competitive outcomes. Interacting fungi may limit each other's growth through the production of lytic enzymes and antibiosis, where secondary compounds limit mycelial growth, spore production or spore germination of the opposing fungi. Interacting fungi may also compete for nutrient if they use the same nutritional resource which is the case in mycoparasitic interactions (Lopes et al. 2012; Malmierca et al. 2012; Nicoletti et al. 2004)

Mycoparasitism, the direct attack of one fungus on another, involves changes in the biochemistry and physiology of both partners. Less well studied are the fluctuations in metabolites during the *in vitro* interactions between a mycoparasite and a pathogen. Analysis of metabolites that are expressed during mycoparasite-host interaction represents a powerful strategy to obtain insight into the biochemical events underlying these changes.

The intimate interaction between the mycoparasite, *Stachybotrys elegans* and the soilborne pathogen *Rhizoctonia solani* involves morphogenetic processes that result in the formation of specific structures including hyphal coils, and appressoria or penetration pegs after 3-5 days of hyphal interaction (Benyagoub et al. 1994). This process is partly accompanied by the production of cell wall degrading enzymes by the mycoparasite (Archambault et al. 1998; Morissette et al. 2003; Taylor et al. 2002) and the differential expression of mycoparasitism associated genes involved in the pathogenic process (Morissette et al. 2008). In response to infection by *S. elegans*, a handful of genes were putatively identified in *R. solani* and belonged to different metabolic categories including lipid and vitamin metabolism (Morissette et al. 2008). Of significance was the finding that

during mycoparasitism the host's response to attack is characterized by elevated levels of the pyridoxal reductase-encoding gene whose role in ROS quenching as a result to stress conditions is established in fungi (Chamoun and Jabaji 2011).

Studies investigating metabolic aspects of microbes are mainly focused on fungal classification (Aliferis et al. 2013; Smedsgaard and Frisvad 1996; Smedsgaard et al. 2004) with few focusing on the metabolic profiles produced during an antagonistic interaction of endophytic fungi with pathogens or during a competitive interaction of primary and secondary fungal colonizers of wood (Combès et al. 2012; Jonkers et al. 2012; Peiris et al. 2008; Rodriguez Estrada et al. 2011). However, metabolic profiling during a mycoparasitic interaction has not been studied.

Broadly, the term fungal metabolomics refers to the comprehensive (qualitative and quantitative) analysis of the complete set of all low molecular weight organic and inorganic metabolites present in and around growing cells at a given time during their growth or production cycle (Mashego et al. 2007). Microbial metabolomic strategies generally aim at quantifying microbial substrates and products at two levels, i.e. outside the cells (extracellular) representing the exo-metabolome which is the sum of the metabolites excreted into the growth medium or extracellular fluids, and inside the cells (intracellular) representing the endo-metabolome which is the sum of intracellular primary and secondary metabolites (Mashego et al. 2007). The combined exo-metabolome and the unspent growth medium components compose the metabolic footprint which is used for taxonomy purposes (Frisvad et al. 2008; Pope et al. 2007, 2009; Smedsgaard et al. 2004) and fungal-fungal interactions (Peiris et al. 2008; Rodriguez Estrada et al. 2011). In this work, we studied the expression of metabolites produced by *R. solani* (exo-metabolome) in response to infection by *S. elegans.* To explore this idea, we co-cultivated the fungi together on agar plates that allowed easy extraction of metabolites for profiling and for comparison with the exo-metabolome of *R. solani* single cultures. Metabolic profiles were differentially analyzed by direct infusion Orbitrap MS (DI-MS) using an in-house

built library of 409 fungal metabolites, and searches against public databases (KEGG, PlantCyc, Lipidmaps, KNApSAcK, and YMDB).

6.3. MATERIALS AND METHODS

6.3.1. Chemicals and reagents

All chemicals used for extraction and sample preparation for direct infusion Orbitrap MS (DI-MS) analysis were of the highest available purity. Methanol, ethyl acetate, formic acid, ammonium acetate (Optima® grade), and water (HPLC grade) were purchased from Fisher Scientific Company (Ottawa, ON, Canada).

6.3.2. Fungal cultures

Starter cultures of the mycoparasite *Stachybotrys elegans* (ATCC 18825) and the pathogen, *Rhizoctonia solani* AG-3 (ATCC 10183) were revived from pre-colonized oat kernels on 1% potato dextrose agar (PDA; Difco Laboratories, Michigan, USA) and were incubated at 24^{o}C for 7 and 5 d respectively. Induction and collection of conidia of *S. elegans* were performed as described in Chapter 3.

6.3.3. Experimental design

Co-cultivation of the mycoparasite and the pathogen were conducted in 9 mm Petri plates containing 20 mL of minimal synthetic media (MSMA). The medium is composed (in g/liter) of: $MgSO_4.7H_2O$, 0.2; K_2HPO_4, 0.9; KCl, 0.2; $FeSO_4.7H_2O$, 0.002; $MnSO_4$, 0.002; $ZnSO_4$, 0.002; $NaNO_3$, 1.0; biotin, 10 mg; gellan gum, 1 % (composed of glucose, glucuronic acid and rhamnose in the molar ratio of 2:1:1) (Phytagel, Sigma, St. Louis, USA).

PDA plugs (8 mm) covered with mycelia of a 5-day old growth of *R. solani* were placed on MSMA media and let to grow for 48 hours after which they were sprayed with 100 µL of *S. elegans* conidia (10^6 mL^{-1} water) or with the same volume of sterile distilled water using a Badger 350 air brush and MC-80 mini air

compressor calibrated at 1 kg/cm^2. Additionally, non-inoculated MSMA plates were sprayed with sterile distilled water. This water control was used as a negative control to determine compounds attributed to the MSMA medium. All culture plates were incubated at 24^{o}C until harvest. Metabolite analysis was monitored on the fifth day following co-cultivation. This period ensured that infection and colonization of *R. solani* hyphal cells by *S. elegans* had occurred. There were five replicates for each treatment.

6.3.4. Optic microscopy

To associate the metabolic changes with the development of biological steps of the mycoparasitic process, agar pieces (5 x 5 mm) from interaction plates and from single cultures of *R. solani* (control) were excised. All sections were stained with lactophenol blue or water and viewed under a light microscope at 40X magnification. Presence of hyphal coiling and penetration pegs and colonization of the host were digitally documented with the Moticam 2300 digital camera (GENEQ Inc. Montreal, Quebec).

6.3.5. Sampling, quenching and metabolite extraction

Four plugs (8 mm x 7 mm thickness) were collected from the single cultures of *R. solani* (Fig. 6.1A), the co-cultivation zones (Fig. 6.1B), and non-inoculated MSMA plates, and placed in screw thread vials (Fisher Scientific). Quenching was performed by adding liquid N_2 and samples were kept at -80^{o}C until further use. For metabolite extraction, one ml of a mixture of methanol/ethyl acetate (50:50, v/v) (Fisher Scientific Company) was added in the vials, followed by sonication for 25 min. Samples were further extracted for 2 h under continuous agitation (250 rpm) at 25°C and filtered through 0.2-µm filters (Millex-FG; Millipore, Billerica, MA, USA). The volume of samples was adjusted to 1 ml and subsequently divided into two equal portions (0.5 ml) for analyses in positive (ESI^+) and negative (ESI^-) electrospray modes. Finally, extracts were dried using

a Labconco CentriVap refrigerated vacuum concentrator equipped with a cold trap (Labconco, Kansas City, MO, USA).

6.3.6. Direct infusion mass spectrometry analysis (DI-MS) and DI-tandem MS (DI-MS/MS)

For DI-MS and DI-MS/MS analyses, a Linear ion trap (LTQ) Orbitrap MS Classic (Thermo Scientific, San Jose, CA, USA) was used acquiring in ESI^+ or ESI^- modes and all experimental events were controlled by the software Xcalibur v.2 (Thermo Scientific, San Jose, CA, USA). The analyzer was equipped with an Orbitrap electrostatic Fourier transform mass spectrometer (FTMS) with a Proxeon nanoelectrospray ion source, a quadrupole linear ion trap and an Accela pump. For analysis in ESI^+, 100 µl of a mixture of methanol/formic acid (0.2% v/v) (50-50, v/v) or 100 µl methanol/ammonium acetate (4 mM) for analysis in ESI^- was added in the dried samples, and the extracts were transferred into glass microinserts which were consecutively placed into glass autosampler vials. Samples (10 µl) were injected performing flow infusion at a flow rate of 10 µl min^{-1} using a 100 µl syringe (Hamilton, Reno, NV, USA). Full scan mass spectra were acquired in the range between 50 and 1200 Da at a rate of 0.6 scans/sec at a mass resolution of 100,000 (full width at half maximum, FWHM) for 3.5 min. The source and capillary voltages were set to 3.2 kV and 5.0 V (ESI^+) and 4.0 kV and -35 V (ESI^-), respectively. The capillary temperature for both modes was set to 275^oC. Sheath gas flow was set to 10 (ESI^+), and 20 (ESI^-) whereas no auxiliary and sweep gases were used. For selected samples MS/MS spectra were recorded. Target ions were dynamically excluded for 60 s and overall 120 MS/MS spectra were recorded per sample.

6.3.7. Data processing and analyses

Mass spectra were processed using the MZmine2 software (Pluskal et al. 2010) following the procedures recommended by the developers after

optimization for our datasets (See on-line manuals, http://mzmine.sourceforge.net/docs.shtml). Cumulative spectra were collected between 0.8-1.2 min (ESI^+) and 0.6-1.0 min (ESI^-). Signals were detected using the centroid mass detector and the noise levels were optimized for each sample. The FTMS shoulder filter was then applied at a mass resolution of 100,000 using the Lorentzian extended model function. Finally chromatograms were built using an m/z tolerance < 3 ppm. Alignment was performed using the Join aligner function with an m/z tolerance < 3 ppm. Following alignment, gap-filling was performed using the Peak finder function and m/z tolerance < 3 ppm. This procedure accounted for the presence of missing peaks in the matrix as a result of the performance of the peak detection algorithm or possible mistakes in the alignment. Subsequently, the matrices were subjected to filtering by removing rows with 50% missing values among replications of the same treatment. During the alignment step, ions of non-biological origin corresponding to the blank samples (containing only culture medium) and detected in the biological samples were excluded for further analysis. The matrices were then exported to SIMCA-P+ v.12.0 software (Umetrics, MKS Instruments Inc., Andover, MA, USA) for multivariate statistical analysis according to Aliferis and Jabaji (2010). Principal component analysis (PCA) was first performed to evaluate the data and examine the variation in the data set through the detection of outliers. The discovery of biomarker-ions was based on partial least squares-discriminant analysis (PLS-DA) regression coefficients ($P < 0.05$). Based on the variability in the model parameters encountered in the different cross-validation cycles, standard errors were calculated with 95% confidence interval using Jack-knifing (Efron and Gong 1983).

6.3.8. Metabolite identification

The lack of chromatographic separation performing DI-MS analysis makes the identification of metabolites a challenging task, even with high mass accuracy (< 1 ppm). For example, the possible presence of metabolites with identical molecular formulae or isomers makes their absolute identification even more

complex. Here, identification of metabolites was performed following a biologically-driven approach. An in-house built targeted-library was constructed and was composed of 409 compounds (Appendix IV) reported to be involved in primary and secondary fungal metabolism. The library includes information on monoisotopic masses, names and molecular formulae. Information was retrieved from the databases KEGG, PubChem, and Chemspider. On-line searches within an error < 3 ppm were performed against five biological databases, the Kyoto Encyclopedia of Genes and Genomes (KEGG, http://www.genome.jp/kegg/ligand.html), the Plant Metabolic pathway database (PMN/PlantCyc, http://plantcyc.org/), LIPID Metabolites and Pathways Strategy Lipidomics Gateway (http://www.lipidmaps.org/), the Yeast Metabolome Database (http://www.ymdb.ca/), and KNApSAcK (http://kanaya.naist.jp/KNApSAcK/) and the in-house built library were performed with different adducts for each of the ionization mode (Table 6.1). Identification of metabolites was based on mass accuracy (< 3 ppm), MS/MS fragmentation and isotope patterns (where available), following the heuristic rules of Kind and Fiehn (2007), which are implemented in mzMine2 (Pluskal et al. 2010). These rules provide a valuable tool for reducing the number of possible molecular formulas for a given detected ion.

Metabolites were considered putatively identified when a single hit was returned from the performed searches against the on-line searches, within an error < 3 ppm, taking into account the isotopic and MS/MS patterns where available, and references from the literature. Detection of mass errors was confirmed by the Molecular Weight Calculator v.1.0 and the elemental composition calculator, both accessible at www.wsearch.com.au.

Metabolites with their corresponding MS/MS spectra were identified using public tandem MS databases, Metlin: Metabolite and tandem MS database (http://metlin.scripps.edu/metabo_advanced.php) and MassBank (http://www.massbank.jp/QuickSearch.html).

6.4. RESULTS

6.4.1. Morphological and microscopical observations

S. elegans conidia germinated within 24 hours, made contact with hyphae of *R. solani* and overgrew over the *R. solani* culture after 5 days of co-culturing. Conspicuous accumulation of *S. elegans* aerial hyphae over *R. solani* colony (Fig. 6.1B) is observed and accompanied by infection characterized by heavy coiling and formation of infection pegs and intracellular colonization of *R. solani* cells (Fig. 6.1 D and E). In the presence of the mycoparasite, infected cultures of *R. solani* appeared more pigmented compared to the non-inoculated cultures and the cytoplasm of infected cells appeared disorganized and devoid of granules (Fig. 6.1 D and E). Additionally, the growth medium which supported the growth of both partners underwent color change from white to dark brown suggesting the release of fungal metabolites into the growth medium as a result of the interaction (data not shown).

6.4.2. Multivariate analysis highlights different metabolic profiles between pure and parasitized cultures of *Rhizoctonia solani* and corresponding biomarkers

In order to test the hypothesis that the metabolic profiles of *R. solani* change and that some metabolites could be specifically induced during its interaction with *S. elegans*, DI-MS profiles of pure *R. solani* cultures were compared to those of co-cultures with *S. elegans*. Using bioinformatic softwares along with five metabolic databases and an in-house built metabolite library, differences in the metabolic profiles between parasitized and non-parasitized *R. solani* cultures were investigated.

Following data pre-processing, two data matrices were obtained [DIMS-D5-ESI^+-3473 rows (features) x 10 columns (biological replications), DIMS-D5-ESI^--977 rows x 10 columns]. Ions corresponding to the control (growth medium alone) were detected and removed from further analyses. Therefore, the analyzed metabolite profiles were composed of extracellular metabolites excreted in the

media (exo-metabolome) and intracellular metabolites found in the fungal hyphae (endo-metabolome). Metabolic profiles of single and co-cultures were subjected to multivariate analysis for their classification and detection of corresponding biomarkers.

Initially, PCA was performed for the overview of the dataset. Results revealed no outliers and tight clustering between the biological replications of the same treatment (data not shown), which is indicative of the robustness and reliability of the applied bioanalytical protocols and instrument performance.

In a second step, PLS-DA was applied for the detection of biomarkers which represent those metabolites detected only in the corresponding treatment without excluding the possibility of their presence in concentrations below the detection limits in other treatments. Analyses showed an excellent discrimination between the metabolic profiles of single and co-cultures of *R. solani* with *S. elegans* (Fig. 6.2) as it is indicated by the high values of R^2X (0.57 – 0.71), R^2Y (0.99) and $Q^2(cum)$ of 0.90-0.98 (2 principal components, PCs) and the tight clustering. The detection of biomarkers was based on PLS-DA regression coefficients ($P < 0.05$). Here and throughout, biomarkers are defined as metabolites or features whose relative intensities are significantly different between the two treatments ($P < 0.05$). In total, applying PLS-DA 486 features were detected as biomarkers (Tables 6.2; 6.3; Fig. 6.3A; Appendix V-XI), from which 108 were assigned unique chemical formulae. From the latter, 42 metabolites were putatively identified (Tables 6.2; 6.3).

6.4.2.1. DI-Orbitrap MS analysis reveals differences in the chemical groups detected in *R. solani* single cultures and during mycoparasitism in co-cultures

Performing DI Orbitrap MS analyses to *R. solani* monocultures, metabolites belonging to ten chemical groups were identified (Fig. 6.4A). Metabolites belonging to carboxylic acids (23%), heterocyclic compounds (20%), terpenoids (11%), and fatty acids (8%) were the most abundant (Fig 6.4A) followed by

indoles, alkaloids, cyanogenic glucosides and fatty amides (3%). During the mycoparasitic interaction, some groups present in *R. solani* single cultures were not detected in the metabolomics matrix, while chemical groups such as carboxylic acids (34%), and alkaloids (22%) were detected in increased levels during interaction (Fig. 6.4B). Generally, the number of metabolites detected during the interaction was lower compared to that in the fungal pathogen monoculture.

6.4.2.2. Metabolites detected in the fungal pathogen *R. solani*

Metabolic profile of *R. solani* monocultures showed that metabolites related to fungal growth and nutrient acquisition, and belonging to amino acid pathways (arginine and proline, cysteine and methionine, tryptophan, lysine and histidine) and fatty acids (2S-hydroxytetradecanoic acid) were the dominant groups followed by metabolites belonging to the folate biosynthetic pathway (tetrahydrobiopterin (BH4) and 4a-hydroxytetrahydrobiopterin) which belongs to the pteridines representing 42% of the heterocyclic compounds detected in *R. solani* monoculture.

6.4.2.3. Metabolites detected in cocultures and during mycoparasitism

In response to parasitism of *R. solani* hyphal cells, metabolites belonging to the carboxylic acids, indoles, aldehydes and alkaloids made up the majority of the biomarkers detected in co-cultures (Table 6.3). Of interest, was the 2.6 fold increase in relative intensity of the alkaloid 11-hydroxycanthin-6-one that was found also in *R. solani* single cultures (Fig. 6.5).

6.4.2.4. Changes in the metabolic content of *R. solani* monoculture and mycoparasitism

Using PLS regression coefficients with 95% Jack-knifed confidence intervals, significant metabolic changes between *R. solani* monoculture and co-cultures

were detected (Fig. 6.5). *R. solani* monoculture showed a 1.26 significant increase in the content of the fatty amide octadecanamide, in addition to other features/metabolites (m/z 404.1036; m/z 214.1057; m/z 519.2778 and $C_{20}H_{30}O_2$) whereas an increase in the concentrations of the alkaloid 11-hydroxycanthin-6-one (2.6) and other features were observed during mycoparasitism (Fig. 6.5).

Table 6.1 Adducts for which databases were searched

Target database(s)/ ionization mode	Adducts
In-house built library/ESI^+	$[M+H]^+$, $[M+K]^+$, $[M+Na]^+$, $[M+NH_4]^+$, $[M+H_2O+H]^+$, $[M+Na-H]^+$, $[M+K-H]^+$, $[M+Mg-2H]^+$, $[M+NH_3]^+$, $[M+H_3PO_4]^+$, $[M+H_2SO_4]^+$, $[M+H_2CO_3]^+$, $[M+3H]^+$, $[M+2H+Na]^+$, $[M+H+2Na]^+$, $[M+3Na]^+$, $[M+2H]^+$, $[M+H+NH_4]^+$, $[M+H+Na]^+$, $[M+H+K]^+$, $[M+CH_3CN+2H]^+$, $[M+2CH_3CN+2H]^+$, $[M+3CH_3CN+2H]^+$, $[M-3H_2O+H]^+$, $[M-2H_2O+H]^+$, $[M-H_2O+H]^+$, $[M+CH_3CN-H_2O+H]^+$, $[M+CH_3OH+H]^+$, $[M+CH_3CN+H]^+$, $[M+CH_3CN+Na]^+$, $[M+DMSO+H]^+$, $[M+2CH_3CN+H]^+$, $[M+CH_3CN+HCOOH+H]^+$, $[M+FeCOO+CH_3CN^+]^+$, $[M+FeCOOH+CH_3CN]^+$.
In-house built library/ESI^-	$[M-2H]^-$, $[M-3H]^-$, $[M+H_2O-H]^-$, $[M+Na-2H]^-$, $[M+2H_2O-H]^-$, $[M+K-2H]^-$, $[M+CH_3CN-H]^-$, $[M+HCOOH-H]^-$, $[M+H_2O+O_2-H]^-$, $[M+NaCOOH-H]^-$, $[M+KCOOH-H]^-$, $[M+2COOH-H]^-$, $[M+H_2SO_4-H]^-$, $[M+H_3PO_4-H]^-$, $[M+Ca[COOH]_2-H]^-$, $[M+2NaCOOH-H]^-$, $[M+Fe[COOH]_2-H]^-$, $[2M-H]^-$.
On-line public databases/ ESI^+	$[M+H]^+$, $[M+K]^+$, $[M+Na]^+$, $[M+NH_4]^+$
On-line public databases/ ESI^-	$[M-H]^-$, $[M+CO_3^-]^-$, $[M+H_2PO_4^-]^-$

Table 6.2. Putatively identified metabolites detected only in monocultures of *Rhizoctonia solani* after 120 h of growth. Identification of metabolites was performed with searches against five biological databases (KEGG, PlantCyc, LIPID MAPS, YMDB, and KNApSAcK) with a mass accuracy (Δppm < 3). Pathway and compound identification (ID) is provided according to KEGG database (http://www.genome.jp/kegg/ligand.html). Chemical group is assigned according to the PubChem database (http://pubchem.ncbi.nlm.nih.gov/).

Detected m/z	Metabolite	Molecular Formula	Monoisotopic mass	Pathway	ID	Chemical group	Adduct	Relative Intensity
145.0291	3-(Methylthio) propionic acid	$C_4H_8O_2S$	120.0245	ko00270 Cysteine and methionine metabolism	C08276	Carboxylic acid	$[M+2H+Na]^+$	0.002
147.9931	2,2-Dichloro-1,1-ethanediol	$C_2H_4Cl_2O_2$	129.9588	ko00980 Metabolism of xenobiotics by cytochrome P450	C14860	n/a[a]	$[M+NH_4]^+$	0.0009
159.0627	2,3-Dihydroxy-3-methylbutanoate	$C_5H_{10}O_4$	134.0549	ko00770 Pantothenate and CoA biosynthesis	C04039	Carboxylic acid	$[M+2H+Na]^+$	0.0015
171.1010	Furfural diethyl acetal	$C_9H_{14}O_3$	170.0942	n/a	C14280	Aldehyde	$[M+H]^+$	0.0008

190.9964	Xanthine	$C_5H_4N_4O_2$	152.0334	Many pathways	C00385	Purine: heterocyclic compound	$[M+K]^+$	0.0016
219.0088	5-Methylthio-D-ribose	$C_6H_{12}O_4S$	180.0456	ko00270 Cysteine and methionine metabolism	C03089	Carbohydrate	$[M+K]^+$	0.0023
221.0664	6-Acetyl-D-glucose	$C_8H_{14}O_7$	222.0739	n/a	C02655	Carbohydrate	$[M-H]^-$	0.00234
235.0501	11-Hydroxycanthin-6-one	$C_{14}H_8N_2O_2$	236.0585	n/a	C09212	Alkaloid	$[M-H]^-$	0.0022
250.1552	N-acetyl-5-methoxytryptamine (melatonin)	$C_{13}H_{16}N_2O_2$	232.1211	ko00380 Tryptophan metabolism	C01598	Indole	$[M+NH_4]^+$	0.0017
259.1516	Tetrahydrobiopterin	$C_9H_{15}N_5O_3$	241.1174	ko00790 Folate biosynthesis	C00272	Pteridine; heterocyclic compound	$[M+NH_4]^+$	0.0013
262.0692	Diethyl 2-methyl-3-oxosuccinate	$C_9H_{14}O_5$	202.0841	n/a	C04067	Carboxylic acid	$[M+CO_3^-]^-$	0.00621
265.1406	linamarin	$C_{10}H_{17}NO_6$	247.1055	ko00460 Cyanoamino acid metabolism	C01594	Cyanogenic glucoside	$[M+NH_4]^+$	0.001

267.1931	2S-Hydroxytetradecanoic acid	$C_{14}H_{28}O_3$	244.2038	ko00061 Fatty acid biosynthesis	C13790	Fatty acid	$[M+Na]^+$	0.0026
275.1465	4a-Hydroxytetrahydrobiopterin	$C_9H_{15}N_5O_4$	257.1124	ko00790 Folate biosynthesis	C15522	Pteridine; heterocyclic compound	$[M+NH_4]^+$	0.0015
281.0571/ 321.028	N-(p-Nitrobenzyl) phthalimide	$C_{15}H_{10}N_2O_4$	282.0640	n/a	C14265	Carboxylic acid	$[M-H]^-$/ $[M+K]^+$	0.0015
290.1088	2-Amino-4-oxo-6-(1',2',3'-trihydroxypropyl)-diquinoid-7,8-dihydroxypterin	$C_9H_{15}N_5O_6$	289.1022	n/a	C05253	Pteridine: heterocyclic compound	$[M+H]^+$	0.0021
291.1780	4-Guanidinobutanoate	$C_5H_{11}N_3O_2$	145.0851	ko00330 Arginine and proline metabolism	C01035	Fatty acid	$[2M+H]^+$	0.0016
291.2033	(2R,3R)-3-Methylglutamyl-5-semialdehyde-N6-lysine	$C_{12}H_{23}N_3O_4$	273.1688	ko00300 Lysine biosynthesis	C20279	n/a	$[M+NH_4]^+$	0.0012
304.1159	Linatine	$C_{10}H_{17}N_3O_5$	259.1168	Ko00330 Arginine and proline metabolism	C05939	Carboxylic acid	$[M+HCOOH-H]^-$	0.0023

306.2757	Octadecanamide	$C_{18}H_{37}NO$	283.2875	n/a	C13846	Fatty amide	$[M+Na]^+$	0.0019
307.1128	N-Succinyl-2-L-amino-6-oxoheptanedioate	$C_{11}H_{15}NO_8$	289.0797	ko00300 Lysine biosynthesis	C04462	Carboxylic acid	$[M+NH_4]^+$	0.0015
311.1470	L-Histidine	$C_6H_9N_3O_2$	155.0694	Many pathways	C00135	Amino acid	$[2M+H]^+$	0.0022
323.0274	Cinnavalininate	$C_{14}H_8N_2O_6$	300.0382	ko00380 Tryptophan metabolism	C05640	Oxazine; Heterocyclic compound	$[M+Na]^+$	0.0019
327.1562	Prosolanapyrone II	$C_{18}H_{24}O_4$	304.1674	n/a	C19933	Carboxylic ester	$[M+Na]^+$	0.0022
334.0622	3-[(2-Chlorobenzylidene)amino]-6H-dibenzo[b,d]pyran-6-one	$C_{20}H_{12}ClNO_2$	333.0556	n/a	C14951	Lactone	$[M+H]^+$	0.0017
355.2011	5-(7-(4-(4,5-Dihydro-4-methyl-2-oxazolyl)phenoxy)heptyl)-3-methylisoxazole [WIN I(S)]	$C_{21}H_{28}N_2O_3$	356.2099	n/a	C06497	Azole; Heterocyclic compound	$[M-H]^+$	0.0036
357.2398	Arachidonyltrifluoromethane	$C_{21}H_{31}F_3O$	356.2327	n/a	C01397	Fatty acid	$[M+H]^+$	0.0016

401.1280	2-(1-ethylpyrrolidin-2-yl)-5-(5-ethylsulfonyl-2-methoxyphenyl)-1H-pyrrole	$C_{19}H_{26}N_2O_3S$	362.1664	n/a	C11709	Pyrole; Heterocyclic compound	$[M+K]^+$	0.0017
421.2255	1,4-Bis(2-ethylhexyl) sulfosuccinate	$C_{20}H_{38}O_7S$	422.2338	n/a	C07874	Carboxylic acid	$[M-H]^-$	0.01958
436.2544	17beta-Hydroxy-4-mercaptoandrost-4-en-3-one 4-acetate 17-propionate	$C_{24}H_{34}O_4S$	418.2177	n/a	C15180	Carboxylic acid	$[M+NH_4]^+$	0.0013
451.2024	Dihydrogeranylgeranyl-PP	$C_{20}H_{38}O_7P_2$	452.2092	n/a	C17439	Terpenoid	$[M-H]^-$	0.00093
497.2358	Glaucarubin	$C_{25}H_{36}O_{10}$	496.2308	n/a	C08760	Terpenoid	$[M+H]^+$	0.0011
639.3292	Phorbol 12-tiglate 13-decanoate	$C_{35}H_{52}O_8$	600.3662	ko00061 Fatty acid biosynthesis	C09157	Terpenoid	$[M+K]^+$	0.0012
815.5118	Solanesyl diphosphate	$C_{45}H_{76}O_7P_2$	790.5066	ko00900 Terpenoid backbone biosynthesis	C04145	Terpenoid	$[M+Na+2H]^+$	0.0014
919.4033	Glycopeptide	$C_{36}H_{64}N_8O_{17}$	880.4389	n/a	C00528	Peptide	$[M+K]^+$	0.0006

[a]n/a = not applicable

Table 6.3. Putatively identified metabolites detected exclusively in the interaction between *Stachybotrys elegans* and *Rhizoctonia solani* after 120 h of contact. Identification of metabolites was performed with searches against five biological databases (KEGG, PlantCyc, LIPID MAPS, YMDB, and KNApSAcK) with a mass accuracy (Δppm < 3). Pathway and compound identification (ID) is provided according to KEGG database (http://www.genome.jp/kegg/ligand.html). Chemical group is assigned according to the PubChem database (http://pubchem.ncbi.nlm.nih.gov/).

Detected m/z	Metabolite	Molecular Formula	Monoisotopic mass	Pathway	ID	Chemical group	Adduct	Relative Intensity
125.096	Octadienal	$C_8H_{12}O$	124.0888	n/a[a]	LMFA 06000034[b]	Aldehyde	$[M+H]^+$	0.0015
133.0313	2-n-Tetrahydrothiophenecarboxylic acid	$C_5H_8O_2S$	132.0245	n/a	C11074	Carboxylic acid	$[M+H]^+$	0.0025
148.0433	Thiomorpholine 3-carboxylate	$C_5H_9NO_2S$	147.0353	n/a	C03901	Carboxylic acid	$[M+H]^+$	0.0012
234.0186	S-Methyl-3-phospho-1-thio-D-glycerate	$C_4H_9O_6PS$	215.9857	n/a	C04399	Carboxylic acid	$[M+NH_4]^+$	0.0017
235.0501	11-Hydroxycanthin-6-one	$C_{14}H_8N_2O_2$	236.0585	n/a	C09212	Alkaloid	$[M-H]^-$	0.0057

291.1850	2,4-Dimethylindole	$C_{10}H_{11}N$	145.0891	n/a	CID7053	Indole	$[2M+H]^+$	0.0014
306.2762	Octadecanamide	$C_{18}H_{37}NO$	283.2875	n/a	C13846	Fatty amide	$[M+Na]^+$	0.0024
314.0436	1-(6-Oxo-6H-dibenzo[b,d]pyran-3-yl)-1H-pyrrole-2,5-dione	$C_{17}H_9NO_4$	291.0531	n/a	C15433	n/a	$[M+Na]^+$	0.0018
371.1006	camptothecin	$C_{20}H_{16}N_2O_4$	348.1110	map01063 Biosynthesis of alkaloids derived from shikimate pathway	C01897	Alkaloid	$[M+Na]^+$	0.0084

[a]n/a = not applicable [b] : ID provided according to LIPID MAPS

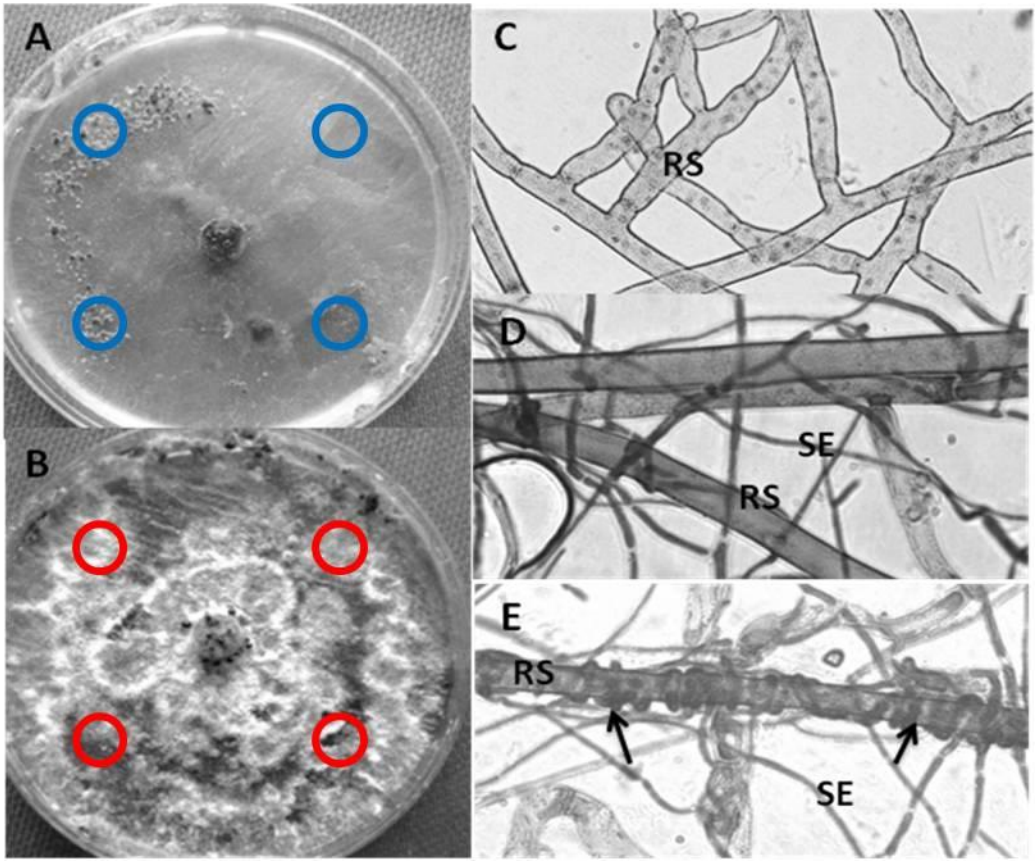


Figure 6.1. Mycoparasitism between *Stachybotrys elegans* and *Rhizoctonia solani* after 120 h of growth. Single cultures of *R. solani* hyphae (A) and co-cultures of *S. elegans* and *R. solani* (B). Microscope image of hyphae of *R. solani* monoculture (C). Microscope image of the interaction between *S. elegans* and *R. solani* (D, E). Arrows indicate the formation of infection pegs of *S. elegans* on *R. solani* hyphae. Sections were stained with lactophenol blue and viewed under a light microscope at 40X magnification. Circles indicate the location of the sampled plugs from single (A) and parasitized cultures of *R. solani* (B).

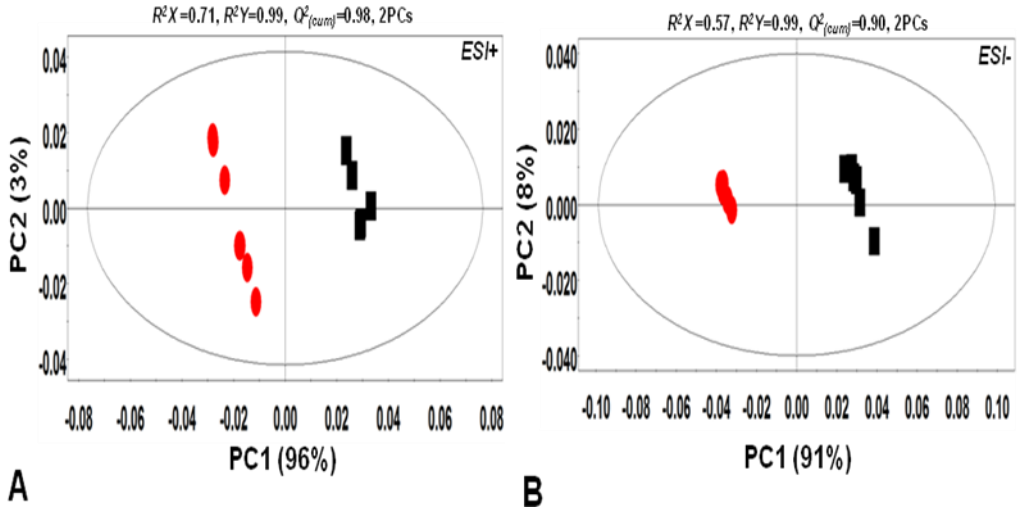


Figure 6.2 Partial least squares-discriminant analyses (PLS-DA) PC1/PC2 score plots of direct infusion Orbitrap MS metabolite profiles of *Rhizoctonia solani* (■) and *Rhizoctonia solani-Stachybotrys elegans* interaction (●) culture extracts, recorded in positive (ESI^+) and negative (ESI^-) electrospray modes (A and B) 120 h following inoculation. The ellipse represents the Hotelling T^2 with 95% confidence interval. Five (5) biological replications were performed per treatment [$Q^2_{(cum)}$; cumulative fraction of the total variation of the *X*'s that can be predicted by the extracted components, R^2X and R^2Y; the fraction of the sum of squares of all *X*'s and *Y*'s explained by the current component, respectively].

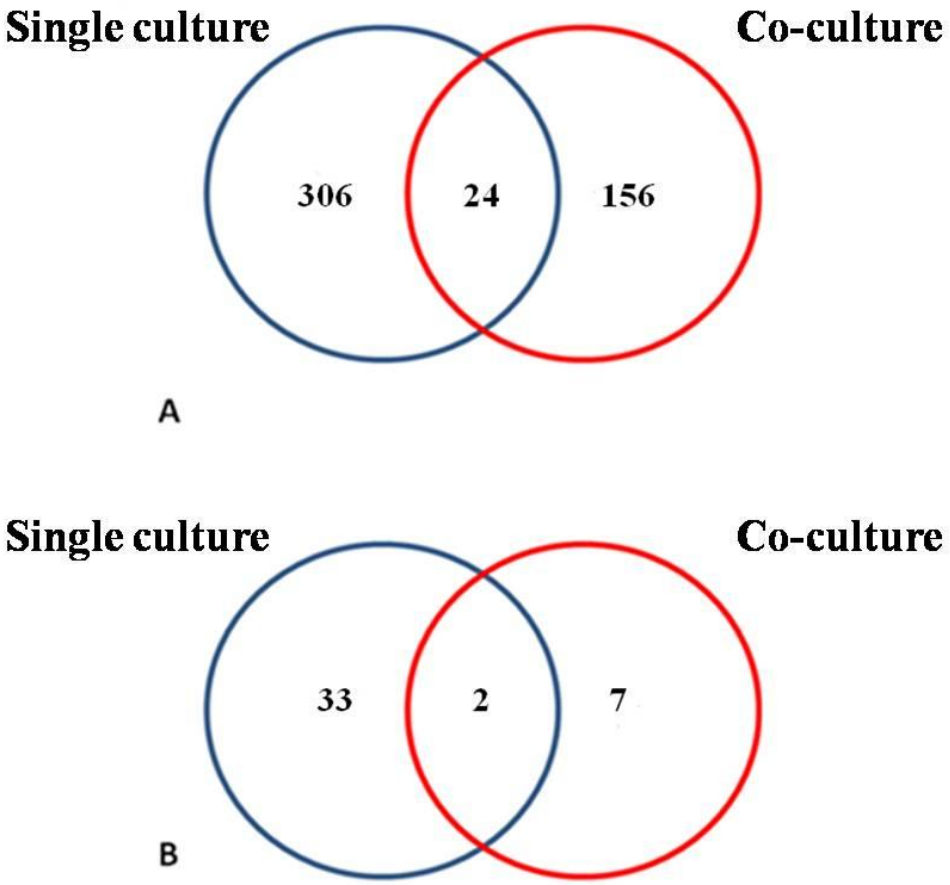


Figure 6.3. Venn diagram shows shared and unique metabolic features or biomarkers for *R. solani* single and co-cultures of *R. solani* and *S. elegans*. (A) Features detected in *R. solani* single culture (306). Features detected only during interaction of co-cultures (156). (B) Putatively identified features. Putatively identified metabolites in *R. solani* monoculture (33). Metabolites putatively identified during interaction of co-cultures (7).

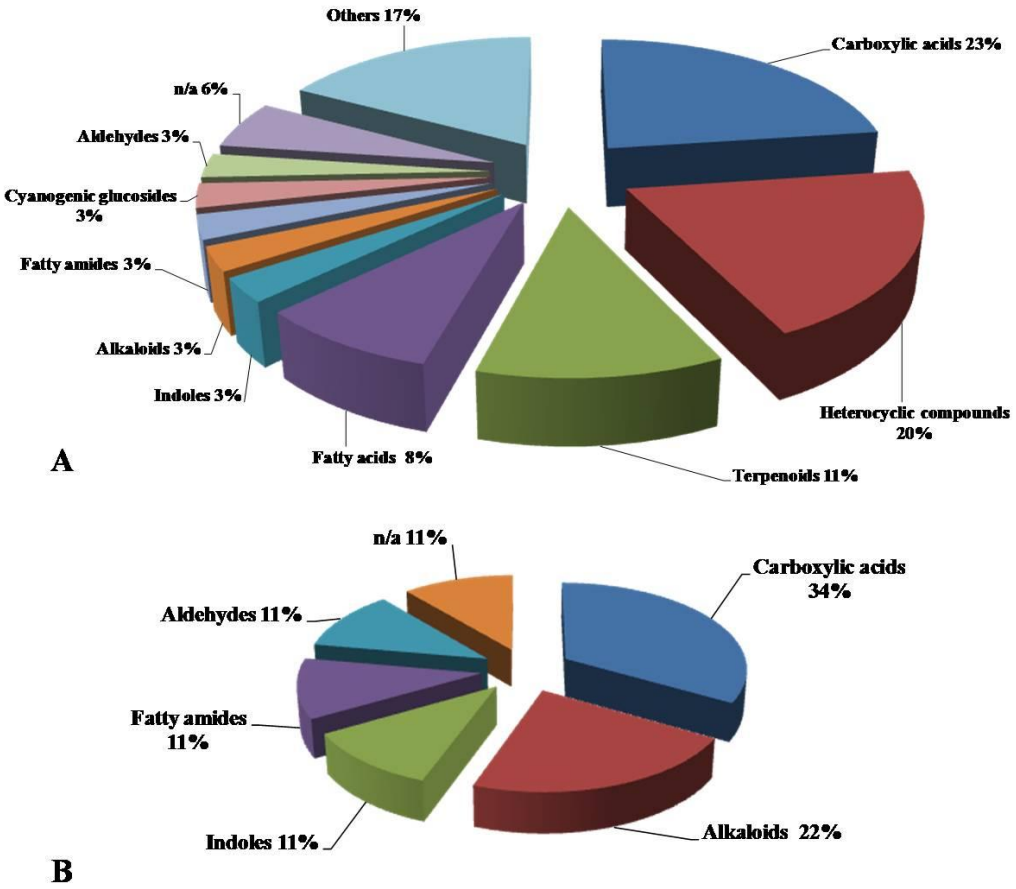


Figure 6.4. Percentages of chemical groups detected in *Rhizoctonia solani* single cultures (A) and co-cultures during the interaction between *Stachybotrys elegans* and *Rhizoctonia solani* (B) after 120 h of growth applying DI-MS analysis. n/a represents metabolites without the possibility of chemical group identification

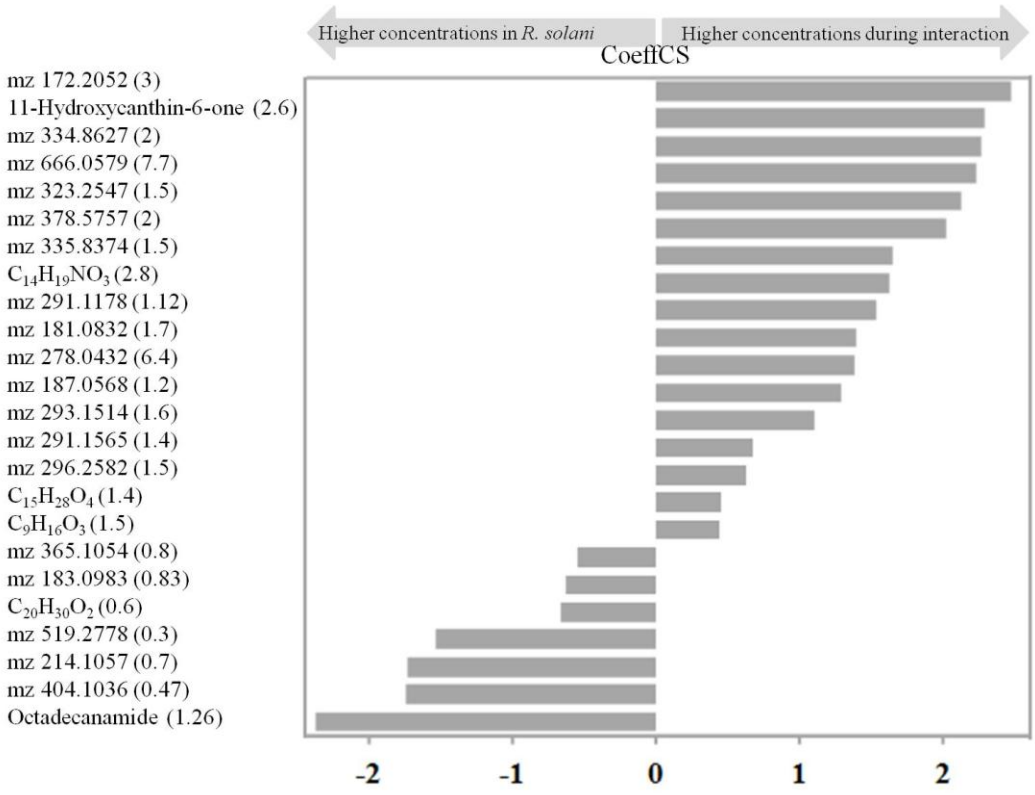


Figure 6.5. Partial least squares (PLS) coefficient plots for direct infusion mass spectrometry selected common metabolites in *R. solani* single cultures and during mycoparasitism in co-cultures with values of scaled and centered PLS regression coefficients (CoeffCS). Negative values of coefficients denote metabolites with higher concentration in *R. solani* single cultures whereas positive values correspond to those with higher concentration during mycoparasitism in co-cultures. Values between brackets correspond to fold change in the relative intensity of the corresponding compound between *R. solani* monoculture and mycoparasitism. Jack-knifed confidence intervals ($P < 0.05$).

6.5. DISCUSSION

In contrast to the great progress that has been reached in understanding and dissecting the metabolomes of plants, human and food, fungal metabolomics is still in its infancy. Although fungal cultures have been utilized for decades for the isolation of bioactive metabolites, only few studies focusing on the targeted metabolite profiling of fungal-fungal interaction have been published (Combès et al. 2012; Jonkers et al. 2012; Peiris et al. 2008). However, comprehensive non-targeted profiling of metabolites during fungal-fungal interaction is lacking. Among the main challenges for fungal metabolomics are the complexity of fungal secondary metabolites and the lack of comprehensive metabolite libraries, therefore the implementation and/or integration of powerful analyzers is required for the deconvolution of fungal metabolomes (Mashego et al. 2007; van der Werf et al. 2007).

Because of their high selectivity and sensitivity, mass spectrometry-based analyzers have a high potential for fungal metabolomics studies (El-Aneed et al. 2009). In the present study, and due to the superior accuracy and resolution (Villas-Bôas et al. 2005), direct infusion orbitrap mass spectrometry (DI-MS) was applied in an effort to dissect the undergoing biochemical changes during *Rhizoctonia solani*-*Stachybotrys elegans* mycoparasitic interaction. With comparable capabilities to LC-MS and a short analysis time, DI-MS represents an alternative to LC/MS for high-throughput metabolomics (Lin et al. 2010). Analyses can be completed in less than 1 min (typically below 5 min), features desirable for high-throughput screening studies without the need of chromatographic separation (Castrillo et al. 2003; Goodacre et al. 2002; Koulman et al. 2007; Smedsgaard and Frisvad 1996).

However, performing DI-MS on metabolites with identical molecular formulae cannot be distinguished due to the absence of chromatographic separation. Additionally, the complexity of the analyzed samples results in ion suppression which can hinder the ionization of low abundance ions leading to an incorrect assignment of metabolites as biomarkers (Annesley 2003; Lin et al. 2010). However, in the present study, the analysis of samples of similar chemical

composition is expected to produce similar ion suppression across the analyzed samples, therefore minimizing the effect of ion suppression during biomarker discovery.

Fungi are an important source of secondary metabolites with pronounced biological activities (Brakhage 2013). Among those, are metabolites that play key roles in fungal virulence and have evolved in the microorganisms to protect them in their ecological niches when they are exposed to a harsh environment with a diverse array of competing organisms (Calvo et al. 2002). Species of *Rhizoctonia* genus are known to produce bioactive compounds exhibiting antimicrobial (Arditti et al. 1972; Ma et al. 2004) or glycoprotein processing inhibitors (Elbein et al. 1981; Schneider et al. 1982). The pathogen *R. solani* produces phenylacetic acid and many of its derivatives that are reported to have phytotoxic activities (Iacobellis and DeVay 1987), and also polyaromatic material with melanin-like compounds found in its cell walls (Potgieter and Alexander 1966) that render the pathogen resistant against degradation, and also it produces glycoprotein processing inhibitors (Elbein et al. 1981; Schneider et al. 1982).

Given that microorganisms interact with each other in the natural environment and these interactions are, arguably, the driving force to produce necessary secondary metabolites, simulating microbial habitats by culturing two different microbial strains in one culture plate (i.e. co-culture) would seem to be an effective way to detect new molecules. Therefore we have under-taken this study with a two-fold aim. Firstly, to dissect the metabolome of the fungal pathogen *R. solani* when grown on culture plates, and compare its metabolic profile to that produced in co-cultures with the mycoparasite *S. elegans*. Secondly, to identify secondary metabolites or biomarkers which are induced during the interaction. In this context, biomarkers that were detected in *R. solani* but not during the mycoparasitic interaction could be attributed to the direct effect of the mycoparasite or because they are below the detection limit.

6.5.1. Biomarkers belonging to the carboxylic acids and terpenoids groups

Our study demonstrated that co-culturing of both fungal partners on MSMA resulted not only in a 1.5 fold increase in the percentage of the carboxylic acid group but in the appearance of new compounds. Indeed, several co-culturing experiments dealing with endophytic fungi have been reported, resulting in an increase in metabolite production including new compounds (Oh et al. 2007; Park et al. 2009). One possible explanation for such an increase could be attributed to the activity of cell wall degrading enzymes (CWDEs) by *S. elegans* (Archambault et al. 1998; Tweddell et al. 1995) releasing reducing sugars that are easily oxidized to yield carboxylic acids. Certainly, other examples of the activity of CWDEs by fungal antagonists and mycoparasites attest to the up-regulation of carboxylic acid as a result of oxidation of reducing sugars released from fungal cell walls (Inglis and Kawchuk 2002). Equally, the increase in carboxylic acid group during interaction could be related to the modification of another secondary metabolite group, the terpenoids which were not detected in co-cultures. It has been reported that terpenoids in fungi and bacteria undergo many chemical modifications (i.e. oxidation, reduction, glycosidation, alkylation, and acetylation) that will lead to the formation of carboxylic acids (Mikami 1988).

6.5.2. Biomarkers belonging to fatty acids (FAs) group

Among the chemical groups detected in *R. solani* single cultures that were absent during the mycoparasitic interaction are the fatty acids (FA), which are known as an essential component of fungal plasma membranes and can also serve as a nutrient source (Van Bogaert et al. 2011). In addition to these functions, FA can be modified by cytochrome P450 monooxygenases to produce secondary metabolites possessing antimicrobial activities (Liu et al. 2008; Van Bogaert et al. 2011). In this perspective, FA can either inhibit protein synthesis, or lead to cell death by altering the membrane fluidity and making the cells devoid of their internal structures (Pohl et al. 2011). The fact that the FA group was present in *R. solani* monoculture only leads us to believe that FAs metabolism and/or

production may be suppressed by the mycoparasite. In accordance with this notion, 2S-hydroxytetradecanoic acid, a metabolite reported to trigger hyphal growth (Nagahashi and Douds 2011), was not detected during the interaction but represented a significant proportion (45%) of the total fatty acids in *R. solani* monoculture.

6.5.3. Biomarkers belonging to alkaloids group

The presence of alkaloids in fungi has been mostly attributed to their biocidal activities in grass endophytes against insects and herbivores (Bush et al. 1997; Zhang et al. 2012). In our study, there was a general increase in the percentage of the alkaloids produced during interaction and detected in co-cultures compared to those detected in *R. solani* monoculture. One particular alkaloid that was commonly detected in *R. solani* single and co-cultures is the pathogen-derived alkaloid, 11-hydroxycanthin-6-one. As far as we are aware, this alkaloid has been isolated from plants (Ouyang et al. 1994) with no existing reports on its presence in fungi. Based on this finding, 11-hydroxycanthin-6-one can be considered a *de novo* produced metabolite. The antifungal property of canthin-6-one derivatives and analogues is well documented against filamentous fungi (Soriano-Agatón et al. 2005; Thouvenel et al. 2003). The fact that 11-hydroxycanthin-6-one is pathogen-derived and has accumulated during mycoparasitism is sufficient to assume that its production could be related to *R. solani* defense against *S. elegans*. How does 11-hydroxycanthin-6-one mediate its effect on *S. elegans* is unclear and requires further investigation. However it is tempting to speculate that its mode of action on *S. elegans* is related to fatty acid metabolism. It has been shown that canthin-6-one rapidly entered fungal cells and accumulated in lipid droplets with an increase in the levels of unsaturated fatty acids (Lagoutte et al. 2008).

Another alkaloid that was detected during interaction in co-cultures but whose origin was not established to belong to either fungal partner is camptothecin. Camptothecin, a plant alkaloid has been found to possess antifungal activity against many fungi causing root rots and leaf spots including *Pestalotia guepinii,*

Alternaria alternata and *Fusarium avenaceum* (Li et al. 2005; Rehman et al. 2008; Zhang et al. 2005). The mode of action is believed to target the intra-nuclear enzyme DNA topoisomerase I, which is involved in loosening DNA during its replication and transcription (Chandra 2012). The presence of camptothecin during the interaction could be related to the mycoparasitic activity of *S. elegans* against *R. solani* or could represent a defense reaction by the *R. solani* to limit the growth of the mycoparasite.

6.5.4. Biomarkers belonging to heterocyclic compounds and their implication in metabolism of *R. solani*

The detection of the heterocyclic compounds 4a-hydroxytetrahydrobiopterin and tetrahydrobiopterin (BH4), both intermediates in the folate biosynthetic pathway, in monocultures of *R. solani* only is an indication that the pathogen produces these metabolites for nutrient and energy acquisition. Folate has been reported to enhance the capacity for different metabolic processes in microorganisms leading to an increase in nutrient consumption (Shane and Stokstad 1975). Another heterocyclic compound detected in *R. solani* monoculture only and believed to be utilized as a nitrogen source by *R. solani* is purine xanthine. This metabolite is reported to be utilized for nutrient acquisition by *Penicillium chrysogenum* as a nitrogen source (Gupta 2011). Although the MSMA growth medium that we used is a carbon poor medium, it contains nitrogen sources that will help synthesizing metabolites with nitrogen moieties.

Interestingly, heterocyclic compounds were not detected during interaction of both fungi which could be attributed to the ability of *S. elegans* to block nutrients access for *R. solani* or that the fungal pathogen is implicating other metabolite groups in nutrient acquisition.

6.5.5. Biomarkers belonging to cyanogenic glucosides and indoles groups

The lack of a carbon source in the culture medium has led to the production of metabolites implicated in stress. Among those, is the presence of cyanogenic glucosides group represented by linamarin, a precursor for the production of hydrogen cyanide (HCN). HCN production in Basidiomycetes has been correlated with virulence and pathogenicity (Stevens and Strobel 1968). The fact that linamarin was absent during *S. elegans* colonization of *R. solani* lead us to speculate that the mycoparasite is able to detoxify HCN production by *R. solani*. HCN detoxification has been previously reported in fungi that are able to convert HCN into formamide through formamide hydrolyase (Fry and Evans 1977; Voisard et al. 1989).

Another metabolite that is produced under stressful conditions is the indole melatonin whose role as an antioxidant and free radical scavenger in organisms including fungi is well reported (Hardeland and Poeggeler 2003; Hardeland et al. 2006; Tamura et al. 2012).

To better understand the mechanism underlying the interaction between a mycoparasite and a fungal pathogen, we adopted a non-target metabolic profiling approach that, although challenging, led to the discovery of several putatively identified biomarkers produced during the interaction and when the pathogen is grown alone. The challenge was surmountable by the application of direct-infusion mass spectrometry along with online public metabolic databases and an in-house fungal library. The co-culturing set up involving the spraying of the mycoparasite over the host posed few challenges and made it difficult to assign the identified metabolites to their fungal origin. Future experiments should focus on the distribution of the metabolites, and the elucidation of metabolic pathways using stable isotopic labeling.

6.6. ACKNOWLEDGMENTS

This work was supported by a research grant to S. Jabaji from the Natural Sciences and Engineering Research Council of Canada (NSERC-Discovery).

CHAPTER 7

General Conclusions and Future Work

7.1. General Conclusions

The studies presented in this thesis represent an important contribution to understanding the mechanisms of attack and defense governing the process of mycoparasitism that takes place between a plant pathogen and a fungal mycoparasite. Chapters 3 to 6 of this thesis report on investigating the mycoparasitic relationship at the transcriptomic and metabolomic levels. It is hoped that this knowledge will lead to a better understanding of the mycoparasites' efficacy and use as biological control agents.

In Chapter 3, we studied the differential transcript abundance of mycoparasitism-induced genes and host-response genes during in vivo interactions between the mycoparasite *S. elegans* and hyphae and sclerotia of the host *R. solani* over an extended period of mycoparasitism. We presented evidence that parasitized hyphal and sclerotial structures by the mycoparasite triggered different expression patterns of host-response and mycoparasitism-induced genes, indicating that some of these genes play an important role during the mycoparasitic process and host defense, respectively. Furthermore, these results lead us to believe that multiple regulatory mechanisms might be involved. The induction of oxidoreductase and several encoding genes involved in toxin production in the mycoparasite during interaction with the host cells was correlated with excessive coiling, peg-like formation and heavy colonization of host structures. The over-expression of these genes strengthens our assumption that they could be related to detoxifying compounds emitted from the host that could affect *S. elegans* in a dreadful way. Hosts are also known to exhibit some sort of a defense reaction such as the formation of vitamin B6 or derivatives that are known to act as antioxidants and quenchers of reactive oxygen species. In this context, we provided evidence that pryidoxal reductase, a gene encoding an upstream enzyme in vitamin B6 biosynthesis was highly induced in hyphae and

sclerotia of *R. solani* during mycoparasitism. This finding can serve as basis for broader exploitation of *R. solani* behavior and response during mycoparasitism.

Signal transduction via MAPK modules is among other processes involved in the parasitic interaction. In Chapter 4, we concentrated our efforts on the importance of signal transduction during cross talk between the host and the mycoparasite. Established knowledge on the role of signaling pathways in the mycoparasitism process led us to fully clone and characterize *smkA*, the first mitogen-activated protein kinase (MAPK) in *S. elegans* and monitor its expression and the abundance of the phosphorylated MAP kinase (ERK1/2) under different stress conditions (i.e., mycoparasitism and starvation). Applying a phospho-proteomic approach, we identified one phosphopeptide with a TXY motif, a signature of MAPK proteins, which was activated during mycoparasitism and in response to nutrient starvation. We also provided evidence that *smkA* is phylogenetically related to the MAPK subcategory (ERK1/2) and constitutes a small multi-gene family. The fact that differential expression of *smkA* in *S. elegans* is influenced by the type of stress led us to believe that *smkA* might be implicated in multifunction pathways.

In Chapter 5, we aimed for the construction of disruptants that will help in elucidating *smkA* functional role in mycoparasitism and growth and how the mycoparasite perceives different cues from its environment. An over-expressing (pSMKA) and silencing (pSMKAi) plasmids were constructed in order to study the impact of over-expressing and down-regulating *smkA* on the mycoparasitic efficacy of *S. elegans.* Both plasmids were designed so that the *smkA* insert would be driven by constitutive promoters. Two transformation methods (polyethylene glycol and *Agrobacterium tumefaciens*) were used, but were unsuccessful for the production of transformants. Possible factors such as osmotic stabilizers, digesting enzymes, conidia:bacteria ratio, and amendment of acetosyringone in the pre-culture step that require optimization in future experiments are discussed.

The aim of Chapter 6 is to elucidate key biochemical mechanisms that regulate the mycoparasitic process via the in-depth profiling of metabolites that are host and pathogen derived. Platforms such as LTQ Orbitrap MS allowed the

wide coverage of potential metabolites in positive and negative ionization modes. Putative metabolite biomarkers were identified through searches against public databases (KEGG, YMDB, PlantCyc, LIPID MAPS, KNApSAcK), and an in-house built library of 409 fungal metabolites and MS/MS spectra whenever available. Several compounds belonging to different chemical groups were detected in monocultures of *R. solani*. Carboxylic acids, heterocyclic compounds, terpenoids, fatty acids, and indoles were the predominant ones. While some of these groups did not appear during the interaction, carboxylic acids and indoles relative levels remained the highest, highlighting their importance and role during mycoparasitism. The number of chemical groups and metabolites detected during the interaction was significantly less than those found in *R. solani* monocultures, highlighting the possible suppressive role of the mycoparasite. During interaction between *S. elegans* and *R. solani,* the relative levels of the alkaloid camptothecin and the fungal pathogen derived indole, 11-hydroxycanthin-6-one significantly increased. The latter finding presents evidence of a defense reaction by fungal pathogen against the mycoparasite *S. elegans*.

In conclusion, the findings of this thesis will lay the foundation for innovative knowledge-based approaches for long-term objectives including plant disease management strategies. The discovery of biomarkers (Chapter 6) is expected to have an impact on the field of biological control and enable us to develop novel strategies to enhance plant disease tolerance. The knowledge on high-throughput metabolomics combined with biometrics and integrated with other 'omics' approaches will provide solid expertise for application to metabolite discovery and network construction. Collectively, such knowledge could be exploited in research dealing with biotechnology such as genetic engineering and/or biomarker-assisted plant breeding.

7.2. Future Work

Future work should target the following ideas:

1. Information is lacking on how pathogens respond to attack and what mechanisms dominate to counteract mycoparasitism. Understanding the pathogen's reaction mechanisms provides an innovative approach to improving the durability of biologically based disease control strategies. Therefore, an in-depth exploration of *R. solani* genetic regulation during mycoparasitism is required.
2. Generation of transgenic lines of *S. elegans* over-expressing and silencing *smkA* to study the function, role and the contribution of this signal transduction gene under different stresses. This will be accompanied by a thorough study investigating the impact of these transformations on several downstream pathways (secretion of CWDEs, transcript abundance control) and on other "omics" (proteomics and metabolomics) fields.
3. Since a large part of fungal metabolomes, especially the primary metabolites, are common in fungi, the origin of detected metabolites is a challenging task during fungal-fungal interactions. This obstacle can be overcome by stable isotope-labeling which is essential to differentiate between fungal metabolites belonging to each organism and also for metabolic network analysis.
4. Integration of multiple layers of information, i.e. the multi-'omics' approach, is required to acquire a holistic view of the mycoparasitism process.

REFERENCES

Abdel-Farid, I., M. Jahangir, C. van den Hondel, H. Kim, Y. Choi and R. Verpoorte. 2009. Fungal infection-induced metabolites in *Brassica rapa*. Plant Sci. 176: 608-615.

Abdulnour, R.-E.E., X. Peng, J.H. Finigan, E.J. Han, E.J. Hasan, K.G. Birukov, S.P. Reddy, J.E. Watkins, U.S. Kayyali and J.G. Garcia. 2006. Mechanical stress activates xanthine oxidoreductase through MAP kinase-dependent pathways. Am. J. Physiol. Lung Cell. Mol. Physiol. 291: 345-353.

Adams, P.B. 1990. The potential of mycoparasites for biological control of plant diseases. Annu. Rev. Phytopathol. 28: 59-72.

Adejumo, T.O. 2005. Crop protection strategies for major diseases of cocoa, coffee and cashew in Nigeria. Afr. J. Biotechnol. 4: 143-150.

Akella, R., T.M. Moon and E.J. Goldsmith. 2008. Unique MAP kinase binding sites. Biochim. Biophys. Acta. 1784: 48-55.

Aliferis, K. and S. Jabaji. 2010. ^{1}H NMR and GC-MS metabolic fingerprinting of developmental stages of *Rhizoctonia solani* sclerotia. Metabolomics 6: 96-108.

Aliferis, K.A. and S. Jabaji. 2010. Metabolite composition and bioactivity of *Rhizoctonia solani* sclerotial exudates. J. Agric. Food Chem. 58: 7604-7615.

Aliferis, K.A. and S. Jabaji. 2012. FT-ICR/MS and GC-EI/MS metabolomics networking unravels global potato sprout's responses to *Rhizoctonia solani* infection. PLoS One 7: e42576.

Allwood, J.W., D.I. Ellis and R. Goodacre. 2008. Metabolomic technologies and their application to the study of plants and plant–host interactions. Physiol. Plantarum 132: 117-135.

Allwood, J.W., J. Heald, A.J. Lloyd, R. Goodacre and L.A. Mur. 2012. Separating the inseparable: the metabolomic analysis of plant-pathogen interactions. Method. Mol. Biol. 860: 31-49.

Amin, F., V. Razdan, K. Bhat and S. Banday. 2010. Potential of *Trichoderma* species as biocontrol agents of soil borne fungal propagules. J. Phytol. 2: 38-41.

Andrews, D.L., J.D. Egan, M.E. Mayorga and S.E. Gold. 2000. The *Ustilago maydis ubc4* and *ubc5* genes encode members of a MAP kinase cascade required for filamentous growth. MPMI 13: 781-786.

Anitha, R. and K. Murugesan. 2005. Production of gliotoxin on natural substrates by *Trichoderma virens*. J. Basic. Microbiol. 45: 12-19.

Annesley, T.M. 2003. Ion suppression in mass spectrometry. Clin. Chem. 49: 1041-1044.

Archambault, C., G. Coloccia, S. Kermasha and S.H. Jabaji-Hare. 1998. Characterization of an endo-1,3-*β*-D-glucanase produced during the interaction between the mycoparasite *Stachybotrys elegans* and its host *Rhizoctonia solani*. Can. J. Microbiol. 44: 989-997.

Arditti, J., R.E.M. Fisch and B. Flick. 1972. Ergosterol peroxide from *Rhizoctonia repens*: composition, conformation, and origin. J. Chem. Soc., Chem. Commun. 22: 1217-1218.

Baek, J.M., C.R. Howell and C.M. Kenerley. 1999. The role of extracellular chitinase from *Trichoderma virens* Gv29-8 in the biocontrol of *Rhizoctonia solani*. Curr. Genet. 35: 41-50.

Bains, P., H. Bennypaul, D. Lynch, L. Kawchuk and r.C. Schaupmete. 2002. *Rhizoctonia* disease of potatoes (*Rhizoctonia solani*): fungicide efficacy and cultivar susceptibility. Am. J. Potato Res. 79: 99-106.

Balasubramanian, N., G.A. Juliet, P. Srikalaivani and D. Lalithakumari. 2003. Release and regeneration of protoplasts from the fungus *Trichothecium roseum*. Can. J. Microbiol. 49: 263-268.

Bangera, M.G. and L.S. Thomashow. 1999. Identification and characterization of a gene cluster for synthesis of the polyketide antibiotic 2,4-diacetylphloroglucinol from *Pseudomonas fluorescens* Q2-87. J. Bacteriol. 181: 3155-3163.

Banuett, F. 1998. Signalling in the yeasts: an informational cascade with links to the filamentous fungi. Microbiol. Mol. Biol. Rev. 62: 249-274.

Bell, A.A. and M.H. Wheeler. 1986. Biosynthesis and functions of fungal melanins. Annu. Rev. Phytopathol. 24: 411-451.

Benabdellah, K., C. Azcon-Aguilar, A. Valderas, D. Speziga, T.B. Fitzpatrick and N. Ferrol. 2009. *GintPDX1* encodes a protein involved in vitamin B6 biosynthesis that is up-regulated by oxidative stress in the arbuscular mycorrhizal fungus *Glomus intraradices*. New Phytol. 184: 682-693.

Benyagoub, M., S.H. Jabaji-Hare, G. Banville and P.M. Charest. 1994. *Stachybotrys elegans*: a destructive mycoparasite of *Rhizoctonia solani*. Mycol. Res. 98: 493-505.

Benyagoub, M., S.H. Jabaji-Hare, H. Chamberland and P.M. Charest. 1996. Cytochemical and immunocytochemical investigation of the mycoparsitic interaction between *Stachybotrys elegans* and its host *Rhizoctonia solani* (AG-3). Mycol. Res. 100: 79-86.

Berg, G. 2009. Plant-microbe interactions promoting plant growth and health: perspectives for controlled use of microorganisms in agriculture. Appl. Microbiol. Biotechnol. 84: 11-18.

Beri, R.K. and G. Turner. 1987. Transformation of *Penicillium chrysogenum* using the *Aspergillus nidulans amds* gene as a dominant selective marker. Curr. Genet. 11: 639-641.

Bertagnolli, B.L., S. Daly and J.B. Sinclair. 1998. Antimycotic compounds from the plant pathogen *Rhizoctonia solani* and its antagonist *Trichoderma harzianum*. J. Phytopathol. 146: 131-135.

Bhatnagar, D., K. Ehrlich and T. Cleveland. 2003. Molecular genetic analysis and regulation of aflatoxin biosynthesis. Appl. Microbiol. Biotechnol. 61: 83-93.

Bilski, P., M. Li, M. Ehrenshaft, M. Daub and C. Chignell. 2000. Vitamin B6 (pyridoxine) and its derivatives are efficient singlet oxygen quenchers and potential fungal antioxidants. Photochem. Photobiol. 71: 129-134.

Bloom, E., K. Bal, E. Nyman, A. Must and L. Larsson. 2007. Mass spectrometry-based strategy for direct detection and quantification of some mycotoxins

produced by *Stachybotrys* and *Aspergillus* spp. in indoor environments. Appl. Environ. Microbiol. 73: 4211-4217.

Bolker, M. 1998. Sex and crime: heterotrimeric G proteins in fungal mating and pathogenesis. Fungal Genet. Biol. 25: 143-156.

Brakhage, A.A. 2013. Regulation of fungal secondary metabolism. Nat. Rev. Microbiol. 11: 21-32.

Brakhage, A.A. and V. Schroeckh. 2011. Fungal secondary metabolites - strategies to activate silent gene clusters. Fungal Genet. Biol. 48: 15-22.

Brand, T. and B.W. Alsanius. 2004. Induction and impact of cell wall degrading enzymes in nutrient solution of closed hydroponic systems. J. Phytopathol. 152: 313-319.

Brian, P.W. and H.G. Hemming. 1945. Gliotoxin, a fungistatic metabolic product of *Trichoderma viride*. Ann. Appl. Biol. 32: 214-220.

Bush, L.P., H.H. Wilkinson and C.L. Schardl. 1997. Bioprotective alkaloids of grass-fungal endophyte symbioses. Plant. Physiol. 114: 1-7.

Calvo, A.M., R.A. Wilson, J.W. Bok and N.P. Keller. 2002. Relationship between secondary metabolism and fungal development. Microbiol. Mol. Biol. Rev. 66: 447-459.

Carpenter, M.A., A. Stewart and H.J. Ridgway. 2005. Identification of novel *Trichoderma hamatum* genes expressed during mycoparasitism using subtractive hybridisation. FEMS Microbiol. Lett. 251: 105-112.

Castrillo, J.I., A. Hayes, S. Mohammed, S.J. Gaskell and S.G. Oliver. 2003. An optimized protocol for metabolome analysis in yeast using direct infusion electrospray mass spectrometry. Phytochemistry 62: 929-937.

Catalano, V., M. Vergara, J.R. Hauzenberger, B. Seiboth, S. Sarrocco, G. Vannacci, C.P. Kubicek and V. Seidl-Seiboth. 2011. Use of a non-homologous end-joining-deficient strain (delta-*ku70*) of the biocontrol fungus *Trichoderma virens* to investigate the function of the laccase gene *lcc1* in sclerotia degradation. Curr. Genet. 57: 13-23.

Chamoun, R., K. Aliferis and S. Jabaji. 2013. Characterization and transcriptional regulation of *Stachybotrys elegans* mitogen-activated-protein kinase gene

smkA following mycoparasitism and starvation conditions. Curr. Genet. 59: 43-54.

Chamoun, R. and S. Jabaji. 2011. Expression of genes of *Rhizoctonia solani* and the biocontrol *Stachybotrys elegans* during mycoparasitism of hyphae and sclerotia. Mycologia 103: 483-493.

Chandra, S. 2012. Endophytic fungi: novel sources of anticancer lead molecules. Appl. Microbiol. Biotechnol. 95: 47-59.

Chang, S.S., Z. Zhang and Y. Liu. 2012. RNA interference pathways in fungi: Mechanisms and Functions. Annu. Rev. Microbiol. 66: 305-323.

Chang, Y.C., R. Baker, O. Kleifeld and I. Chet. 1986. Increased growth of plants in the presence of the biological control agent *Trichoderma harzianum*. Plant Dis. 70: 145-148.

Chatterjee, A., C.T. Jurgenson, F.C. Schroeder, S.E. Ealick and T.P. Begley. 2006. Thiamin biosynthesis in eukaryotes: Characterization of the enzyme-bound product of thiazole synthase from *Saccharomyces cerevisiae* and its implications in thiazole biosynthesis. J. Am. Chem. Soc. 128: 7158-7159.

Chaveroche, M.K., J.M. Ghigo and C. D'Enfert. 2000. A rapid method for efficient gene replacement in the filamentous fungus *Aspergillus nidulans*. Nucleic Acids Res. 28: E97.

Chaves Barreto, C., L. Cardoso Alves, F.J. Lima Aragão, E. Rech, A. Schrank and M. Henning Vainstein. 2006. High frequency gene transfer by microprojectile bombardment of intact conidia from the entomopathogenic fungus *Paecilomyces fumosoroseus*. FEMS Microbiol. Lett. 156: 95-99.

Cherkasova, V., D.M. Lyons and E.A. Elion. 1999. Fus3p and Kss1p control G1 arrest in *Saccharomyces cerevisiae* through a balance of distinct arrest and proliferative functions that operate in parallel with Far1p. Genetics 151: 989-1004.

Chet, I. and J. Inbar. 1994. Biological control of fungal pathogens. Appl. Biochem. Biotechnol. 48: 37-43.

Chiu, B.C.H., D.D. Weisenburger, S.H. Zahm, K.P. Cantor, S.M. Gapstur, F. Holmes, L.F. Burmeister and A. Blair. 2004. Agricultural pesticide use,

familial cancer, and risk of non-Hodgkin lymphoma. Cancer Epidem. Biomar. 13: 525-531.

Cho, Y., R.A. Cramer, K.H. Kim, J. Davis, T.K. Mitchell, P. Figuli, B.M. Pryor, E. Lemasters and C.B. Lawrence. 2007. The *Fus3/Kss1* MAP kinase homolog *Amk1* regulates the expression of genes encoding hydrolytic enzymes in *Alternaria brassicicola*. Fungal Genet. Biol. 44: 543-553.

Chuang, S.M., I.C. Wang and J.L. Yang. 2000. Roles of JNK, p38 and ERK mitogen-activated protein kinases in the growth inhibition and apoptosis induced by cadmium. Carcinogenesis 21: 1423-1432.

Clapham, D. and E. Neer. 1993. New Roles for G-protein βγ-dimer in transmembrane signalling Nature 365: 403-406.

Cogoni, C. and G. Macino. 1999. Gene silencing in *Neurospora crassa* requires a protein homologous to RNA-dependent RNA polymerase. Nature 399: 166-169.

Coley-Smith, J. and R. Cooke. 1971. Survival and germination of fungal sclerotia. Annu. Rev. Phytopathol. 9: 65-92.

Collopy, P.D., R.C. Amey, M.J. Sergeant, M.P. Challen, P.R. Mills, G.D. Foster and A.M. Bailey. 2010. The *pmk*1-like mitogen-activated protein kinase from *Lecanicillium* (*Verticillium*) *fungicola* is not required for virulence on *Agaricus bisporus*. Microbiology 156: 1439-1447.

Colot, H.V., G. Park, G.E. Turner, C. Ringelberg, C.M. Crew, L. Litvinkova, R.L. Weiss, K.A. Borkovich and J.C. Dunlap. 2006. A high-throughput gene knockout procedure for *Neurospora* reveals functions for multiple transcription factors. PNAS 103: 10352-10357.

Combès, A., I. Ndoye, C. Bance, J. Bruzaud, C. Djediat, J. Dupont, B. Nay and S. Prado. 2012. Chemical communication between the endophytic fungus *Paraconiothyrium variabile* and the phytopathogen *Fusarium oxysporum*. PLoS One 7: e47313.

Cook, J.G., L. Bardwell, S.J. Kron and J. Thorner. 1996. Two novel targets of the MAP kinase Kss1 are negative regulators of invasive growth in the yeast *Saccharomyces cerevisiae*. Genes Dev. 10: 2831-2848.

Covert, S.F., P. Kapoor, M. Lee, A. Briley and C.J. Nairn. 2001. *Agrobacterium tumefaciens*-mediated transformation of *Fusarium circinatum*. Mycol. Res. 105: 259-264.

Cubeta, M.A., R. Vilgalys and D. Gonzalez. 1996. Molecular analysis of ribosomal RNA genes in *Rhizoctonia* fungi. Rhizoctonia Species: Taxonomy, Molecular Biology, Ecology, Pathology and Disease Control 578: 81-86.

Cundliffe, E. and J.E. Davies. 1977. Inhibition of initiation, elongation, and termination of eukaryotic protein synthesis by trichothecene fungal toxins. Antimicrob. Agents Ch. 11: 491-499.

D'Souza, C.A. and J. Heitman. 2001. Conserved cAMP signaling cascades regulate fungal development and virulence. FEMS Microbiol. Rev. 25: 349-364.

De Boer, W., P. Verheggen, P.J.A.K. Gunnewiek, G.A. Kowalchuk and J.A. van Veen. 2003. Microbial community composition affects soil fungistasis. Appl. Environ. Microbiol. 69: 835-844.

de Groot, M.J., P. Bundock, P.J. Hooykaas and A.G. Beijersbergen. 1998. *Agrobacterium tumefaciens*-mediated transformation of filamentous fungi. Nat. Biotechnol. 16: 839-842.

de la Cruz, J., J.A. Pintor-Toro, T. Benitez, A. Llobell and L.C. Romero. 1995. A novel endo-beta-1,3-glucanase, BGN13.1, involved in the mycoparasitism of *Trichoderma harzianum*. J. Bacteriol. 177: 6937-6945.

Degenkolb, T., H. Von Dohren, K.F. Nielsen, G.J. Samuels and H. Bruckner. 2008. Recent advances and future prospects in peptaibiotics, hydrophobin, and mycotoxin research, and their importance for chemotaxonomy of *Trichoderma* and *Hypocrea*. Chem. Biodivers. 5: 671-680.

Denoth, M., L. Frid and J.H. Myers. 2002. Multiple agents in biological control: improving the odds? Biol. Control 24: 20-30.

Denslow, S.A., A.A. Walls and M.E. Daub. 2005. Regulation of biosynthetic genes and antioxidant properties of vitamin B6/vitamers during plant defense responses. Physiol. Mol. Plant Pathol. 66: 244-255.

DeRisi, J.L., V.R. Iyer and P.O. Brown. 1997. Exploring the metabolic and genetic control of gene expression on a genomic scale. Science 278: 680-686.

Dettmer, K., P.A. Aronov and B.D. Hammock. 2007. Mass spectrometry-based metabolomics. Mass Spectrom. Rev. 26: 51-78.

Di Pietro, A., F.I. García Maceira, E. Meglecz and M.I.G. Roncero. 2001. A MAP kinase of the vascular wilt fungus *Fusarium oxysporum* is essential for root penetration and pathogenesis. Mol. Microbiol. 39: 1140-1152.

Dickman, M.B. and O. Yarden. 1999. Serine/threonine protein kinases and phosphatases in filamentious fungi. Fungal Genet. Biol. 26: 99-117.

Djonovic, S., M.J. Pozo and C.M. Kenerley. 2006. Tvbgn3, a β-1,6-Glucanase from the biocontrol fungus *Trichoderma virens*, is involved in mycoparasitism and control of *Pythium ultimum*. Appl. Environ. Microbiol. 72: 7661-7670.

Djulic, A., A. Schmid, H. Lenz, P. Sharma, C. Koch, S.G.R. Wirsel and R.T. Voegele. 2011. Transient transformation of the obligate biotrophic rust fungus *Uromyces fabae* using biolistics. Fungal Biol. 115: 633-642.

Duffy, B., A. Schouten and J.M. Raaijmakers. 2003. Pathogen self-defense: mechanisms to counteract microbial antagonism. Annu. Rev. Phytopathol. 41: 501-538.

Dutton, M.V. and C.S. Evans. 1996. Oxalate production by fungi: its role in pathogenicity and ecology in the soil environment. Can. J. Microbiol. 42: 881-895.

Efron, B. and G. Gong. 1983. A leisurely look at the bootstrap, the jackknife, and cross-validation. Am. Stat. 37: 36-48.

Ehrlich, K.C., B.G. Montalbano and J.W. Cary. 1999. Binding of the C6-zinc cluster protein, AFLR, to the promoters of aflatoxin pathway biosynthesis genes in *Aspergillus parasiticus*. Gene 230: 249-257.

El-Aneed, A., A. Cohen and J. Banoub. 2009. Mass spectrometry, review of the basics: Electrospray, MALDI, and commonly used mass analyzers. Appl. Spectrosc. Rev. 44: 210-230.

Elbein, A.D., R. Solf, P.R. Dorling and K. Vosbeck. 1981. Swainsonine: an inhibitor of glycoprotein processing. Proc. Natl. Acad. Sci. USA 78: 7393-7397.

Engel, L.S., D.A. Hill, J.A. Hoppin, J.H. Lubin, C.F. Lynch, J. Pierce, C. Samanic, D.P. Sandler, A. Blair and M.C. Alavanja. 2005. Pesticide use and breast cancer risk among farmers' wives in the Agricultural Health Study. Am. J. Epidemiol. 161: 121-135.

Errampalli, D. and H.W. Johnston. 2001. Control of tuber-borne black scurf [*Rhizoctonia solani*] and common scab [*Streptomyces scabies*] of potatoes with a combination of sodium hypochlorite and thiophanate-methyl preplanting seed tuber treatment. Can. J. Plant. Pathol. 23: 68-77.

Finking, R. and M.A. Marahiel. 2004. Biosynthesis of nonribosomal peptides. Annu. Rev. Microbiol. 58: 453-488.

Flores, A., I. Chet and A. Herrera-Estrella. 1997. Improved biocontrol activity of *Trichoderma harzianum* by over-expression of the proteinase-encoding gene *prb1*. Curr. Genet. 31: 30-37.

Fravel, D.R. 1988. Role of antibiosis in the biocontrol of plant diseases. Annu. Rev. Phytopathol. 26: 75-91.

Frisvad, J.C., B. Andersen and U. Thrane. 2008. The use of secondary metabolite profiling in chemotaxonomy of filamentous fungi. Mycol. Res. 112: 231-240.

Frisvad, J.C., J. Smedsgaard, R.A. Samson, T.O. Larsen and U. Thrane. 2007. Fumonisin B2 production by *Aspergillus niger*. J. Agric. Food Chem. 55: 9727-9732.

Fry, W.E. and P.H. Evans. 1977. Association of formamide hydro-lyase with fungal pathogenicity to cyanogenic plants. Phytopathology 67: 1001-1006.

Gao, F.K., C.C. Dai and X.Z. Liu. 2010. Mechanisms of fungal endophytes in plant protection against pathogens. Afr. J. Microbiol. Res. 4: 1346-1351.

Gao, S.G., F.H. Zhou, T. Liu, Y.Y. Li and J. Chen. 2012. A MAP kinase gene, *Clk1*, is required for conidiation and pathogenicity in the phytopathogenic fungus *Curvularia lunata*. J. Basic Microbiol. 52: 1-10.

Garcia, I., J.M. Lora, J. de la Cruz, T. Benitez, A. Llobell and J.A. Pintor-Toro. 1994. Cloning and characterization of a chitinase (CHIT 42) cDNA from the mycoparasitic fungus *Trichoderma harzianum*. Curr. Genet. 27: 83-89.

Gardes, M. and T. Bruns. 1993. ITS primers with enhanced specificity for basidiomycetes-application to the identification of mycorrhizae and rusts. Mol. Ecol. 2: 113-118.

Gardiner, D.M., K. Kazan and J.M. Manners. 2009. Novel genes of *Fusarium graminearum* that negatively regulate deoxynivalenol production and virulence. MPMI 22: 1588-1600.

Gartner, A., K. Nasmyth and G. Ammerer. 1992. Signal transduction in *Saccharomyces cerevisiae* requires tyrosine and threonine phosphorylation of FUS3 and KSS1. Genes Dev. 6: 1280-1292.

Georgiou, C.D., N. Tairis and A. Sotiropoulou. 2000. Hydroxyl radical scavengers inhibit sclerotial differentiation and growth in *Sclerotinia sclerotiorum* and *Rhizoctonia solani*. Mycol. Res. 104: 1191-1196.

Gerhardson, B. 2002. Biological substitutes for pesticides. Trends Biotechnol. 20: 338-343.

Gershater, M.C. and R. Edwards. 2007. Regulating biological activity in plants with carboxylesterases. Plant Sci. 173: 579-588.

Gheinani, A.H., N.H. Jahromi, E. Feuk-Lagerstedt and M.J. Taherzadeh. 2011. RNA silencing of lactate dehydrogenase gene in *Rhizopus oryzae*. J. RNAi Gene Silencing 7: 443-448.

Gilman, A. 1984. G Proteins and dual control of adenylate cyclase. Cell 36: 577-579.

Glass, N.L. and G.C. Donaldson. 1995. Development of primer sets designed for use with the PCR to amplify conserved genes from filamentous Ascomycetes. Appl. Environ. Microbiol. 61: 1323-1330.

Gleave, A.P. 1992. A versatile binary vector system with a T-DNA organizational-structure conducive to efficient integration of cloned DNA into the plant genome. Plant Mol. Biol. 20: 1203-1207.

Goodacre, R., S. Vaidyanathan, G. Bianchi and D.B. Kell. 2002. Metabolic profiling using direct infusion electrospray ionisation mass spectrometry for the characterisation of olive oils. Analyst 127: 1457-1462.

Goulard, C., S. Hlimi, S. Rebuffat and B. Bodo. 1995. Trichorzins HA and MA, antibiotic peptides from *Trichoderma harzianum*. I. Fermentation, isolation and biological properties. J. Antibiot. 48: 1248-1253.

Gramss, G. 2010. The universe of basidiomycetous ground fungi. Current research, technology and education topics in applied microbiology and microbial biotechnology. A. Méndez-vilas (Ed). © Formatex

Gronover, C.S., D. Kasulke, P. Tudzynski and B. Tudzynski. 2001. The role of G protein alpha subunits in the infection process of the gray mold fungus *Botrytis cinerea*. MPMI 14: 1293-1302.

Grosh, R., F. Faltin, J. Lottmann, A. Kofoet and G. Berg. 2005. Effectiveness of 3 antagonistic isolates to control *Rhizoctonia solani* Kuhn on lettuce and potato. Can. J. Microbiol. 51: 345-353.

Guengerich, F.P. 2001. Common and uncommon cytochrome P450 reactions related to metabolism and chemical toxicity. Chem. Res. Toxicol. 14: 611-650.

Guo, J., X. Dai, J.R. Xu, Y. Wang, P. Bai, F. Liu, Y. Duan, H. Zhang, L. Huang and Z. Kang. 2011. Molecular characterization of a Fus3/Kss1 type MAPK from *Puccinia striiformis* f. sp. *tritici*, PsMAPK1. PLoS One: e21895.

Gupta, A. and S. Saxena. 2011. Screeing of endophytic fungi for xanthine oxidase producer(s). Master of Science in Biotechnology. Thapar University. Patiala-India.

Ha, T.N. 2010. Using *Trichoderma* species for biological control of plant pathogens in Vietnam. J. ISSAAS 16: 17-21.

Hammerschmidt, R. 1999. Induced disease resistance: how do induced plants stop pathogens? Physiol. Mol. Plant Pathol. 55: 77-84.

Hao, J.J., C. Geng, W. Xie, Z. Gong, W.Y. Liu and E. Wang. 1999. Isolation and characterization of viridin, a new 65 kDa antifungal protein from the mould *Trichoderma viride*. Biol. Chem. 380: 1243-1245.

Hardeland, R., S.R. Pandi-Perumal and D.P. Cardinali. 2006. Melatonin. Int. J. Biochem. Cell Biol. 38: 313-316.

Hardeland, R. and B. Poeggeler. 2003. Non-vertebrate melatonin. J. Pineal Res. 34: 233-241.

Harman, G.E., C.R. Howell, A. Viterbo, I. Chet and M. Lorito. 2004. *Trichoderma* species-opportunistic, avirulent plant symbionts. Nat. Rev. Microbiol. 2: 43-56.

Havaux, M., B. Ksas, A. Szewczyk, D. Rumeau, F. Franck, S. Caffarri and C. Triantaphylides. 2009. Vitamin B6 deficient plants display increased sensitivity to high light and photo-oxidative stress. BMC Plant Biol. 9: 130-153.

Hinkley, S.F. and B.B. Jarvis. 2001. Chromatographic method for *Stachybotrys* toxins. Method. Mol. Biol. 157: 173-194.

Hoffmeister, D. and N.P. Keller. 2007. Natural products of filamentous fungi: enzymes, genes, and their regulation. Nat. Prod. Rep. 24: 393-416.

Hong, Y.S., A. Martinez, G. Liger-Belair, P. Jeandet, J.M. Nuzillard and C. Cilindre. 2012. Metabolomics reveals simultaneous influences of plant defense system and fungal growth in *Botrytis cinerea*-infected *Vitis vinifera* cv. *Chardonnay* berries. J. Exp. Bot. 63: 5773-5785.

Howell, C.R. 1999. Selective isolation from soil and separation in vitro of P and Q strains of *Trichoderma virens* with differential media. Mycologia 91: 930-934.

Howell, C.R. 2003. Mechanisms employed by *Trichoderma* species in the biological control of plant diseases: The history and evolution of current concepts. Plant Dis. 87: 4-10.

Howell, C.R. 2006. Understanding the mechanisms employed by *Trichoderma virens* to effect biological control of cotton diseases. Phytopathology 96: 178-180.

Howell, C.R. and R.D. Stipanovic. 1983. Gliovirin, a new antibiotic from *Gliocladium virens*, and its role in the biological control of *Pythium ultimum*. Can. J. Microbiol. 29: 321-324.

Huang, D., T. Zhou, K. Lafleur, C. Nevado and A. Caflisch. 2010. Kinase selectivity potential for inhibitors targeting the ATP binding site: a network analysis. Bioinformatics 26: 198-204.

Hynes, J., C.T. Müller, T.H. Jones and L. Boddy. 2007. Changes in volatile production during the course of fungal mycelial interactions between *Hypholoma fasciculare* and *Resinicium bicolor*. J. Chem. Ecol. 33: 43-57.

Iacobellis, N. and J. DeVay. 1987. Studies on pathogenesis of *Rhizoctonia solani* in beans: an evaluation of the possible roles of phenylacetic acid and its hydroxy derivatives as phytotoxins. Physiol. Mol. Plant P. 30: 421-432.

Iakovlev, A., Å. Olson, M. Elfstrand and J. Stenlid. 2006. Differential gene expression during interactions between *Heterobasidion annosum* and *Physisporinus sanguinolentus*. FEMS Microbiol. Lett. 241: 79-85.

Inglis, G.D. and L.M. Kawchuk. 2002. Comparative degradation of oomycete, ascomycete, and basidiomycete cell walls by mycoparasitic and biocontrol fungi. Can. J. Microbiol. 48: 60-70.

Insell, J.P., N. Huner, W.J. Newsted and R. Van Huystee. 1985. Light microscopic and polypeptide analyses of sclerotia from mesophilic and psychrophilic pathogenic fungi. Can. J. Botany 63: 2305-2310.

Jager, G. and H. Velvis. 1988. Inactivation of sclerotia of *Rhizoctonia solani* on potato tubers by *Verticillium biguttatum*, a soil borne mycoparasite. Neth. J. Pl. Path. 94: 225-231.

Jain, R., V. Valiante, N. Remme, T. Docimo, T. Heinekamp, C. Hertweck, J. Gershenzon, H. Haas and A.A. Brakhage. 2011. The MAP kinase MpkA controls cell wall integrity, oxidative stress response, gliotoxin production and iron adaptation in *Aspergillus fumigatus*. Mol. Microbiol. 82: 39-53.

Jain, S., K. Akiyama, K. Mae, T. Ohguchi and R. Takata. 2002. Targeted disruption of a G protein alpha subunit gene results in reduced pathogenicity in *Fusarium oxysporum*. Curr. Genet. 41: 407-413.

Jamalizadeh, M., H. Etebarian, H. Aminian and A. Alizadeh. 2011. A review of mechanisms of action of biological control organisms against post-harvest fruit spoilage. EPPO Bulletin 41: 65-71.

Jarvis, B.B. 2003. *Stachybotrys chartarum*: a fungus for our time. Phytochemistry 64: 53-60.

Jeffries, P. 1995. Biology and ecology of mycoparasitism. Can. J. Botany 73: 1284-1290.

Jiang, F., Y. Zhang and G.J. Dusting. 2011. NADPH oxidase-mediated redox signaling: roles in cellular stress response, stress tolerance, and tissue repair. Pharmacol. Rev. 63: 218-242.

John, R.P., R.D. Tyagi, D. Prevost, S.K. Brar, S. Pouleur and R.Y. Surampalli. 2010. Mycoparasitic *Trichoderma viride* as a biocontrol agent against *Fusarium oxysporum* f. sp. *adzuki* and *Pythium arrhenomanes* and as a growth promoter of soybean. Crop Prot. 29: 1452-1459.

Jonkers, W., A.E. Estrada, K. Lee, A. Breakspear, G. May and H.C. Kistler. 2012. Metabolome and transcriptome of the interaction between *Ustilago maydis* and *Fusarium verticillioides* in vitro. Appl. Environ. Microbiol. 78: 3656-3667.

Joseph-Horne, T. and D.W. Hollomon. 2000. Functional diversity within the mitochondrial electron transport chain of plant pathogenic fungi. Pest Manag. Sci. 56: 24-30.

Kadotani, N., H. Nakayashiki, Y. Tosa and S. Mayama. 2003. RNA silencing in the phytopathogenic fungus *Magnaporthe oryzae*. MPMI 16: 769-776.

Kahmann, R., C. Basse and M. Feldbrügge. 1999. Fungal-plant signalling in the *Ustilago maydis*-maize pathosystem. Curr. Opin. Microbiol. 2: 647-650.

Kahmann, R. and J. Kämper. 2004. *Ustilago maydis*: how its biology relates to pathogenic development. New Phytol. 164: 31-42.

Kays, A.M., P.S. Rowley, R.A. Baasiri and K.A. Borkovich. 2000. Regulation of conidiation and adenylyl cyclase levels by the G alpha protein GNA-3 in *Neurospora crassa*. Mol. Cell. Biol. 20: 7693-7705.

Khosla, C. 2009. Structures and mechanisms of polyketide synthases. J. Org. Chem. 74: 6416-6420.

Kim, H.S., S.Y. Park, S. Lee, E.L. Adams, K. Czymmek and S. Kang. 2011. Loss of cAMP-dependent protein kinase A affects multiple traits important for root pathogenesis by *Fusarium oxysporum*. MPMI 24: 719-732.

Kind, T. and O. Fiehn. 2007. Seven Golden Rules for heuristic filtering of molecular formulas obtained by accurate mass spectrometry. BMC Bioinformatics 8: 105-126.

Koulman, A., B.A. Tapper, K. Fraser, M. Cao, G.A. Lane and S. Rasmussen. 2007. High-throughput direct-infusion ion trap mass spectrometry: a new method for metabolomics. Rapid. Commun. Mass Spectrom. 21: 421-428.

Kronstad, J., A.D. De Maria, D. Funnell, R.D. Laidlaw, N. Lee, M.M. de Sa and M. Ramesh. 1998. Signaling via cAMP in fungi: interconnections with mitogen-activated protein kinase pathways. Arch. Microbiol. 170: 395-404.

Kültz, D. 1998. Phylogenetic and functional classification of mitogen-and stress-activated protein kinases. J. Mol. Evol. 46: 571-588.

Kumar, A., K. Scher, M. Mukherjee, E. Pardovitz-Kedmi, G.V. Sible, U.S. Singh, S.P. Kale, P.K. Mukherjee and B.A. Horwitz. 2010. Overlapping and distinct functions of two *Trichoderma virens* MAP kinases in cell-wall integrity, antagonistic properties and repression of conidiation. Biochem. Bioph. Res. Co. 398: 765-770.

Kuo, C.Y. and C.T. Huang. 2008. A reliable transformation method and heterologous expression of beta-glucuronidase in *Lentinula edodes*. J. Microbiol. Methods 72: 111-115.

Lagoutte, D., V. Nicolas, E. Poupon, A. Fournet, R. Hocquemiller, D. Libong, P. Chaminade and P. Loiseau. 2008. Antifungal canthin-6-one series accumulate in lipid droplets and affect fatty acid metabolism in *Saccharomyces cerevisiae*. Biomed. Pharmacother. 62: 99-103.

Larkin, R.P. and D.R. Fravel. 2002. Effects of varying environmental conditions on biological control of *Fusarium* wilt of tomato by nonpathogenic *Fusarium* spp. Phytopathology 92: 1160-1166.

Leclerque, A., H. Wan, A. Abschutz, S. Chen, G.V. Mitina, G. Zimmermann and H.U. Schairer. 2004. Agrobacterium-mediated insertional mutagenesis (AIM)

of the entomopathogenic fungus *Beauveria bassiana*. Curr. Genet. 45: 111-119.

Lee, S. and J. Chappell. 2008. Biochemical and genomic characterization of terpene synthases in *Magnolia grandiflora*. Plant Physiol. 147: 1017-1033.

Lee S.B., J.W. Taylor. 1990. Isolation of DNA from fungal mycelia and single spores. In: Innis D, Sninsky J, White T (eds) PCR Protocols: A Guide to Methods and Applications. Academic Press, New York, pp 282-287

Lee, S.K., B.G. Kim, T.R. Kwon, M.J. Jeong, S.R. Park, J.W. Lee, M.O. Byun, H.B. Kwon, B.F. Matthews, C.B. Hong and S.C. Park. 2011. Overexpression of the mitogen-activated protein kinase gene *OsMAPK33* enhances sensitivity to salt stress in rice (*Oryza sativa* L.). J. Biosci. 36: 139-151.

Lee, Y.H. and R.A. Dean. 1993. cAMP regulates infection structure formation in the plant pathogenic fungus *Magnaporthe grisea*. Plant Cell 5: 693-700.

Lehtonen, M., P. Ahvenniemi, P. Wilson, M. German- Kinnari and J. Valkonen. 2008. Biological diversity of *Rhizoctonia solani* (AG- 3) in a northern potato- cultivation environment in Finland. Plant Pathol. 57: 141-151.

Leitgeb, B., A. Szekeres, L. Manczinger, C. Vagvolgyi and L. Kredics. 2007. The history of alamethicin: A review of the most extensively studied peptaibol. Chem. Biodivers. 4: 1027-1051.

Lev, S., A. Sharon, R. Hadar, H. Ma and B.A. Horwitz. 1999. A mitogen-activated protein kinase of the corn leaf pathogen *Cochliobolus heterostrophus* is involved in conidiation, appressorium formation, and pathogenicity: diverse roles for mitogen-activated protein kinase homologs in foliar pathogens. PNAS 96: 13542-13547.

Levy, E., Z. Eyal, I. Chet and A. Hochman. 1992. Resistance mechanisms of *Septoria tritici* to antifungal products of Pseudomonas. Physiol. Mol. Plant Pathol. 40: 163-171.

Lewis, J.A. and R.D. Lumsden. 1995. Do pathogenic fungi have the potential to inhibit biocontrol fungi ? J. Phytopathol. 143: 585-588.

Li, D.C., S.H. Zhang, K.Q. Liu and J. Lu. 2004. Purification and partial characterization of a chitinase from the mycoparasitic fungus *Trichothecium roseum*. J. Gen. Appl. Microbiol. 50: 35-39.

Li, S., Z. Zhang, A. Cain, B. Wang, M. Long and J. Taylor. 2005. Antifungal activity of camptothecin, trifolin, and hyperoside isolated from *Camptotheca acuminata*. J. Agric. Food. Chem. 53: 32-37.

Limón, M.C., J.A. Pintor-Toro and T. Benítez. 1999. Increased antifungal activity of *Trichoderma harzianum* transformants that overexpress a 33-kDa chitinase. Phytopathology 89: 254-261.

Lin, L., Q. Yu, X. Yan, W. Hang, J. Zheng, J. Xing and B. Huang. 2010. Direct infusion mass spectrometry or liquid chromatography mass spectrometry for human metabonomics? A serum metabonomic study of kidney cancer. Analyst 135: 2970-2978.

Liu, C., D.K. Lakshman and S.M. Tavantzis. 2003. Quinic acid induces hypovirulence and expression of a hypovirulence-associated double-stranded RNA in *Rhizoctonia solani*. Curr. Genet. 43: 103-111.

Liu, G., J. Casqueiro, O. Bañuelos, R.E. Cardoza, S. Gutiérrez and J.F. Martín. 2001. Targeted inactivation of the *mecB* gene, encoding cystathione-gamma-lyase, shows that the reverse transsulfuration pathway is required for high-level cephalosporin biosíntesis in *Acremonium chysogenum* C10 but not for methionine induction of the cephalosporin genes. J. Bacteriol. 183: 1765-1772.

Liu, S., J.-P. Sun, B. Zhou and Z.-Y. Zhang. 2006. Structural basis of docking interactions between ERK2 and MAP kinase phosphatase 3. PNAS 103: 5326-5331.

Liu, S., W. Ruan, J. Li, H. Xu, J. Wang, Y. Gao and J. Wang. 2008. Biological control of phytopathogenic fungi by fatty acids. Mycopathologia 166: 93-102.

Lopes, F.A.C., A.S. Steindorff, A.M. Geraldine, R.S. Brandão, V.N. Monteiro, M.L. Júnior, A.S. Guedes Coelho, C.J. Ulhoa and R.N. Silva. 2012. Biochemical and metabolic profiles of *Trichoderma* strains isolated from

common bean crops in the Brazilian Cerrado, and potential antagonism against *Sclerotinia sclerotiorum*. Fungal Biol. 116: 815-824.

López Gresa, M.P., F. Maltese, J.M. Bellés, V. Conejero, H.K. Kim, Y.H. Choi and R. Verpoorte. 2010. Metabolic response of tomato leaves upon different plant–pathogen interactions. Phytochem. Analysis 21: 89-94.

Lu, Z. and T. Hunter. 2009. Degradation of activated protein kinases by ubiquitination. Annu. Rev. Biochem. 78: 435-475.

Lucas, J. 2010. Advances in plant disease and pest management. J. Agr. Sci. 1: 1-24.

Ma, Y., Y. Li, J. Liu, Y. Song and R. Tan. 2004. Anti *Helicobacter pylori* metabolites from *Rhizoctonia* sp. Cy064, an endophytic fungus in *Cynodon dactylon*. Fitoterapia 75: 451-456.

Ma, Z., T.J. Proffer, J.L. Jacobs and G.W. Sundin. 2006. Overexpression of the 14 alpha-demethylase target gene (*CYP51*) mediates fungicide resistance in *Blumeriella jaapii*. Appl. Environ. Microbiol. 72: 2581-2585.

Malmierca, M.G., R.E. Cardoza, N.J. Alexander, S.P. McCormick, R. Hermosa, E. Monte and S. Gutierrez. 2012. Involvement of *Trichoderma* trichothecenes in the biocontrol activity and induction of plant defense-related genes. Appl. Environ. Microbiol. 78: 4856-4868.

Mandeel, Q. and R. Baker. 1991. Mechanisms involved in biological control of *Fusarium* wilt of cucumber with strains of nonpathogenic *Fusarium oxysporum*. Phytopathology 81: 462-469.

Manikonda, P.K. and A. Jagota. 2012. Melatonin administration differentially affects age-induced alterations in daily rhythms of lipid peroxidation and antioxidant enzymes in male rat liver. Biogerontology 13: 511-524.

Martin, K.L., B.M. McDougall, S.E. Unkles and R.J. Seviour. 2006. The three β-1, 3-glucanases from *Acremonium blochii* strain C59 appear to be encoded by separate genes. Mycol. Res. 110: 66-74.

Mashego, M.R., K. Rumbold, M. De Mey, E. Vandamme, W. Soetaert and J.J. Heijnen. 2007. Microbial metabolomics: past, present and future methodologies. Biotechnol. Lett. 29: 1-16.

May, G.S., T. Xue, D.P. Kontoyiannis and M.C. Gustin. 2005. Mitogen activated protein kinases of *Aspergillus fumigatus*. Med. Mycol. 43 Suppl 1: S83-S86.

McCormick, S.P., A.M. Stanley, N.A. Stover and N.J. Alexander. 2011. Trichothecenes: from simple to complex mycotoxins. Toxins 3: 802-814.

McQuilken, M.P. and J. Gemmell. 2004. Enzyme production by the mycoparasite *Verticillium biguttatum* against *Rhizoctonia solani*. Mycopathologia 157: 201-205.

McQuilken, M.P., J. Gemmell, R.A. Hill and J.M. Whipps. 2003. Production of macrosphelide A by the mycoparasite *Coniothyrium minitans*. FEMS Microbiol. Lett. 219: 27-31.

Mehrabi, R., X. Zhao, K. Yangseon and J.-R. Xu. 2009. The cAMP signaling and MAP kinase pathways in plant pathogenic fungi. In: Hloger Deising, ed. The Mycota XXII, Plant Relationships, volume V, 2nd edition, pp 157-172.

Melo, I.S., J.L. Faull and R.S. Nascimento. 2006. Antagonism of *Aspergillus terrus* to *Sclerotinia sclerotiorum* Braz. J. Microbiol. 37: 417-419.

Mendoza-Mendoza, A., M.J. Pozo, D. Grzegorski, P. Martínez, J.M. García, V. Olmedo-Monfil, C. Cortés, C. Kenerley and A. Herrera-Estrella. 2003. Enhanced biocontrol activity of Trichoderma through inactivation of a mitogen-activated protein kinase. PNAS 100: 15965-15970.

Meyer, V. 2008. Genetic engineering of filamentous fungi-progress, obstacles and future trends. Biotechnol. Adv. 26: 177-185.

Meyer, V., D. Mueller, T. Strowig and U. Stahl. 2003. Comparison of different transformation methods for *Aspergillus giganteus*. Curr. Genet. 43: 371-377.

Meyer, V., F. Wanka, J. van Gent, M. Arentshorst, C.A. van den Hondel and A.F. Ram. 2011. Fungal gene expression on demand: an inducible, tunable, and metabolism-independent expression system for *Aspergillus niger*. Appl. Environ. Microbiol. 77: 2975-2983.

Michielse, C.B., P.J. Hooykaas, C.A. van den Hondel and A.F. Ram. 2008. *Agrobacterium*-mediated transformation of the filamentous fungus *Aspergillus awamori*. Nat. Protoc. 3: 1671-1678.

Michielse, C.B., P.J.J. Hooykaas, C.A.M.J.J. van den Hondel and A.F.J. Ram. 2005. *Agrobacterium*-mediated transformation as a tool for functional genomics in fungi. Curr. Genet. 48: 1-17.

Michielse, C.B., K. Salim, P. Ragas, A.F. Ram, B. Kudla, B. Jarry, P.J. Punt and C.A. van den Hondel. 2004. Development of a system for integrative and stable transformation of the zygomycete *Rhizopus oryzae* by *Agrobacterium*-mediated DNA transfer. Mol. Genet. Genomics 271: 499-510.

Mikami, Y. 1988. Microbial conversion of terpenoids. Biotechnol. Genet. Eng. 6: 271-320.

Mischke, S. 1998. Mycoparasitism of selected sclerotia-forming fungi by *Sporidesmium sclerotivorum*. Can. J. Bot. 76: 460-466.

Mitchell, T.K. and R.A. Dean. 1995. The cAMP-Dependent Protein kinase catalytic subunit is required for appressorium formation and pathogenesis by the rice blast pathogen *Magnaporthe grisea*. The Plant Cell 7: 1869-1878.

Miyoshi, S. and S. Shinoda. 2000. Microbial metalloproteases and pathogenesis. Microbes Infect. 2: 91-98.

Montero-Barrientos, M., R. Hermosa, C. Nicolás, R.E. Cardoza, S. Gutiérrez and E. Monte. 2008. Overexpression of a *Trichoderma* HSP70 gene increases fungal resistance to heat and other abiotic stresses. Fungal Genet. Biol. 45: 1506-1513.

Morissette, D. 2006. Characterization of *Stachybotrys elegans*' genes regulated during its interaction with *Rhizoctonia solani*. McGill University.

Morissette, D., A. Dauch, R. Beech, L. Masson, R. Brousseau and S.H. Jabaji-Hare. 2008. Isolation of mycoparasitic-related transcripts by SSH during interaction of the mycoparasite *Stachybotrys elegans* with its host *Rhizoctonia solani*. Curr. Genet. 53: 67-80.

Morissette, D., B.T. Driscoll and S.H. Jabaji-Hare. 2003. Molecular cloning, characterization, and expression of a cDNA encoding an endochitinase gene from the mycoparasite *Stachybotrys elegans*. Fungal Genet. Biol. 39: 276-285.

Morissette, D.C., P. Seguin and S.H. Jabaji-Hare. 2006. Expression regulation of the endochitinase-encoding gene *sechi44* from the mycoparasite *Stachybotrys elegans*. Can. J. Microbiol. 52: 1103-1109.

Morita, T., K. Takegawa and T. Yagi. 2004. Disruption of the *plr1+* gene encoding pyridoxal reductase of *Schizosaccharomyces pombe*. J. Biochem. 135: 225-230.

Morris, R.A.C., D.F. Ewing, J.M. Whipps and J.R. Coley-Smith. 1995. Antifungal hydroxymethyl-phenols from the mycoparasite *Verticillium biguttatum*. Phytochemistry 39: 1043-1048.

Mukherjee, M., B.A. Horwitz, P.D. Sherkhane, R. Hadar and P.K. Mukherjee. 2006. A secondary metabolite biosynthesis cluster in *Trichoderma virens*: evidence from analysis of genes underexpressed in a mutant defective in morphogenesis and antibiotic production. Curr. Genet. 50: 193-202.

Mukherjee, M., P.K. Mukherjee and S.P. Kale. 2007. cAMP signalling is involved in growth, germination, mycoparasitism and secondary metabolism in *Trichoderma virens*. Microbiol-Sgm 153: 1734-1742.

Mukherjee, P., J. Latha, R. Hadar and B. Horwitz. 2004. Role of Two G-Protein alpha subunits, *TgaA* and *TgaB*, in the antagonism of plant pathogens by *Trichoderma virens*. Appl. Environ. Microbiol. 70: 542-549.

Mukherjee, P.K., J. Latha, R. Hadar and B.A. Horwitz. 2003. TmkA, a mitogen-activated protein kinase of *Trichoderma virens*, is involved in biocontrol properties and repression of conidiation in the dark. Eukaryot. cell 2: 446-455.

Mukherjee, P.K., A. Wiest, N. Ruiz, A. Keightley, M.E. Moran-Diez, K. McCluskey, Y.F. Pouchus and C.M. Kenerley. 2011. Two classes of new peptaibols are synthesized by a single non-ribosomal peptide synthetase of *Trichoderma virens*. J. Biol. Chem. 286: 4544-4554.

Müller, P., C. Aichinger, M. Feldbrügge and R. Kahmann. 1999. The MAP kinase kpp2 regulates mating and pathogenic development in *Ustilago maydis*. Mol. Microbiol. 34: 1007-1017.

Mullins, E.D., X. Chen, P. Romaine, R. Raina, D.M. Geiser and S. Kang. 2001. Agrobacterium-mediated transformation of *Fusarium oxysporum*: An efficient

tool for insertional mutagenesis and gene transfer. Phytopathology 91: 173-180.

Murray, M., P.H. Cui and F. Zhou. 2010. Roles of mitogen-activated protein kinases in the regulation of CYP genes. Curr. Drug. Metab. 11: 850-858.

Muthumeenakshi, S., S. Sreenivasaprasad, C.W. Rogers, M.P. Challen and J.M. Whipps. 2007. Analysis of cDNA transcripts from *Coniothyrium minitans* reveals a diverse array of genes involved in key processes during sclerotial mycoparasitism. Fungal Genet. Biol. 44: 1262-1284.

Nagahashi, G. and D.D. Douds, Jr. 2011. The effects of hydroxy fatty acids on the hyphal branching of germinated spores of AM fungi. Fungal. Biol. 115: 351-358.

Nicoletti, R., M. De Stefano, S. De Stefano, A. Trincone and F. Marziano. 2004. Antagonism against *Rhizoctonia solani* and fungitoxic metabolite production by some *Penicillium* isolates. Mycopathologia 158: 465-474.

Nielsen, K.F., J. Smedsgaard, T.O. Larsen, F. Lund, U. Thrane, and J.C. Frisvad. 2004. Chemical identification of fungi: metabolite profiling and metabolomics. In: Arora DK, ed. Fungal biotechnology in agricultural, food, and environmental application. New York: Marcel Dekker, pp 19-35.

Nishida, E. and Y. Gotoh. 1993. The MAP kinase cascade is essential for diverse signal transduction pathways. Trends Biochem. Sci. 18: 128-131.

O'Brien, J. and G.D. Wright. 2011. An ecological perspective of microbial secondary metabolism. Curr. Opin. Biotechnol. 22: 552-558.

O'Donnell, G. and S. Gibbons. 2007. Antibacterial activity of two canthin-6-one alkaloids from *Allium neapolitanum*. Phytother. Res. 21: 653-657.

Oh, D.C., C.A. Kauffman, P.R. Jensen and W. Fenical. 2007. Induced production of emericellamides A and B from the marine-derived fungus *Emericella* sp. in competing co-culture. J. Nat. Prod. 70: 515-520.

Oh, Y., N. Donofrio, H.Q. Pan, S. Coughlan, D.E. Brown, S.W. Meng, T. Mitchell and R.A. Dean. 2008. Transcriptome analysis reveals new insight into appressorium formation and function in the rice blast fungus *Magnaporthe oryzae*. Genome Biol. 9 (5): R85.

Ouyang, Y., K. Koike and T. Ohmoto. 1994. Canthin-6-one alkaloids from *Brucea mollis* var. *tonkinensis*. Phytochemistry 36: 1543-1546.

Osbourn, A. 2010. Secondary metabolic gene clusters: evolutionary toolkits for chemical innovation. Trends Genet. 26: 449-457.

Pandya, U. and M. Saraf. 2010. Application of fungi as a biocontrol agent and their biofertilizer potential in agriculture. J. Adv. Dev. Res 1: 90-99.

Park, H.B., H.C. Kwon, C.-H. Lee and H.O. Yang. 2009. Glionitrin A, an antibiotic-antitumor metabolite derived from competitive interaction between abandoned mine microbes. J. Nat. Prod. 72: 248-252.

Pearson, G., F. Robinson, T.B. Gibson, B. Xu, M. Karandikar, K. Berman and M.H. Cobb. 2001. Mitogen-activated protein (MAP) kinase pathways: regulation and physiological functions. Endocr. Rev. 22: 153-183.

Peberdy, J.F. 1979. Fungal protoplasts: isolation, reversion, and fusion. Annu. Rev. Microbiol. 33: 21-39.

Peiris, D., W.B. Dunn, M. Brown, D.B. Kell, I. Roy and J.N. Hedger. 2008. Metabolite profiles of interacting mycelial fronts differ for pairings of the wood decay basidiomycete fungus, *Stereum hirsutum* with its competitors *Coprinus micaceus* and *Coprinus disseminatus*. Metabolomics 4: 52-62.

Pimentel, D., L. Mclaughlin, A. Zepp, B. Lakitan, T. Kraus, P. Kleinman, F. Vancini, W.J. Roach, E. Graap, W.S. Keeton and G. Selig. 1993. Environmental and economic-effects of reducing pesticide use in agriculture. Agr. Ecosyst. Environ. 46: 273-288.

Pluskal, T., S. Castillo, A. Villar-Briones and M. Oresic. 2010. MZmine 2: modular framework for processing, visualizing, and analyzing mass spectrometry-based molecular profile data. BMC Bioinformatics 11: 395.

Pöggeler, S. and U. Kück. 2006. Highly efficient generation of signal transduction knockout mutants using a fungal strain deficient in the mammalian ku70 ortholog. Gene 378: 1-10.

Pohl, C.H., J.L. Kock and V.S. Thibane. 2011. Antifungal free fatty acids. Science against microbial pathogens: Communicating current research and technological advances, Badajoz: Formatex 1: 61-71.

Pope, G.A., D.A. MacKenzie, M. Defemez, M.A.M.M. Aroso, L.J. Fuller, F.A. Mellon, W.B. Dunn, M. Brown, R. Goodacre, D.B. Kell, M.E. Marvin, E.J. Louis and I.N. Roberts. 2007. Metabolic footprinting as a tool for discriminating between brewing yeasts. Yeast 24: 667-679.

Pope, G.A., D.A. MacKenzie, M. Defernez and I.N. Roberts. 2009. Metabolic footprinting for the study of microbial biodiversity. Cold Spring Harb. Protoc. 4: pdb prot5222.

Potgieter, H. and M. Alexander. 1966. Susceptibility and resistance of several fungi to microbial lysis. J. Bacteriol. 91: 1526-1532.

Punt, P.J., R.P. Oliver, M.A. Dingemanse, P.H. Pouwels and C.A. van den Hondel. 1987. Transformation of Aspergillus based on the hygromycin B resistance marker from *Escherichia coli*. Gene 56: 117-124.

Rao, M.B., A.M. Tanksale, M.S. Ghatge and V.V. Deshpande. 1998. Molecular and biotechnological aspects of microbial proteases. Microbiol. Mol. Biol. Rev. 62: 597-635.

Rautio, J.J., M. Bailey, T. Kivioja, H. Soderlund, M. Penttila and M. Saloheimo. 2007. Physiological evaluation of the filamentous fungus *Trichoderma reesei* in production processes by marker gene expression analysis. BMC Biotechnol. 7: 28-45.

Reddy, K.R.N., C.S. Reddy and K. Muralidharan. 2009. Potential of botanicals and biocontrol agents on growth and aflatoxin production by *Aspergillus flavus* infecting rice grains. Food Control 20: 173-178.

Rehman, S., A.S. Shawl, V. Verma, A. Kour, M. Athar, R. Andrabi, P. Sultan and G.N. Qazi. 2008. An endophytic *Neurospora* sp. from *Nothapodytes foetida* producing camptothecin. App. Biochem. Microbiol. 44: 225-231.

Rehman, S.U., R. Lawrence, E.J. Kumar and Z.A. Badri. 2012. Comparative efficacy of *Trichoderma viride, T. harzianum* and carbendazim against damping-off disease of cauliflower caused by *Rhizoctonia solani* Kuehn. J. Biopest. 5: 23-27.

Reino, J.L., R.F. Guerrero, R. Hernandez-Galan and I.G. Collado. 2008. Secondary metabolites from species of the biocontrol agent *Trichoderma*. Phytochem. Rev. 7: 89-123.

Rey, P., G. Le Floch, N. Benhamou, M.I. Salerno, E. Thuillier and Y. Tirilly. 2005. Interactions between the mycoparasite *Pythium oligandrum* and two types of sclerotia of plant-pathogenic fungi. Mycol. Res. 109: 779-788.

Reyes, G., A. Romans, C.K. Nguyen and G.S. May. 2006. Novel mitogen-activated protein kinase MpkC of *Aspergillus fumigatus* is required for utilization of polyalcohol sugars. Eukaryot. cell 5: 1934-1940.

Rho, H.S., S. Kang and Y.H. Lee. 2001. *Agrobacterium tumefaciens*-mediated transformation of the plant pathogenic fungus, *Magnaporthe grisea*. Mol. Cells 12: 407-411.

Ridgway, R.L., J.C. Tinney, J.T. Macgregor and N.J. Starler. 1978. Pesticide use in agriculture. Environ. Health Persp. 27: 103-112.

Rippa, S., M. Eid, F. Formaggio, C. Toniolo and L. Béven. 2010. Hypersensitive-like response to the pore-former peptaibol alamethicin in *Arabidopsis thaliana*. Chem. Bio. Chem. 11: 2042-2049.

Rodriguez Estrada, A.E., A. Hegeman, H. Corby Kistler and G. May. 2011. In vitro interactions between *Fusarium verticillioides* and *Ustilago maydis* through real-time PCR and metabolic profiling. Fungal Genet. Biol. 48: 874-885.

Rotem, Y., O. Yarden and A. Sztejnberg. 1999. The mycoparasite *Ampelomyces quisqualis* expresses *exgA* encoding an exo-beta-1,3-glucanase in culture and during mycoparasitism. Phytopathology 89: 631-638.

Rowan, D.D. 1993. Lolitrems, peramine and paxilline: mycotoxins of the ryegrass/endophyte interaction. Agr. Ecosys. Environ. 44: 103-122.

Rozen, S. and H. Skaletsky. 2000. Primer3 on the WWW for general users and for biologist programmers. Methods in molecular biology 132: 365-386.

Ruiz-Diez, B. 2002. Strategies for the transformation of filamentous fungi. J. Appl. Microbiol. 92: 189-195.

Sambrook, J., E. Fritsh and T. Maniatis. 1989. Molecular Cloning: a laboratory manual.

N.Y., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, ISBN 0-87969-309-6.

Samudio-Ruiz, S.L. and L.G. Hudson. 2012. Increased DNA methyltransferase activity and DNA methylation following epidermal growth factor stimulation in ovarian cancer cells. Epigenetics 7: 216-224.

Sang, Y., J.M. Barbosa, H. Wu, R.D. Locy and N.K. Singh. 2007. Identification of a pyridoxine (pyridoxamine) 5′-phosphate oxidase from *Arabidopsis thaliana*. FEBS Lett. 581: 344-348.

Sattler, C., H. Kachele and G. Verch. 2007. Assessing the intensity of pesticide use in agriculture. Agr. Ecosys. Environ. 119: 299-304.

Sauer, S. and M. Kliem. 2010. Mass spectrometry tools for the classification and identification of bacteria. Nat. Rev. Microbiol. 8: 74-82.

Schaeffer, H.J. and M.J. Weber. 1999. Mitogen-activated protein kinases: specific messages from ubiquitous messengers. Mol. Cell. Biol. 19: 2435-2444.

Schneider, M.J., F.S. Ungemach, H.P. Broquist and T.M. Harris. 1982. Biosynthesis of swainsonine in *Rhizoctonia leguminicola*. Epimerization at the ring fusion. J. Am. Chem. Soc. 104: 6863-6864.

Schumacher, J., L. Kokkelink, C. Huesmann, D. Jimenez-Teja, I.G. Collado, R. Barakat, P. Tudzynski and B. Tudzynski. 2008. The cAMP-dependent signaling pathway and its role in conidial germination, growth, and virulence of the gray mold *Botrytis cinerea*. MPMI 21: 1443-1459.

Seidl, V., L. Song, E. Lindquist, S. Gruber, A. Koptchinskiy, S. Zeilinger, M. Schmoll, P. Martinez, J. Sun, I. Grigoriev, A. Herrera-Estrella, S.E. Baker and C.P. Kubicek. 2009. Transcriptomic response of the mycoparasitic fungus *Trichoderma atroviride* to the presence of a fungal prey. BMC Genomics 10: 567-581.

Shane, B. and E.L. Stokstad. 1975. Transport and metabolism of folates by bacteria. J. Biol. Chem. 250: 2243-2253.

Sharma, P., K. Vignesh, R. Ramesh, K. Saravanan, S. Deep, M. Sharma, M. Saini and D. Singh. 2011. Biocontrol genes from *Trichoderma* species. Afr. J. Biotechnol. 10: 19898-19907.

Shi-Wang, L., W. Zheng-Yi and G. Ze-Jian. 2004. Isolation and transformation of *Trichoderma viride* protoplasts. Chinese. J. Agr. Biotechnol. 1: 67-72.

Shishido, M., F. Ogura, T. Usami and Y. Amemiya. 2001. Phenotypic analysis of pathogenicity-impaired mutants of the *Fusarium* Wilt fungus generated by linearized plasmid insertion. Tech. Bull. Fac. Hort. Chiba Univ. 55: 11-20.

Shoji, J., J. Maruyama, M. Arioka and K. Kitamoto. 2006. Development of *Aspergillus oryzae thiA* promoter as a tool for molecular biological studies. FEMS Microbiol. Lett. 244: 41-46.

Skory, C.D., J.S. Horng, J.J. Pestka and J.E. Linz. 1990. Transformation of *Aspergillus parasiticus* with a homologous gene (*pyrG*) involved in pyrimidine biosynthesis. Appl. Environ. Microbiol. 56: 3315-3320.

Smedsgaard, J. and J.C. Frisvad. 1996. Using direct electrospray mass spectrometry in taxonomy and secondary metabolite profiling of crude fungal extracts. J. Microbiol. Meth. 25: 5-17.

Smedsgaard, J., M.E. Hansen and J.C. Frisvad. 2004. Classification of terverticillate Penicillia by electrospray mass spectrometric profiling. Stud. Mycol. 49: 243-251.

Sohn, J., R.T. Voegele, K. Mendgen and M. Hahn. 2000. High level activation of vitamin B1 biosynthesis genes in haustoria of the rust fungus *Uromyces fabae*. MPMI 13: 629-636.

Solomon, P.S., O.D. Waters, J. Simmonds, R.M. Cooper and R.P. Oliver. 2005. The *Mak2* MAP kinase signal transduction pathway is required for pathogenicity in *Stagonospora nodorum*. Curr. Genet. 48: 60-68.

Sontag, R.L. and T.J. Weber. 2012. Ectopic ERK expression induces phenotypic conversion of C10 cells and alters DNA methyltransferase expression. BMC Res. Notes 5: 217-223.

Soriano-Agatón, F., D. Lagoutte, E. Poupon, F. Roblot, A. Fournet, J.-C. Gantier and R. Hocquemiller. 2005. Extraction, hemisynthesis, and synthesis of

canthin-6-one analogues. Evaluation of their antifungal activities. J. Nat. Prod. 68: 1581-1587.

Staunton, J. and K.J. Weissman. 2001. Polyketide biosynthesis: a millennium review. Nat. Prod. Rep. 18: 380-416.

Stevens, D.L. and G.A. Strobel. 1968. Origin of cyanide in cultures of a psychrophilic basidiomycete. J. Bacteriol. 95: 1094-1102.

Steyaert, J.M., H.J. Ridgway, Y. Elad and A. Stewart. 2003. Genetic basis of mycoparasitism: a mechanism of biological control by species of *Trichoderma*. New Zeal. J. Crop Hort. 31: 281-291.

Strnisková, M., M. Barancík and T. Ravingerová. 2002. Mitogen-Activated Protein kinases and their role in regulation of cellular processes. Gen. Physiol. Biophys. 21: 231-255.

Suárez, M.B., J.A. Vizcaíno, A. Llobell and E. Monte. 2007. Characterization of genes encoding novel peptidases in the biocontrol fungus *Trichoderma harzianum* CECT 2413 using the TrichoEST functional genomics approach. Curr. Genet. 51: 331-342.

Sun, H., J. Yang, C. Lin, X. Huang, R. Xing and K.Q. Zhang. 2006. Purification and properties of a β-1, 3-glucanase from *Chaetomium* sp. that is involved in mycoparasitism. Biotechnol. Lett. 28: 131-135.

Takano, Y., T. Kikuchi, Y. Kubo, J.E. Hamer, K. Mise and I. Furusawa. 2000. The *Colletotrichum lagenarium* MAP kinase gene CMK1 regulates diverse aspects of fungal pathogenesis. MPMI 13: 374-383.

Tamova, G., V. Betina and V. Farkaš. 1993. An efficient method for the preparation of protoplasts from *Trichoderma viride*. Folia Microbiol. 38: 214-218.

Tamura, H., A. Takasaki, T. Taketani, M. Tanabe, F. Kizuka, L. Lee, I. Tamura, R. Maekawa, H. Aasada and Y. Yamagata. 2012. The role of melatonin as an antioxidant in the follicle. J. Ovarian Res. 5: 5-13.

Tamura, K., D. Peterson, N. Peterson, G. Stecher, M. Nei and S. Kumar. 2011. MEGA5: molecular evolutionary genetics analysis using maximum

likelihood, evolutionary distance, and maximum parsimony methods. Mol. Biol. Evol. 28: 2731-2739.

Tanguay, P., J. Coupal and L. Bernier. 2003. Genetic transformation, electrophoretic karyotyping and isolation of insertional mutants in the tree pathogenic fungus *Neonectria galligena*. Forest Pathol. 33: 413-428.

Taylor, G., S.H. Jabaji-Hare, P.M. Charest and W. Khan. 2002. Purification and characterization of an extracellular exochitinase, β-N-acetylhexosaminidase, from the fungal mycoparasite *Stachybotrys elegans*. Can. J. Microbiol. 48: 311-319.

Thouvenel, C., J.C. Gantier, P. Duret, C. Fourneau, R. Hocquemiller, M.E. Ferreira, A. Rojas de Arias and A. Fournet. 2003. Antifungal compounds from *Zanthoxylum chiloperone* var. *angustifolium*. Phytother. Res. 17: 678-680.

Tsror, L., R. Barak and B. Sneh. 2001. Biological control of black scurf on potato under organic management. Crop Prot. 20: 145-150.

Tsuji, G., S. Fujii, N. Fujihara, C. Hirose, S. Tsuge, T. Shiraishi and Y. Kubo. 2003. *Agrobacterium tumefaciens*-mediated transformation for random insertional mutagenesis in *Colletotrichum lagenarium*. J. Gen. Plant Pathol. 69: 230-239.

Tsuruoka, A., Y. Kaku, H. Kakinuma, I. Tsukada, M. Yanagisawa, K. Nara and T. Naito. 1998. Synthesis and antifungal activity of novel thiazole-containing triazole antifungals. II. Optically active ER-30346 and its derivatives. Chem. Pharm. Bull. 46: 623-630.

Tulp, M. and L. Bohlin. 2005. Rediscovery of known natural compounds: nuisance or goldmine? Bioorgan. Med. Chem. 13: 5274-5282.

Tweddell, R.J., S.H. Jabaji-Hare, M. Goetghebeur, P.M. Charest and S. Kermasha. 1995. Purification and partial characterization of a β-1,3-glucanase secreted by the mycoparasite *Stachybotrys elegans*. Biosci. Biotechnol. Biochem. 59: 2223-2227.

Van Bogaert, I.N., S. Groeneboer, K. Saerens and W. Soetaert. 2011. The role of cytochrome P450 monooxygenases in microbial fatty acid metabolism. FEBS J. 278: 206-221.

van der Werf, M.J., K.M. Overkamp, B. Muilwijk, L. Coulier and T. Hankemeier. 2007. Microbial metabolomics: toward a platform with full metabolome coverage. Anal. Biochem. 370: 17-25.

Van Loon, L., P. Bakker and C. Pieterse. 1998. Systemic resistance induced by rhizosphere bacteria. Annu. Rev. Phytopathol. 36: 453-483.

Varavallo, M.A., M.V.d. Queiroz, J.F. Pereira and E.F.d. Araújo. 2004. Isolation and regeneration of *Penicillium brevicompactum* protoplasts. Acta Sci. Biol. Sci. 26: 475-479.

Viiri, H., E. Annila, V. Kitunen and P. Niemelä. 2001. Induced responses in stilbenes and terpenes in fertilized Norway spruce after inoculation with blue-stain fungus, *Ceratocystis polonica*. Trees-Struct. Funct. 15: 112-122.

Villas-Bôas, S.G., S. Mas, M. Åkesson, J. Smedsgaard and J. Nielsen. 2005. Mass spectrometry in metabolome analysis. Mass Spec. Rev. 24: 613-646.

Viterbo, A., M. Harel, B.A. Horwitz, I. Chet and P.K. Mukherjee. 2005. *Trichoderma* mitogen-activated protein kinase signaling is involved in induction of plant systemic resistance. Appl. Environ. Microbiol. 71: 6241-6246.

Viterbo, A., A. Wiest, Y. Brotman, I. Chet and C. Kenerley. 2007. The 18mer peptaibols from *Trichoderma virens* elicit plant defense responses. Mol. Plant Pathol. 8: 737-746.

Vizcaino, J.A., J. Redondo, M.B. Suarez, R.E. Cardoza, R. Hermosa, F.J. Gonzalez, M. Rey and E. Monte. 2007. Generation, annotation, and analysis of ESTs from four different Trichoderma strains grown under conditions related to biocontrol. Appl. Microbiol. Biotechnol. 75: 853-862.

Voisard, C., C. Keel, D. Haas and G. Defago. 1989. Cyanide production by *Pseudomonas fluorescens* helps suppress black root rot of tobacco under gnotobiotic conditions. EMBO J. 8: 351-358.

von Döhren, H. 2009. A survey of nonribosomal peptide synthetase (NRPS) genes in *Aspergillus nidulans*. Fungal Genet. Biol. 46: S45–S52

Wagle, S., A.V. Adhikari and N.S. Kumari. 2008. Synthesis of some novel 2,4-disubstituted thiazoles as possible antimicrobial agents. Phosphorus Sulfur 183: 1285-1300.

Walters, D., D. Walsh, A. Newton and G. Lyon. 2005. Induced resistance for plant disease control: maximizing the efficacy of resistance elicitors. Phytopathology 95: 1368-1373.

Wei, X., F. Yang and D.C. Straney. 2005. Multiple non-ribosomal peptide synthetase genes determine peptaibol synthesis in *Trichoderma virens*. Can. J. Microbiol. 51: 423-429.

Wei, Y.D., W.Y. Shen, M. Dauk, F. Wang, G. Selvaraj and J.T. Zou. 2004. Targeted gene disruption of glycerol-3-phosphate dehydrogenase in *Colletotrichum gloeosporioides* reveals evidence that glycerol is a significant transferred nutrient from host plant to fungal pathogen. J. Biol. Chem. 279: 429-435.

Whipps, J.M. 2001. Microbial interactions and biocontrol in the rhizosphere. J. Exp. Bot. 52: 487-511.

White T., T. Bruns, S. Lee, and J. Taylor. 1990. Amplification and direct sequencing of fungal ribosomal RNA genes for phylogenetics. In: Innis D, Sninsky J, White T, eds. PCR protocols: a guide to methods and applications. New York: Academic Press Inc. p 315-322.

Wicklow, D.T. and J.C. Zak. 1979. Ascospore germination of carbonicolous ascomycetes in fungistatic soils: an ecological interpretation. Mycologia 71: 238-242.

Wiest, A., D. Grzegorski, B.W. Xu, C. Goulard, S. Rebuffat, D.J. Ebbole, B. Bodo and C. Kenerley. 2002. Identification of peptaibols from *Trichoderma virens* and cloning of a peptaibol synthetase. J. Biol. Chem. 277: 20862-20868.

Wilhite, S.E., R.D. Lumsden and D.C. Straney. 2001. Peptide synthetase gene in *Trichoderma virens*. Appl. Environ. Microbiol. 67: 5055-5062.

Wilhite, S.E. and D.C. Straney. 1996. Timing of gliotoxin biosynthesis in the fungal biological control agent *Gliocladium virens* (*Trichoderma virens*). Appl. Microbiol. Biotechnol. 45: 513-518.

Willetts, H.J. and S. Bullock. 1992. Developmental biology of sclerotia. Mycol. Res. 96: 801-816.

Wnendt, S., M. Jacobs and U. Stahl. 1990. Transformation of *Aspergillus giganteus* to hygromycin B resistance. Curr. Genet. 17: 21-24.

Woo, S.L., B. Donzelli, F. Scala, R. Mach, G.E. Harman, C.P. Kubicek, G. Del Sorbo and M. Lorito. 1999. Disruption of the *ech42* (endochitinase-encoding) gene affects biocontrol activity in *Trichoderma harzianum* P1. MPMI 12: 419-429.

Woodhall, J.W., A.K. Lees, S.G. Edwards and P. Jenkinson. 2007. Characterization of *Rhizoctonia solani* from potato in Great Britain. Plant Pathol. 56: 286-295.

Xiao-Yan, S., S. Qing-Tao, X. Shu-Tao, C. Xiu-Lan, S. Cai-Yun and Z. Yu-Zhong. 2006. Broad-spectrum antimicrobial activity and high stability of Trichokonins from *Trichoderma koningii* SMF2 against plant pathogens. FEMS Microbiol. Lett. 260: 119-125.

Xu, J.R. 2000. Map kinases in fungal pathogens. Fungal Genet. Biol. 31: 137-152.

Xu, J.R. and J.E. Hamer. 1996. MAP kinase and cAMP signaling regulate infection structure formation and pathogenic growth in the rice blast fungus *Magnaporthe grisea*. Genes Dev. 10: 2696-2706.

Xue, L., J.H. Murray and A.M. Tolkovsky. 2000. The Ras/phosphatidylinositol 3-kinase and Ras/ERK pathways function as independent survival modules each of which inhibits a distinct apoptotic signaling pathway in sympathetic neurons. J. Biol. Chem. 275: 8817-8824.

Xue, T., C.K. Nguyen, A. Romans and G.S. May. 2004. A mitogen-activated protein kinase that senses nitrogen regulates conidial germination and growth in *Aspergillus fumigatus*. Eukaryot. cell 3: 557-560.

Yamagishi, K., T. Kimura, M. Suzuki, K.J. Yamaki and S. Oita. 2005. Identification and overexpression of genes encoding cAMP-dependent protein

kinase catalytic subunits in homobasidiomycete *Schizophyllum commune*. Biosci. Biotechnol. Biochem. 69: 2333-2342.

Yanar, Y., G. Yilmaz, I. Cesmeli and S. Coskun. 2005. Characterization of *Rhizoctonia solani* isolates from potatoes in Turkey and screening potato cultivars for resistance to AG-3 isolates. Phytoparasitica 33: 370-376.

Yedidia, I.I., N. Benhamou and I.I. Chet. 1999. Induction of defense responses in cucumber plants (*Cucumis sativus* L.) by the biocontrol agent *Trichoderma harzianum*. Appl. Environ. Microbiol. 65: 1061-1070.

Yu, J., P.K. Chang, K.C. Ehrlich, J.W. Cary, D. Bhatnagar, T.E. Cleveland, G.A. Payne, J.E. Linz, C.P. Woloshuk and J.W. Bennett. 2004. Clustered pathway genes in aflatoxin biosynthesis. Appl. Environ. Microbiol. 70: 1253-1262.

Yudelman, M., A. Ratta and D. Nygaard. 1998. Pest management and food production. Looking to the future. Food Agr. Environ. Discussion paper 25. Copyright 1998 International Food Policy Research Institute.

Zabalgogeazcoa, I. 2008. Fungal endophytes and their interaction with plant pathogens. Span. J. Agric. Res. 6: 138-146.

Zarnowski, R. and J.P. Woods. 2005. Glutathione-dependent extracellular ferric reductase activities in dimorphic zoopathogenic fungi. Microbiology 151: 2233-2240.

Zeilinger, S. 2004. Gene disruption in *Trichoderma atroviride* via *Agrobacterium*-mediated transformation. Curr. Genet. 45: 54-60.

Zeilinger, S. and M. Omann. 2007. *Trichoderma* biocontrol: signal transduction pathways involved in host sensing and mycoparasitism. Gene Regul. Syst. Bio. 1: 227-234.

Zeilinger, S., B. Reithner, V. Scala, I. Peissl, M. Lorito and R.L. Mach. 2005. Signal transduction by *Tga3*, a novel G protein alpha subunit of *Trichoderma atroviride*. Appl. Environ. Microbiol. 71: 1591-1597.

Zhang, A., P. Lu, A. Dahl-Roshak, P. Paress, S. Kennedy, J. Tkacz and Z. An. 2003. Efficient disruption of a polyketide synthase gene (*pks1*) required for melanin synthesis through *Agrobacterium*-mediated transformation of *Glarea lozoyensis*. Mol. Genet. Genomics 268: 645-655.

Zhang, H. and Q. Yang. 2007. Expressed sequence tags-based identification of genes in the biocontrol agent *Chaetomium cupreum*. Appl. Microbiol. Biotechnol. 74: 650-658.

Zhang, Y., T. Han, Q. Ming, L. Wu, K. Rahman and L. Qin. 2012. Alkaloids produced by endophytic fungi: a review. Nat. Prod. Commun. 7: 963-968.

Zhang, Z., S. Li, S. Zhang, C. Liang, D. Gorenstein and R.S. Beasley. 2005. New camptothecin and ellagic acid analogues from the root bark of *Camptotheca acuminata*. Planta Med. 70: 1216-1221.

Zhao, S. and R.D. Fernald. 2005. Comprehensive algorithm for quantitative real-time polymerase chain reaction. J. Comput. Biol. 12: 1047-1064.

Zhao, X., R. Mehrabi and J.R. Xu. 2007. Mitogen-activated protein kinase pathways and fungal pathogenesis. Eukaryot. Cell 6: 1701-1714.

Zheng, L., M. Campbell, J. Murphy, S. Lam and J.R. Xu. 2000. The BMP1 gene is essential for pathogenicity in the gray mold fungus *Botrytis cinerea*. MPMI 13: 724-732.

Zhou, B., J.F. Xiao, L. Tuli and H.W. Ressom. 2012. LC-MS-based metabolomics. Mol. Biosyst. 8: 470-481.

Zhou, X.W., Y.M. Wei, H.F. Zhu, Z.N. Wang, J.A. Lin, L. Liu and K.X. Tang. 2008. Protoplast formation, regeneration and transformation from the taxol-producing fungus *Ozonium* sp. Afr. J. Biotechnol. 7: 2017-2024.

Zwiers, L.H. and M.A. De Waard. 2001. Efficient *Agrobacterium tumefaciens*-mediated gene disruption in the phytopathogen *Mycosphaerella graminicola*. Curr. Genet. 39: 388-393.

APPENDICES

Appendix I. LC-MS/MS analytical conditions

Protein identification

For the construction of the target in-house-built protein library, data were retrieved from the National Center for Biotechnology Information (NCBI, http://www.ncbi.nlm.nih.gov/) and the Gene Ontology database (http://www.geneontology.org/). For Proteome Discoverer searches, trypsin was selected as the digestion enzyme allowing for 2 missed internal cleavage sites per peptide. Deamidation (N and Q) and oxidation (M) were selected as dynamic modifications, and carbamidomethyl (C) as static. The mass tolerance for the precursor and fragment ions was set to 15 and 0.6 ppm, respectively.

Liquid chromatography-mass spectrometry/mass spectrometry analysis

For LC-MS/MS analyses, during the first 12 min, 5 µL of sample were loaded on column at a flow rate of 600 nL/min of buffer A and, subsequently, the separation was done using a gradient from 2–80% buffer B over 110 min at a flow rate of 250 nL/min and then 2% buffer B for 10 min at a flow rate of 600 nL/min. Full scans were acquired in the mass range between 360 and 1800 Da. Data dependent MS/MS scans were performed in the LTQ for the top ten most abundant masses with intensity higher than 10000 counts. Target ions already selected for MS/MS were dynamically excluded for 25 s. Nanospray and S-lens voltages were set to 0.9–1.8 kV and 50 V, respectively. Capillary temperature was set to 225ºC. Collision induced dissociation (CID) was used with a collision energy of 35 %, activation Q setting of 0.25 and 10 ms activation time for MS.

Appendix II- Target in-house-built protein library in FASTA format

>sp|P38110|ATM_YEAST Serine/threonine-protein kinase TEL1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=TEL1 PE=1 SV=3

MEDHGIVETLNFLSSTKIKERNNALDELTTILKEDPERIPTKALSTTAEALVELLASEHTKYCDLLRNLTV
STTNKLSLSENRLSTISYVLRLFVEKSCERFKVKTLKLLLAVVPELMVKDGSKSLLVSVHLSFALDALIKSD
PFKLKFMIHQWISLVDKICEYFQSQMKLSMVDKTLTNFISILLNLLALDTVGIFQVTRTITWTVIDFLRL
SKKENGNTRLIMSLINQLILKCHCFSVIDTLMLIKEAWSYLIGCTSNELVQDQLSLFDVMSSELMNHKL
PYMIGQENYVEELRSESLVSLYREYILLRLSNYKPQLFTVNHVEFSYIRGSRDKNSWFALPDFRLRDRG
GRSVWLKILGITKSLLTYFALNRKNENYLLKRRKCDSDIPSILRISDDMDTFLIHLLEENSSHEFEVLGLQ
LCSFYGTLQDFTKSFAEQLKELLFSKFEKIQCFNWVCFSFIPLLSQKECELSNGDMARLFKVCLPLVKSN
ESCQLSCLLLANSKFSQLLSDEKTINQIYDLYELSDILGPILVTNESFMLWGYLQYVGKDFQSMNGISS
ADRIFEWLKSKWNQLRGTDAKQDQFCNFISWLGNKYDPENPFNDKKGEGANPVSLCWDESHKIW
QHFQEQEFLLVKPEEKSECFNTPFFNLPKVSLDLTRYNEILYRLLENIESDAFSSPLQKFTWVAKLIQIV
DNLCGDSTFSEFIAAYKRTTLITIPQLSFDSQNSYQSFFEEVLSIRTINVDHLVLDKINMKEVNDFIMQK
NKSQTGTSAINYFEASSEDTTQNNSPYTIGGRFQKPLHSTIDKAVRAYLWSSRNKSISERLVAILEFSD
CVSTDVFISYLGTVCQWLKQAIGEKSSYNKILEEFTEVLGEKLLCNHYSSNQAMLLTSYIEAIRPQWLS
YPEQPLNSDCNDILDWIISRFEDNSFTGVAPTVNLSMLLLSLLQNHDLSHGSIRGGKQRVFATFIKCL
QKLDSSNIINIMNSISSYMAQVSYKNQSIIFYEIKSLFPPQQSIESAFYSLAMSMLSLVSYPSLVFSLED
MMTYSGFNHTRAFIQQALNKITVAFRYQNLTELFEYCKFDLIMYWFNRTKVPTSKLEKEWDISLFGF
ADIHEFLGRYFVEISAIYFSQGFNQKWLDMLHAITNGDAYLVDNSYYLCIPLAFISGGVNELIFDILPQI
SGKTTVKYHKKYRLLMLKWIIRFTDLGSLTELRSTVEKLFPTSYLSPYLFENSSVSMRYQYPLHIPLALG
ATLVQTQFAHEKNTHEFKLLFLVITDLEKTSTYIGKLRCARELKYLFVLYENVLVKSSTLNFIIIRLSKFLID
TQIHDEVITIFSSLLNLADKNTFEIEPSLPNLFCKIFIYLRENKQLSPSFQQAIKLLEHRDLIKIKWKYCLDA
IFGIVQDDIYENTELLDASDCGVDDVVLVSLLFSYARRPVASKIGCSLSKAAAINILKHHVPKEYLSKNF
KLWFAALSRRILQQEVQRERSTNFNNEVHLKNFEMVFRHPEQPHMIYQRSTFNKEAELYDTEVFFIS
ECILTYLVGYSIGNSESEFCFRDNIMNENKDKVAPLDKDVLNAIYPLANNFGMESFICDTYLSVNEPY
NCWLSKFARSLIHQISFNIPPIVCLYPLCKGSTAFCELVLDLFFLSTTYDPKCLNWSNRIFTQIAMLLHV
KDSEIKLKMLFNVIKMIRMGSRCKERNCLRIYSSLDLQEICQISLKIKEFKFGYLLFEEMNMPNIREMNI
NTLQKIYECINDGDFLAGLPVPHSIEVLNSINRIDSDTWRFLFNNADFDANYTTSLEEEKESLIKATEDS
GFYGLTSLLESRLSGSSDVYKWNLELGDWKLLTPKVVDSKAKGLYYAIKNLPQDVGFAEKSLEKSLLTI
FDSRQHFISQTEWDTLNAIIEFIKIAAPQDVTSFPQTLMSIMKADKERLNTIDFYDHKTTLKSRHTLM
NVLSRNSLDENVKCSKYLRLGSIIQLANYVQLAIANGAPQDALRNATLMSKTVKNIAKLYDDPSVVSQ
IEKASFTSANALWESREYAPVMIMRDLLAQNEKNISESILYDDFKLLINVPMDQIKARLVKWSSESRL
EPAAAIYEKIIVNWDINVEDHESCSDVFYTLGSFLDEQAQKLRSNGEIEDREHRSYTGKSTKALELIYKN
TKLPENEKDAKRHYNRVLLQYNRDSEVLKALLLQKEKFLWHALHFYLNTLVFSNRYDNDIIDKFCGL
WFENDDNSKINQLLYKEIGTIPSWKFLPWVNQIASKISMEENEFQKPLQLMKRLLYKLPYDSLYSVMI
LLYEKQSNKDTNISQKIQAVKKILLELQGYDRGAFAKKYLLPVQEFCEMSVELANLKFVQNTKTLRLA
NLKIGQYWLKQLNMEKLPLPTSNFTVKSSADGRKARPYIVVNETVGITTTGLSLPKIVFNISDGTTQK
ALMKGSNDDLRQDAIMEQVFQQVNKVLQNDKVLRNLDLGIRTYKVVPLGPKAGIIEFVANSTSLHQ
ILSKLHTNDKITFDQARKGMKAVQTKSNEERLAYLKITNEIKPQLRNFFFDFPDPLDWFEAKKTYTKG
VAASSIVGYILGLGDRHLNNILLDCSTGEPIHIDLGIAFDQGKLLPIPELVPFRLTRDIVDGFGVTGVDG
LFRRSCERVYAVLRKDYVKVCVLNILKWDPLYSWVMSPVKYEHLFEEEHEITNFDNVSKFISNNDRN
ENQESYRALKGVEEKLMGNGLSVESSVQDLIQQATDPSNLSVIYMGWSPFY

>gi|161075907|ref|NP_001104350.1| rolled, isoform A [Drosophila melanogaster]

MEEFNSSGSVVNGTGSTEVPQSNAEVIRGQIFEVGPRYIKLAYIGEGAYGMVVSADDTLTNQRVAIK
KISPFEHQTYCQRTLREITILTRFKHENIIDIRDILRVDSIDQMRDVYIVQCLMETDLYKKTQVMVLPDI
WLKFIERITTIDMWCIILAITPNTKTEYNCRLSDIFNYGSDSRYAFMRALK

>gi|161075905|ref|NP_001104349.1| rolled, isoform E [Drosophila melanogaster]

MEEFNSSGSVVNGTGSTEVPQSNAEVIRGQIFEVGPRYIKLAYIGEGAYGMVVSADDTLTNQRVAIK
KISPFEHQTYCQRTLREITILTRFKHENIIDIRDILRVDSIDQMRDVYIVQCLMETDLYKKTQRLSNDHIC
YFLYQILRGLKYIHSANVLHRDLKPSNLLLNKTCDLKICDFGLARIADPEHDHTGFLTEYVATRWYRAP
EIMLNSKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGLSPSRDDLECIINEKARNYLESLP
FKPNVPWAKLFPNADALALDLLGKMLTFNPHKRIPVEEALAHPYLEQYYDPGDEPVAEVPFRINME
NDDISRDALKSLIFEETLKFKERQPDNAP

>gi|161075903|ref|NP_001104348.1| rolled, isoform F [Drosophila melanogaster]

MFYAVDFDKSYLRICLKSKKKLSLYIHILSYRLLVKFIINISSFPEETLVMEEFNSSGSVVNGTGSTEVPQS
NAEVIRGQIFEVGPRYIKLAYIGEGAYGMVVSADDTLTNQRVAIKKISPFEHQTYRTLREITILTRFKHE
NIIDIRDILRVDSIDQMRDVYIVQCLMETDLYKLLKTQRLSNDHICYFLYQILRGLKYIHSANVLHRDLK
PSNLLLNKTCDLKICDFGLARIADPEHDHTGFLTEYVATRWRPEIMLNSKGYTKSIDIWSVGCILAEML
SNRPIFPGKHYLDQLNHILGVLGSPSRDDLECIINEKARNYLESLPFKPNVPWAKLFPNADALALDLLG
KMLTFNPHKRIPVEEALAHPYLEQYYDPGEPAEVPFRINMENDDISRDALKSLIFEETLKFKERQPDN
AP

>gi|161075901|ref|NP_001015121.2| rolled, isoform B [Drosophila melanogaster]

MFYAVDFDKSYLRICLKSKKNISSFPEETLVMEEFNSSGSVVNGTGSTEVPQSNAEVIRGQIFEVGPRY
IKLAYIGEGAYGMVVSADDTLTNQRVAIKKISPFEHQTYCQRTLREITILTRFKHENIIRDILRVDSIDQ
MRDVYIVQCLMETDLYKLLKTQRLSNDHICYFLYQILRGLKYIHSANVLHRDLKPSNLLLNKTCDLKIC
DFGLARIADPEHDHTGFLTEYVATRWYRAPEIMLNSKGYTKSIDISGCILAEMLSNRPIFPGKHYLDQL
NHILGVLGSPSRDDLECIINEKARNYLESLPFKPNVPWAKLFPNADALALDLLGKMLTFNPHKRIPVEE
ALAHPYLEQYYDPGDEPVAEVPFRINMENDDISDAKSLIFEETLKFKERQPDNAP

>gi|62861952|ref|NP_001015123.1| rolled, isoform D [Drosophila melanogaster]

MEEFNSSGSVVNGTGSTEVPQSNAEVIRGQIFEVGPRYIKLAYIGEGAYGMVVSADDTLTNQRVAIK
KISPFEHQTYCQRTLREITILTRFKHENIIDIRDILRVDSIDQMRDVYIVQCLMETDLYKKTQRLSNDHIC
YFLYQILRGLKYIHSANVLHRDLKPSNLLLNKTCDLKICDFGLARIADPEHDHTGFLTEYVATRWYRAP
EIMLNSKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGLSPSRDDLECIINEKARNYLESLP
FKPNVPWAKLFPNADALALDLLGKMLTFNPHKRIPVEEALAHPYLEQYYDPGDEPVAEVPFRINME
NDDISRDALKSLIFEETLKFKERQPDNAP

>gi|62861950|ref|NP_001015122.1| rolled, isoform C [Drosophila melanogaster]

MEEFNSSGSVVNGTGSTEVPQSNAEVIRGQIFEVGPRYIKLAYIGEGAYGMVVSADDTLTNQRVAIK
KISPFEHQTYCQRTLREITILTRFKHENIIDIRDILRVDSIDQMRDVYIVQCLMETDLYKKTQRLSNDHIC
YFLYQILRGLKYIHSANVLHRDLKPSNLLLNKTCDLKICDFGLARIADPEHDHTGFLTEYVATRWYRAP
EIMLNSKGYTKSIDIWSVGCILAEMLSNRPIFPGK

HYLDQLNHILGVLGSPSRDDLECIINEKARNYLESLPFKPNVPWAKLFPNADALALDLLGKMLTFNPH
KRIPVEEALAHPYLEQYYDPGDEPVAEVPFRINMENDDISRDALKSLIFEETLKFKERQNAP

>gi|158529765|gb|EDP28108.1| rolled, isoform A [Drosophila melanogaster]

MEEFNSSGSVVNGTGSTEVPQSNAEVIRGQIFEVGPRYIKLAYIGEGAYGMVVSADDTLTNQRVAIK
KISPFEHQTYCQRTLREITILTRFKHENIIDIRDILRVDSIDQMRDVYIVQCLMETDLYKKTQVMVLPDI
WLKFIERITTIDMWCIILAITPNTKTEYNCRLSDIFNYGSDSRYAFMRALK

>gi|158529764|gb|EDP28107.1| rolled, isoform E [Drosophila melanogaster]

MEEFNSSGSVVNGTGSTEVPQSNAEVIRGQIFEVGPRYIKLAYIGEGAYGMVVSADDTLTNQRVAIK
KISPFEHQTYCQRTLREITILTRFKHENIIDIRDILRVDSIDQMRDVYIVQCLMETDLYKKTQRLSNDHIC
YFLYQILRGLKYIHSANVLHRDLKPSNLLLNKTCDLKICDFGLARIADPEHDHTGFLTEYVATRWYRAP
EIMLNSKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGLSPSRDDLECIINEKARNYLESLP
FKPNVPWAKLFPNADALALDLLGKMLTFNPHKRIPVEEALAHPYLEQYYDPGDEPVAEVPFRINME
NDDISRDALKSLIFEETLKFKERQPDNAP

>gi|158529763|gb|EDP28106.1| rolled, isoform F [Drosophila melanogaster]

MFYAVDFDKSYLRICLKSKKKLSLYIHILSYRLLVKFIINISSFPEETLVMEEFNSSGSVVNGTGSTEVPQS
NAEVIRGQIFEVGPRYIKLAYIGEGAYGMVVSADDTLTNQRVAIKKISPFEHQTYRTLREITILTRFKHE
NIIDIRDILRVDSIDQMRDVYIVQCLMETDLYKLLKTQRLSNDHICYFLYQILRGLKYIHSANVLHRDLK
PSNLLLNKTCDLKICDFGLARIADPEHDHTGFLTEYVATRWRPEIMLNSKGYTKSIDIWSVGCILAEML
SNRPIFPGKHYLDQLNHILGVLGSPSRDDLECIINEKARNYLESLPFKPNVPWAKLFPNADALALDLLG
KMLTFNPHKRIPVEEALAHPYLEQYYDPGEPAEVPFRINMENDDISRDALKSLIFEETLKFKERQPDN
AP

>gi|158529762|gb|EAA46312.3| rolled, isoform B [Drosophila melanogaster]

MFYAVDFDKSYLRICLKSKKNISSFPEETLVMEEFNSSGSVVNGTGSTEVPQSNAEVIRGQIFEVGPRY
IKLAYIGEGAYGMVVSADDTLTNQRVAIKKISPFEHQTYCQRTLREITILTRFKHENIIRDILRVDSIDQ
MRDVYIVQCLMETDLYKLLKTQRLSNDHICYFLYQILRGLKYIHSANVLHRDLKPSNLLLNKTCDLKIC
DFGLARIADPEHDHTGFLTEYVATRWYRAPEIMLNSKGYTKSIDISGCILAEMLSNRPIFPGKHYLDQL
NHILGVLGSPSRDDLECIINEKARNYLESLPFKPNVPWAKLFPNADALALDLLGKMLTFNPHKRIPVEE
ALAHPYLEQYYDPGDEPVAEVPFRINMENDDISDAKSLIFEETLKFKERQPDNAP

>gi|51951149|gb|EAA46311.2| rolled, isoform D [Drosophila melanogaster]

MEEFNSSGSVVNGTGSTEVPQSNAEVIRGQIFEVGPRYIKLAYIGEGAYGMVVSADDTLTNQRVAIK
KISPFEHQTYCQRTLREITILTRFKHENIIDIRDILRVDSIDQMRDVYIVQCLMETDLYKKTQRLSNDHIC
YFLYQILRGLKYIHSANVLHRDLKPSNLLLNKTCDLKICDFGLARIADPEHDHTGFLTEYVATRWYRAP
EIMLNSKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGLSPSRDDLECIINEKARNYLESLP
FKPNVPWAKLFPNADALALDLLGKMLTFNPHKRIPVEEALAHPYLEQYYDPGDEPVAEVPFRINME
NDDISRDALKSLIFEETLKFKERQPDNAP

>gi|51951148|gb|EAA46310.2| rolled, isoform C [Drosophila melanogaster]

MEEFNSSGSVVNGTGSTEVPQSNAEVIRGQIFEVGPRYIKLAYIGEGAYGMVVSADDTLTNQRVAIK
KISPFEHQTYCQRTLREITILTRFKHENIIDIRDILRVDSIDQMRDVYIVQCLMETDLYKKTQRLSNDHIC
YFLYQILRGLKYIHSANVLHRDLKPSNLLLNKTCDLKICDFGLARIADPEHDHTGFLTEYVATRWYRAP
EIMLNSKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGLSPSRDDLECIINEKARNYLESLP
FKPNVPWAKLFPNADALALDLLGKMLTFNPHKRIPVEEALAHPYLEQYYDPGDEPVAEVPFRINME
NDDISRDALKSLIFEETLKFKERQPDNAP

>gi|66807963|ref|XP_637704.1| extracellular signal-regulated protein kinase [Dictyostelium discoideum AX4]

MEPEFDHFQSQMDSDNTHQSTMFNVQDNNAILMSGMENVLQSPRQLQAAAQAQQQAAAQA
QQQQVQAQQVQAQQAQQQQQQQQNQQQQQQQQNQQNQQQQQNQQQQSQQMTQQQL
QQLMPPPPTSDTFNDNISYFVYGSQFTVPRRYSIVKCIGHGAYGVVCSAKDNLTGEKVAIKKISKAFD
NLKDTKRTLREIHLLRHFKHENLISIKDILKPNSKEQFEDVYIVSELMDTDLHQIITSPQPLSDDHCQYFY
MLRGLKHIHSANVLHRDLKPSNLLINEDCLLKICDLGLARVEDATHQGFMTEYVATRWYRAPEVILS
WNKYTKAIDIWSVGCIFAELLGRKPLFQGKDYIHQITLIIETIGSPSEEDICNIANEQRQIRNMGNQPK
VNFANMFPKANPDAIDLLERMLYFDPSKRLTVEEALAHPYFQSLHDPSDEPICLHKFSLNFEAWDLN
RDLLKELIYNEMLAYHPEDPQAPYYTDLNNPNFNLSRIQSSSELFNLLQQKQIHQQVNQQSIKN

>gi|327349367|gb|EGE78224.1| MAP kinase [*Ajellomyces dermatitidis* ATCC 18188]

MDRTDSASTPDTEASRATGYFPPHQPYLAPEREFVNGLQTRVLNPQKPPRPANAGFSPVSVPASQS
AYSSWSPILTRPRGSSGSGASMNALEQPLPPDMAAMNDRDLRPQRPSGPARTPSNTYAPARPQFT
PLHSSTQVPLATKRPTRRDPDARYRAQEKAYVQRVRQGPNEWFNFDTQLPGLSFAADSEPEEESPS
SESQFDNDPFDPDTHLVLEDDDAQPTLEELQDPKNKERLEWYSMLASVLKGDVIRQKRLIGTMEQK
SREVWNLEIFVGAKAARFGRPLPLQKKFVEYQISNLGPLIEDIISFEIKGETQVGKPPLKQVEDVVEKIE
KCESLYPSRRILQAEHPRAASEEFQESCDAIIAWHNTTMSINTELALQWVGNEELDFAKPMTMSSLA
ADLSDEGSFLDRIMKEDGLKTLQITDNIYDNDKKKEPSILDGIGGVIKKAKSTLIENAEAFAKRHLPPYI
EELLTLINFPSRLIQEVIRLRLSYARKMKDPALQSILVQMISQFQILLKVAVDIKQRYLIISDPEPGWDLP
PCVDENFDNVVVDGLKYYFKLLNWKLSANKNTFKEAEILEGEWEFSNEIGRQLENGDIEVAEQFSTL
TAKSLQRLMIHFERELHSRPEEDVETERYKQIFDSVRVRQRKLFRFSRLLRQRFENATEFNLREDMVD
TLSEALLASGHFLVTSHDSVGQKGVHLIASPSLYGRPKDIQSILGTSFRSEDSPEDPSNPYVLVVRPEK
GLVWNGKRMEVDLEHPTVRFGKLRLVADGSQQRLQNARLALTRLTGLQLDITIEQRANLGRVNVEL
NKIKKTAYKLSTGIIDSVEIIRRQSKNAENHELIQSCFAFATEFGKRSLMYMDASRRSLNHSKLINLALD
WVFICDDCAADRKTFKWAVAALEFAMIVTHGQNVLAISDEDYCLLRLKVAGCMSLLISHFDIMGAR
SSLAAQAEQQHADPSGQGFRKLDLSRITDDEQASREVQERREELFAEIDLARIEADAKRQALKVLEG
VNADRSVTVLSSSATNVTLRWQQGQFIGGGTSGSVYAAIDLDTSYLMAVKEIRLQEPSVIPGAAQQI
RDEMGVLEVLDHPNIISYYGIEVHRDKVYIFMEYCSGGSLATLLEHGRIEDEMVMVYTLQMLGLAYL
HQAGIVHRDIKPANILLDHNGVIKYVDFGAAMVIARQGKTLAAMDHYSSGARDGRGQAKDALGQ
RKNQKSVTGTPMYMSPELVRGEVGHTSGRHGCMDIWSLGCVILEMATGHPWAGVDNEWIMYKI
AQGSQPQLPTPDQLSPMGIDFIKRCFEIDPVKRPSATELLQHEWIVSIRQQVVAEPQTPSSEGGNMS
GGSGPSSGGNSR

>gi|357500999|ref|XP_003620788.1| MAP kinase, partial [*Medicago truncatula*]

MVKFHDSMHDQGVAEEGLVEALNALRLFLLLLVFMKLTCVEIVIRTASGTFHDGDLMLNQKGMRLI
SEEKESRTDSQTGLTILSRTLSFLRHQSCMTNSQTSSGWSFLRHQSCMKNLQTSSAEIEANKRHSLKS
RAEFISAVSKFHSPTSGHTASACAQPSDAKDLDFDFTLDDLETVKVIGKGSGGVVQLVRHKWVGKLF
ALKAIPMNIQEDIRKQIVQELKINQASQCPHVVVCYHSFYNNGVISLVLEYMRSLVDVIRQVNTILEPY
LAVVCKQVLQGLVYLHNERHVIHRDIKPSNLLVNHKGEVKITDFGVSAMLASTMGQRDTFVGTYNY
MSPERISGSTYDYSCDIWSLGMVVLECAIGRFPYIQSEDQQAWSFELLQAIVESPPPSAPPDQFSPEF
CSFVS

>gi|355495803|gb|AES77006.1| MAP kinase, partial [*Medicago truncatula*]

MVKFHDSMHDQGVAEEGLVEALNALRLFLLLLVFMKLTCVEIVIRTASGTFHDGDLMLNQKGMRLI
SEEKESRTDSQTGLTILSRTLSFLRHQSCMTNSQTSSGWSFLRHQSCMKNLQTSSAEIEANKRHSLKS
RAEFISAVSKFHSPTSGHTASACAQPSDAKDLDFDFTLDDLETVKVIGKGSGGVVQLVRHKWVGKLF
ALKAIPMNIQEDIRKQIVQELKINQASQCPHVVVCYHSFYNNGVISLVLEYMRSLVDVIRQVNTILEPY
LAVVCKQVLQGLVYLHNERHVIHRDIKPSNLLVNHKGEVKITDFGVSAMLASTMGQRDTFVGTYNY
MSPERISGSTYDYSCDIWSLGMVVLECAIGRFPYIQSEDQQAWSFELLQAIVESPPPSAPPDQFSPEF
CSFVS

>gi|317157565|ref|XP_001825893.2| MAP kinase [*Aspergillus oryzae* RIB40]

MDTLKATLLKSWSRLASILGNPSQKAPLCRLNHFRNTEEPDLYTTGGFHRVSLGDTFDHGRYAILRKL
GYGQYSTVWLAQDFKHKKYVTLKLLRADCYGGPHDIFEREILSKISDMSRNSTHDGARHPLIGDFTH
TGPNGDHVCLVFDVLGHHLDFQCAKYEDGRLPVRAVKLIARQLLLGLDFLHRECGVIHTDLKPTNILL
ELENPDRVISRYLEKVPPLMDTQGNAEVPLREVITTPLISEMEAPRIRIIFVASWRDNHLSEQIQSSAL
RAPEVTIGAPWDTGVDIWSLGCLIMELVQGIVPFSGEASERGTWTAEDDRLARTIEILGPFPLELLRK
GSRTPDLFDEKGKYSST

>gi|351693721|gb|AEQ59237.1| MAP kinase [*Cochliobolus lunatus*]

MPPAGSGSSRKISFNVSEQYDIQDVVGEGAYGVVCSALHKPSGQKVAIKKITPFDHSMFCLRTLREM
KLLRYFNHENIISILDIQKPRNYETFTEVYLIQELMETDMHRVIRTQELSDDHCQYFIYQRALKAMHSA
NVLHRDLKPSNLLLNANCDLKVCDFGLARSAASTEDNSGFMTEYVATRWYRAPEIMLTFKEYTKAID
VWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYYGIKSRRAEIRSLPFKKKIPWKAMFP
KTNDLALDLLERLLAFNPVKRITVEEALKHPYLEPYHDPDDEPGADPIPEEFFDFDKNKDNLTKEQLKL
LIYQEIMR

>gi|350296601|gb|EGZ77578.1| MAP kinase [*Neurospora tetrasperma* FGSC 2509]

MASELSPRAVRFSQTDDEPIARLDKHKTVSRPNPRANDSDNSNSSTDAHDDLHVREQIDELGSLSRY
VESHSGSVPSLVPGSLTSSLPLTNGSSSRRGASSETYANGTPSRPQRPTAPARTPSNTYQNQRRPPQ
GQPSSYMANNPHARDGSRPRPLAGTSTFRAQEREYVRRLRQQDYNNDYFDAYGSGEQYDSDSEG
ETPSSEGAFDSYDDAHIMFASNEDIQITEEDLRDPESRERLEWHGMLEAVLTGDVREKKRLIGSNDE
AFGKSAHNVELWLGIRARLCGRHLPVQKRVVEDARAALDRSINDIINFAIAGESEAGKPPFEQVRDV
VNKIERIESLYPSSRELMTALKPGVYSAYQETCDAVISWYNVNEMINELILKKWVGNDALDFSRTKEK
SPSGNGLSDESSFLDRLMKEEGLKSLHEDKGSEPKSLKKKSRLDGISRVITKAKDTLIQNAEGFQKRHL
PPYIEELLTLISFPSRLIEEIIKMRLAYAKKMKDSAQNPMQDQMISQFQVLLKLAIKIKREYMEIARPEP
GWDLPPCIDEDFDRVILEALKYYFKLLNWKLSGNKNTFKEAELLFQEWGFGNEIGRYLAHGDVEVAE
QFSSLTYKAWNRLSQTFEKEVQRRPESVAMTKRYKQILDSVRVRQRMLQRFSRMLSDNYENACDY

TIAFEQPQMLHQLYDRLIETGHFQVYSASPEHKDILIIASPTLHNRDDEIQVLMGTFTYEAAIEDPSDP
YLLIIKAEDPPQWLGPVTLRVREPLDIKLGHMRLIAGGCQPRLLNARKAFVDRIDMQVDPVVEQRSN
LQKVNFRLMEIRKVAFKLSNAFMDSVEAIRRQTRGLNCQELIQTCFIFATEFGQRSLLYMDNNRRTM
NNLKLTKLALDWVSFICDDCISSDRKTFRWAVQALEFAMTRGRHILGLGEDEYARLRAKVAGCMAL
LISHFDIMGARSSVAAQAEKKRLEGLVNQIKRLNKGQMLDDNEAAKYYQEHRLEELAKVDNYRKEIL
LQQSAMGRVLEASNEVDRSLAWLSSTATNFTRQQGHFVGGGTFGNVYAAVNLDTGQLMAVKEIR
LQDPKLIPTIAGQIRDEMRVLETVDHPNVVSYYGIEVHRDRVYMFMEFCSGGSLANLLEHGRIEDEQ
VIMVYALQLLEGLAYLHELKIAHRDIPEILLDHNGIIKYVDFGAAKLIARQGRTLVQDIASTKPNKSMT
GTPMYMSPEVIKGENAGHFGAVDIWSLGCVILEMATGRRPWANLDNEWAIMYNIAQGNPPQLP
SQDQLSPEGIDFLRRCFMRDTKRTAMELLQHEWIMTIRNRVVEPATPSSDAGSTTSQGALNPGNSS
RGGFPGDGMY

>gi|350291063|gb|EGZ72277.1| MAP kinase [*Neurospora tetrasperma* FGSC 2509]

MAPAPAPLLRPAIPGARPGGRGPPRLGLAIPPSLSVKPVGNPGAPPARAAPPQLKLATPMGSTTIPH
EQPAGRPGAQGYSASGASDSSAAHSRSGSFGPESNPTSADTRYSNVSFIGAQRPHGTPDPAVGSLY
SNASEGGVGMERENSLHGLEAFDKLTLEKARTLDVEELDDDGWRIAMMEKRVEELGPLGEGAGGA
VTKARLKGGKTVFALKIITANPDKDVAKQIVRELGFNKQCASEHICRYFGAVVDTSTISIAMEYCEGGS
LDSVYKEVKKLGGRTGERVLGKIAEGVLHGLTYLHSKKIIHRDIKPSNILLCRNGEVKLCDFGVSGDYG
TNGAANTFIGTSYYMAPERITGQSYTITSDVWSLGVTLLEVAQRFFPADGTDSQPRAGLIDLLTYIVR
QPVPKLKDEPDANIFWTDKFKYFIDCCLEKDPNRRASPWRMLDHPWMLEIRSRRVNVARFLATVW
GWEDGKEEA

>gi|350287952|gb|EGZ69188.1| MAP kinase [*Neurospora tetrasperma* FGSC 2509]

MSSAQRGGARKISFNVSEQYDIQDVVGEGAYGVVCSAVHKPSGQKVAIKKITPFDHSMFCLRTLRE
MKLLRYFNHENIISILDIQKPRSYETFNEVYLIQELMETDMHRVIRTQELSDDHCQYFIYQRALKAMH
SANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNSGFMTEYVATRWYRAPEIMLTFKEYTK
AIDVWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYYGIKSRRAEIRSLPFKKKVPFRTL
FPNTSELALDLLEKLLAFNPVKRITVEEALKHPYLEPYHDPDDEPTAPPIPEEFFDFDKHKDNLSKEQLK
QLIYQEIMR

>gi|148228736|ref|NP_001083548.1| mitogen-activated protein kinase 1 [Xenopus laevis]

MAAAGAASNPGGGPEMVRGQAFDVGPRYINLAYIGEGAYGMVCSAHDNVNKVRVAIKKISPFEH
QTYCQRTLREIKILLRFKHENIIGINDIIRAPTIEQMKDVYIVQDLMETDLYKLLKTQHLSNDCYFLYQIL
RGLKYIHSANVLHRDLKPSNLLLNTTCDLKICDFGLARVADPDHDHTGFLTEYVATRWYRAPEIMLN
SKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGILGSPSQEDLCINLKARNYLLSLPHKNKV
PWNRLFPNADPKALDLLDKMLTFNPHKRIEVEAALAHPYLEQYYDPSDEPVAEAPFKFEMELDDLPK
ETLKELIFEETARFQPGY

>gi|148226702|ref|NP_001081344.1| mitogen-activated protein kinase 1 [Xenopus laevis]

MAAAAASSNPGGGPEMVRGQAFDVGPRYTNLSYIGEGAYGMVCSAHCNINKVRVAIKKISPFEHQ
TYCQRTLREIKILLRFKHENIIGINDIIRAPTIEQMKDVYIVQDLMETDLYKLLKTQHLSNDCYFLYQILR
GLKYIHSANVLHRDLKPSNLLLNTTCDLKICDFGLARVADPDHDHTGFLTEYVATRCYRAPEIMLNSK
GYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGILGSPSQEDLCINLKARNYLLSLPHKNKVP

WNRLFPNADPKALDLLDKMLTFNPHKRIEVEAALAHPYLEQYYDPSDEPVAEAPFKFEMELDDLPKE
TLKELIFEETARFQPGY

>gi|344230141|gb|EGV62026.1| MAP kinase [Candida tenuis ATCC 10573]

MASSIKSTNNQANSSMTRSHSKALSSMLANNLQHQNASFMAQERAYIRRIRNQIVDDYYTKGITGA
DDDFKYNDNDNDANINDDDDDDYDEETDGNTSLLADMVDDAYQLDSVSASTLLASRLSDLKPNKN
ITQLEKDSTEDPAVLERLEWQAMLTSVLTGDVVKSEKTKIINNNNLDEQESYLQATYKESLWFGIRAK
LLNRTEDDQRKIISYRRTLVGSLIEDVLNFEINYEDPLGNPPKTQITEILERYECDLWRTQEEMKADKP
ACKTEEFQNRIDSLNAWLSITTAIERESSSLKIWIGNDELDITKSPSEKVTPISTPASEVPERKIFDEDNK
SLAERLMKEKDVHNIFRKRIFLPLAPWMVKSKDTYIRLGFFELKLPDYIHDLIELCLIPMKLIKEIINVRL
GYAKKLQNPTLMMIDQMIDDLRTYLTIALEVKSGVQEYCKSDFGKTWVVGDFFEAENAEFDKVVLE
CLRYKMILLNRKLLDSARSPTNFRTFKEPVLESYNHVKRLGNYIEGGGTVVAEQMTLLTSRLIQRLLAY
FTSQVRSPPSQNPTVSELVRWYSSTTENFGQLRRKLARFTGEISRDFTNSLVFDIASTPNYRTKNLLDV
LRATDHFLVYTGTVETQTYFFSSELFGNEQDILKIINGSYIGLDSNVDTSEFSTLMNILKNCEEGENSAS
ESSIEHALPSHSKDFAYILALCPPKPIVWEGDVVNLSIEKVPITDVKVGQMLLISKLPSYSLHIVKEKFLDI
VDVLFSNGVIKPIEQRCSLAKVHHELTRVNKNFFKMSLAVLDSVKIVREQCNKMCPQGGCQEIINNY
FVYAKDYGKNSVKNLDISRKSTVIMKLIQLCIEWVSFICDDCVPTDRKTFRWCVLALEFAYMTRGFVL
VLKDDQFHKLKLKVARCMSLLISHFDIMGARSSEAEQRKLLRWTSQRQKIENSADDDFIINAYKEDM
MVQINEIEESRSELQGELNSVGRVLDVSDSEYQFVTLLASSFSSVSIRWQKKYIGGGSGDVFGAVNLD
TGGIMAVKEIRFHDSQLVKNLVPSIRDEMTVLEMLNHPNVVQYFGVEVHRDKVYIFMEFCEGGSLA
GLLSHGRIEDEMVIQVYTLQMLEGLAYLHQSGVVHRDIKPENILDHNGVIKVDFGAAKVIATSGRTM
APTQSKPLAGNHSNLNSMTGTPMYMSPEVITGASSDKNGVVDIWSLGCCVLEMATGRRPWANL
DNEWAIMYHIAAGHKPSLPSADQLSEPGIKFIARCLEHDKKRPNAIELNDPWIVSIRQAAFGGSDSLS
TPSSDIGSEP

>gi|343427538|emb|CBQ71065.1| MAP kinase [Sporisorium reilianum SRZ2]

MSIANYSLSSSSSSSPVSDSADAHHVMAGPDASACASTSASASRNNTTIPAPRPFDYRVTYAPVAPA
SGVSAVSVTTQSHRPPSKSHSVSSIESTATVSSIAPSTPPTHDVDDVCFDMATIPKSVRANETYHVDK
RLPPTPHSTATTHQNVASSMAPSHADDTTAAAAAAAAAAAAAAAAAAAPSQFVSRNEKYKSAISF
RVGSKYKVCEIIGEGAYGVVCSAIHRATGQKVAIKKIQPFEHQMFALRTLRELLRFFQECDVSENIISIL
DIIKPNTYEAFTEVYLVQELMETDLHRVIRTQELSDDHCQYFTYQTLRALKPMHCADVIHRDLKPSNV
LLNANCDLKVCDFGLARSVLTADQDTGFMTEYVATRWYRAPIMTFKQYTKAIDVWAVGCILAEML
SGRPLFPGRDYHQQLSLILDVLGTPTLEEFHNINSRRSRDYIRSMPFRKRRDFRTLFPKASPEAIDFLQK
TLTFDPRNRLTVEECLAHPYLSAYHDPDDEPGPRLPDFFYFDMQKESITKEDLRKELWYQVQEFQPL
LR

>gi|210160943|gb|ACJ09358.1| MAP kinase [Phytophthora sojae]

MSSRGASQDAASAGRASEEKAGDGVYVTKNRSLFSMWLHGKAVPNRAHPAVVFRSADVIQEGYL
LKQGLRLKMWSRRYFILRLEERHMTLGYYTSKDSLTLCSETPIGPGHVLDHVNTAKYPRRLELGTKV
MTLEAEDQKAYEAWKSALQEAIRWNHAMVPTKDGSFVTYGKQASEDLKQEERSRAEAAKKLREK
QRADEAAAAANAANKPKYLPATRPGTQCFMTSNTRFEIPSNFEYVKTIGSGAYGVVISTSKSGKTVAI
KNIQRAFDDLTDAKRIVREIKLMRHLNHKCVLGVEDIFEPVALDKFEDVYIVSQLMATDLHRVIYSRH
ALSDEHIAFFMYQMLCAMKYVHSANVIHRDLKPSNVLVNANCELKICDGLRGVFPEEELELTEYVVT
RWYRAPEIMLGCMKYTREVDVWSMGCIFAEMMSRKPLFPGQDYIDQLHLIMNALGAPNDQELYF
LTNARARKFMNAEFQKRGPNPTKPLAHMFTDSPPDALDLLQKMVIDNKRISVDEALAHPYLASIRN
MDDETMATSSFDFDFENEKLTKPVLQRLIWEEMRHFHPIEGEEPGVSSNAAAEGENDSFATTQAS

NTPVTPVTPATAEQDNTSSSSSSEATGTATTAEVEVETTPAEEARPEDDGEASTRPTGDDKQSTNS
DQKIVRTSVGSDNPTDAQTRQEAGEPAREVA

>gi|340521987|gb|EGR52220.1| map kinase [Trichoderma reesei QM6a]

MNSPAPLMRPAIPGSRGRAAPRLGLAIPPSPNAKPVGNLTIQPPARPPLPTLHLATPMGSQVTPVE
QPARPQGIQPGQSAGGGSESSAAHSRSGSFGPLDGRASNPTSAGSQFSALSFASQYGIPVTQGTPD
PVSAVGSMRSEGGVSMERDGSLQGLEGFDRLSIEKARTADVEDLDDEGWRIASLEKRIVELGNLGE
GAGGAVTKAMLKGGKTVFALKVITTNPDPDVKKQIVRELGFNKECASDHICRYYGFDPSTATISIAM
EFCEGGSLDSIYKEVKRLGGRTGEKVLGKIAEGVLGGLTYLHTRRIIHRDIKPSNILLCRDGSVKLCDFG
VSGDFGTKGEANTFIGTSYYMAPERITGQSYTITSDVWSTGVTLEVQHRFPFPADGTEMQPRAGLID
LLTYIVRQPVPKLKDEPDNDVYWSDNFKYFIECCLEKQPNRRASPWKMLEHPWMVEMRSKRVNM
VKYLSFVWGWDEKQVKTSQ

>gi|340520737|gb|EGR50973.1| map kinase [Trichoderma reesei QM6a]

MPNSLDRAVRFSGGSDDDEAAANLAMQSLKHALPEAEDEDSSPESNGADLHHAIERHDDLGSLSR
YADAPNGLTGSLSSLPPASHINGGPPPKAPRPSGGEADAPYLQRPMGPIRTPSNTYNPANSRAAPQ
PQPSFSESARSSSKTRPRQSDSRFRAQERAYVQTLRQGGYTGEYFSQFQPQNGNDSDSEGETPSSE
GPFDDRLDQQETIMFYGNDEIQPTEEDIAIPENRERLEWHSMLEAVLTGDVVRQEKRISATDTTANR
ATYRQELWLELRAESCGRRVPVQKRMVEDGRAMVDKLLDDVINFEVKGTLEAGKPPFEQVKDVVK
KIEKCQSMYPSWNALVAEHKSAVSPQFLEAYEAIMSWYNTNEMINTELAIKKVGNDELDFSRTKQR
SPAVDGITTDETSFLDRLMKEDGLQSLYNENAKVILKGDLVQWGMLMPISHVIKKAKETLIRNSIPFQ
KRHLPPYLDELLTLISFPSRLIEEITKTRLAYARKVKETAQQPLMDQMISQFQLLLQFAIRIKTEYLEIEKP
EPGWDLPPCIDESFDQVALEALKYYFKMLNWKLSGNKNTFKEAELLFQEWDFANDIGGSLHRGNIE
VAEQFSSLTFKALNRLSTTFERELQIKPKEAADMKRYKAALDSVRVRQRMLQRFSRMLSENYEHACD
FSISLPPDQMQLFYDHLVASGHFHVDTHGVFETLGIYLIASPEMRDRLDDVQAMLAITSADRFPDDS
GDQYILILRPEDPFVWIGEVADLIKEQIDLKRGQIRLCTTSSSAIAHARRTFLDAIDMHIDLLQESRSNI
HKVNTRLTEIRRVAYKLSNTFMDSVEIIRRQTQGKDCQELIQTCFIFATEFGQRSLLYMDSNRRQMN
NLKLTKLALDWSFICDDVASDRRTFRWAVLALEFAMGMTRGRHILALGEEEYERIRAKVGGCMSVLI
SHFDIMGARSSLAAQAEKERIENLVSQFRKDKNKMLDDDEATMSVTEQRLEKLARVDEFREGKEAE
RRALRVLETTNADRSLAYLSASATNVTVRWQQGQFVGGGTFGNVYAAMNLDTGHLMAVKEIRLQ
DPKLIPTIAESIREEMRVLEVLDHPNVVSYHGIEVHRDRVYIFMEFCSGGSLANLLEHGRIEEEEVMVY
ALQLLGLAYLHESGIAHRDIKPENILLDHNGIIKYVDFGAAKLIARQGRTMAADLHATKPNKSMTGTP
MYMSPEVIKGENPGKAGAVDIWSLGCVILEMATGRRPWANLDNEWAIMYNIAQGNPQLPTSEQL
PQGIDFLMRCFARDPKQRSSAIELLQHEWIMTIRNQVVEPATPSDASGSSQSPFVSATSTRNSIGPD
GFY

>gi|340520617|gb|EGR50853.1| map kinase [Trichoderma reesei QM6a]

MADPFAPRTMKRKNVKGLALTPAAPRPPPTADTSRRGSEVNKDDAGKEEQLEIGIEYKLDLRPEELE
VIKELGSGNGGTVSKVRHLTTGTVMARKIIHVEAKKEMRRRIVRELQIMHGCHSEHIVTFAFLNHNN
DVIMCMEYMDVGALDRVSRVFGPIRVDVLGKIAEATLGGLTYLYIKHHIMHRDIKPSNILINSRGSIKL
CDFGVSGELVNSIADTFVGTSTYMAPERIQGEKYTVKSDVWSFGLTIMELIKFPFNASEHIDDAESAP
AGILDLLQQIVNEPAPKLPKSDAFPSILEDMVQKCLFKEPEKRPTPQELYERDPFVQAAKRTPVDLKE
WAVGLMERDNRKSHLVPQLSPSGTHELLRSSDSSPQSRNEAPDGPVFGDIPIAGDRLFSPRDQGAT
QNRSPSRNGAATSRTGHPSLAPRNPASGYSDGSHHSSSNPTTFSLPVRPAPPTSSFSREGPPKSAAD
EARGQNRRQVKTYGLPPNPSYGV

>gi|340516404|gb|EGR46653.1| map kinase [Trichoderma reesei QM6a]

MSGSGSVPATPDSVTDGTRELAMQASPYSEDSSVAGTPNGDEVGDSPKRLPSLNTFADPRNMNPS
STALGILGKARHPPQPTSSFVGGVGAMENSVMAKARALHQQRMQKGMAASGSSPVSPMPSPGG
VAGFPNLRMPPAMQRPGAVPHPRSAPVIPKPSLSERRANMGMGMKLSDIGGGGNASPTGGLRR
AGAPSLAGISVNGPSVPNGKPSLGSQLDDFKKYIDAEKGWITFDGAATITRTGVEFTNGQTFILDEVE
ILDELGKGNYGTVYKVKHAKPAVPRFGQGLSGAKLAPHPHRSQSDSAVLDAASLDGRTGKIMAMK
EIRLELDDAKFTTILKELVILHECVSPYIIDFYGAFFQEGAVYMCIEYMDGGSIDLYGGIPENVLKKITFS
AIMGLKSLKDEHNIIHRDVKPTNILANTRGQVKICDFGVSGNLVASIAKTNIGCQSYMAPERISGGA
MAPGTSDGTYSVQSDVWSLGLTIIECAMGQYPYPPEASSTIFSLNAVEGEPPAMPEEGYSDLAKDFV
KGCLHKIPKMRPTYAALLKHPWIQSLSKPETIDEVAEEGEAADKVAEAVGHMDLSSGTEDAEVAEW
VKSVLKKNAEGQNGDGPTKPALHAAPLDSVSPLGSPLHQG

>gi|321262114|ref|XP_003195776.1| MAP kinase [Cryptococcus gattii WM276]

MTSPSNKPMMPRSQPPRPPHTQSTPAISSACSKLSGSPDVIRRAPSVPVNPSTATASGSLSSLLKNG
NVTQSSPPTEPKGLPRPIEPTLMPPITGQTSTSSSSSNPRCGPSSSVSRGPLGTGTLTPAVLEAPIKVSP
PQTGASRMAAAAKRGLDGSSGNNVKVYEKDHPLNEETLKQRGYWTLNILNHPFHLPNRWKLLRPL
GQGAYGLVIQVQDAETEIPIAVKCVTKVFDKIILARRALREITLLRHFGEHNTGLVDMDNVWDGYNE
IYLYMEPMEADLHQIIRSGQPLGNDHIQFFIYQLLRGMKYIHSANVIHRDLKPGNLLVNSDCELKICDF
GLARGFNPVSGEEPQGEEGKLTEYVATRWYRAPEIMLSNRRTTIDVWSIGCILAELLGLKPMFKGKD
YIEQMTLILETVGTPDEETMARVASEKALLFLKTLPTYEKKDLRSIFPDADPLAVDLTDQLLEFDHTRRI
DVPTALKHAYVEKYHDPEDEPSCDKIFDKWEVELRTIDELKAAITREINEFREEVRTAAEEDDEDEEW
AERDYLDEERVIQESPVPGSASILKEVAYPELIAPTGSAPRTREHSPSTNFTPLAEDYFTGQHGFGGPK
GRASRRSSTHSVSGRRPASLFSPGAGMTQIVPTPNTHARPHPQASPEPMVAEKPPRDRRSSGIWRT
RSRAQSQSGNLVLERLSSLEINDSKDGEKNRIDALHAMVGLGGDAEVPPITVSPSDAPASEVPKSFGY

>gi|321261878|ref|XP_003195658.1| MAP kinase [Cryptococcus gattii WM276]

MDNTPRHLFQTPNNVYILQQPWQFVKELGQGAYGCVSSARNSSTGETCAVKKVTNVFQKKILTKR
CLRELRLLHHFRGHKNITCLYDMDIVFDPPGSGQFREVYLYEELMEADLHAIIRSGQPLSDAQSFLYQ
TLCGLKYIHSANVLHRDLKPGNLLVNADCELKICDFGLARGFQPGAVQTDQGQAGFMTEYVATRW
YRAPEIMLSFANYTSSIDMWSVGCILAELLGGKPIFKGEDYVDQLNKILNLLGTPETLRRVGSPRAQD
YIRSLPIKPRVKFETLYPNASPLALDLLSKLLTFDPAKRYGCEEALEHPYLAVWHDPADEPLCEVPFDFS
FEEEDSVSGMRDLILEEVRSFRYLVRQHSMPPIRRDSHDLPPAPAQHPGAGVGPAFHEKANCEGD
MEEHPGSALEKQLERQKLS

>gi|339473242|gb|EGP88336.1| MAP kinase [Mycosphaerella graminicola IPO323]

MASPAPLLRPPIPGAGRQQTGGRMPRLGLSIPASPNQRPVNSVAAPPMTDTSAVPPLSIQTRQAPP
KLSLATPMGSSHTPQENNPARRRGPPLQIAPGLSASGASSDDSAHSRTNSFGANTTQNGSVTSSYS
ALNFVEMLRGDKDPVSATGSMYSSSSAHSVGMEREGSTQGILPDLEKLSLEKGRPLDVEDLDDAG
WKAAKKEGRIVELGSLGEGAGGAVTRCVLKGGTTVFALKIITTDPNPDVKKQIVRESNKSCASAHICQ
YYGAFMDDTAGTIGISMEFCEGGSLDSVYREVKKLGGRTGEKVLGKVAEGVLNGLTYLHGHRIIHRD
IKPSNILLTRQGGVKLCDFGVSGEFGTKGDANTFIGTSYYMAPERITQSTITSDVWSLGVTLLEVAQH
RFPFPADGTEMNPRAGLIDLLTYIVRQPIPKLKDEPENKLKWSENFKYFIECCLEKDANRRATPWHIE
GHPWIVEMKSKRVDMTQFLRTVWDWKD

>gi|339468944|gb|EGP84044.1| MAP kinase [Mycosphaerella graminicola IPO323]

MAEFVRAQIFGTTFEITSRYTDLQPVGMGAFGLVCSAKDQLTGQAVAVKKIMKPFSTPVLSKRTYRE
LKLLKHLKHENVISLSDIFISPLEDIYFVTELLGTDLHRLLTSRPLEKQFIQYFLYQILRKYVHSAGVVHRD
LKPSNILVNENCDLKICDFGLARIQDPQMTGYVSTRYYRAPEIMLTWQKYDVEVDIWSAGCIFAEML
EGKPLFPGKDHVNQFSIITDLLGTPPDDVISTICSENTLRFVQSLPKEQPLKNKFKNADPQAIELLERM
LVFDPRKRVKAGEALADPYLSPYHDPTDEPEAEEKFDWSFNDADLPVDTWKIMMYSEILDYHNVDS
ANNGEGQENGGA

>gi|336469303|gb|EGO57465.1| MAP kinase [Neurospora tetrasperma FGSC 2508]

MAPAPAPLLRPAIPGARPGGRGPPRLGLAIPPSLSVKPVGNPGAPPARAAPPQLKLATPMGSTTIPH
EQPAGRPGAQGYSASGASDSSAAHSRSGSFGPESNPTSADTRYSNVSFIGAQRPHGTPDPAVGSLY
SNASEGGVGMERENSLHGLEAFDKLTLEKARTLDVEELDDDGWRIAMMEKRVEELGPLGEGAGGA
VTKARLKGGKTVFALKIITANPDKDVAKQIVRELGFNKQCASEHICRYFGAVVDTSTISIAMEYCEGGS
LDSVYKEVKKLGGRTGERVLGKIAEGVLHGLTYLHSKKIIHRDIKPSNILLCRNGEVKLCDFGVSGDYG
TNGAANTFIGTSYYMAPERITGQSYTITSDVWSLGVTLLEVAQRFFPADGTDSQPRAGLIDLLTYIVR
QPVPKLKDEPDANIFWTDKFKYFIDCCLEKDPNRRASPWRMLDHPWMLEIRSRRVNVARFLATVW
GWEDGKEEA

>gi|336467405|gb|EGO55569.1| MAP kinase [Neurospora tetrasperma FGSC 2508]

MSSAQRGGARKISFNVSEQYDIQDVVGEGAYGVVCSAVHKPSGQKVAIKKITPFDHSMFCLRTLRE
MKLLRYFNHENIISILDIQKPRSYETFNEVYLIQELMETDMHRVIRTQELSDDHCQYFIYQRALKAMH
SANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNSGFMTEYVATRWYRAPEIMLTFKEYTK
AIDVWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYYGIKSRRAEIRSLPFKKKVPFRTL
FPNTSELALDLLEKLLAFNPVKRITVEEALKHPYLEPYHDPDDEPTAPPIPEEFFDFDKHKDNLSKEQLK
QLIYQEIMR

>gi|300155447|gb|EFJ22079.1| MAP kinase [Selaginella moellendorffii]

MRSLKGESRVVQFLGRVQTGLDDDRCIVMELAYNLSLRALLDASGQSLSGRLKVVIARDLCGGLCSL
HGRGIAHEDVKSDNVLLDFGLRAKLCDFGTARQMGDEKRAAPPGSMYHRLASDIYSLGLVELCLAS
CPLERPSCDEVLDALDHLYSSDDRDFDSFKGLLDHAIGEAERVNLACYWTDAFMDPFSVVAGVVGL
VASIDSIINLLNRVKGLLERLDQEDYARMVLAVEIYKELRSV

>gi|300154649|gb|EFJ21284.1| MAP kinase [Selaginella moellendorffii]

MEARKPYPVAASDYRVLEEIGHGRNATVHRALCVPRGEIVSIKSIDLEKCRSDLDEVRREAQTLSLIDH
PNVVAALALFIVGQRLWVVMPYMAAGSCLTIMRVARPYGLDELLVATVLRECLKALDYFHGHIHRD
VKAGNILVDQHGGVKLGDFGVSACLFDCYNRQIARRTTFAGTPCWMAPEVLDPVCGYDCSADIWS
LGITALELAQGHAPLSDLPPMKMVLVELSSPPPTLEPERAKVFSKSFKDFVACLKEASKRPTAGKLLKH
GFFKHAQSGEYLVEHLLRELPPLWEQVRELRNRDVAELGKKISLPEGEQQKQQEVVSEWNFCVADS
SSSSSTSGKGEAKPEEEEKK

>gi|300153017|gb|EFJ19657.1| MAP kinase [Selaginella moellendorffii]

MFSCLDFVSRSRPEVPAPRAHRIWILWRCLPCHRLPGFAHCGSQMVFFQRVGDVLCCPLLAKRVLR
EVCIMRRLSHRYVITLTDVFISMSMEVSGGIDLYIATEFADGGDMYHLREPLTPEHVKFLMLLTGMSY
IHSCRVWHRDLKSENILLMADMSVKICDFGLSRSAEEVVTPSYRAPEVIMSRGQYSSSIDIWSLGCIF
WVSVSSNDITILNLDVIFNVIGTPGWSDIESVPSESWRSYLKHLPGRVRNLELLGYVDQEALDLLFRM
LAFNPGRRCTAEEALSHIYVSNRLYFAFSYKYSM

>gi|300151715|gb|EFJ18360.1| MAP kinase [Selaginella moellendorffii]

MDCSASSSPIVLLREGYSNEDINDYEIDSREVECGAGSYGSVRLGVYRGQAVAVKSYNRGVSESSIRR
EVEVMRSLKGESRVVQFLGRVQTGLDDDRCIVMELAYNLSLRALLDASGQSLSGRLKVVRDLCGGL
CSLHGRGIAHEDVKSDNVLLDFGLRAKLCDFGTARQMGDNDFGEVLGTPAFMAPEKRAAPPGSM
YHRLASDIYSLGLVLQELLGDVEIVVQCLASCPLERPSCDEVLDALDHLYSSDDRFSFKGLLDHAIGEAE
RVNLACYWTDISSARAGCFSINNNTRRHLTCSPRLKAQWPSCFWVS

>gi|300151075|gb|EFJ17722.1| MAP kinase [Selaginella moellendorffii]

MTHQSPYPAYCPSPRPRVVLCEKLGCGSYSVVYRGENTQTGQQVAVKVLHDDERLSPKEVSVLSRL
DHEHIVKYIGTTTLGDGRAGILLELMKCSLASVIKESNGLDESKLRVYTRQILSGLEYLHRIVHRDVKCG
NILLDPNGKAKLADFGLAKKIDYSVAKSCKGTFVYMAPEVLLTEGTYGLAADVWSLGCTVIEMACGK
PPWSGFGMMPFYERMRDGCSPPIPPKMSTEAVSFIKLCLTRDPRRRPSAALSHPFFQERSLKV

>gi|300149596|gb|EFJ16250.1| MAP kinase [Selaginella moellendorffii]

MKCSLASVIKESNGLDESKLRVYTRQILSGLEYLHRMNIVHRDVKCGNILLDPNGKAKLADFGLAKKI
DYSVAKSCKGTFVYMAPEVLLTEGTYGLAADVWSLGCTVIEMACGKPPWSGFGMMPFYERDGCS
PPIPPKMSTEAVSFINLCLTRDPRRRPSAAALLSHSFFQKCKI

>gi|300144076|gb|EFJ10763.1| MAP kinase [Selaginella moellendorffii]

MRGFASNRRALRVAVPRQDTNISDFLTASGTFQDGDILLNRDGLRVVTQEPTTSPVDGQIALTDLEA
VKVIGKGSSGVVQLVRHKWTGQVFALKAIQMNIQETMRKQIVQEIKINQSSQCPYVVVCYFYNNG
VISIVFEYMDGGSLLDVIKEVNALPEPYLAAICKQVLKGLVYLHLDRRIIHRDIKPSNLLVNHKGEVKITD
FGVSAVLANSMGQRDTFVGTYTYMSPERISGGAYGFESDIWSLGLTLLECTRFPYLPPGQENGYLNF
YELLETIVEQPAPVASPEMFSAEFCSLISACIQKEPKDRMTAAELLKHPFIQKYENEDINLAVLVPRLPP
GA

>gi|20153214|gb|AAM13670.1|AF492766_1 MAP kinase [Gibberella zeae]

MGDLQGRKVFKVFNQDFVVDERYTVTKELGQGAYGIVCAAVNNQTNEGVAIKKVTNVFSKKILAKR
ALREIKLLQHFRGHRNITCLYDMDIPRPDNFNETYLYEELMECDLAAIIRSGQPLTDAHFQIYQILCGL
KYIHSANVLHRDLKPGNLLVNADCELKICDFGLARGFSVDPEENAGYMTEYVATRWYRAPEIMLSFQ
SYTKAIDVWSVGCILAELLGGRPFFKGRDYVDQLNQILHILGTPNEETLSRGPRAQEYVRNLPFMPKK
PFPSLFPQANPDALDLLDKMLAFDPSSRISVEQALEHPYLQIWHDASDEPDCPTTFNFDFEVVEDVG
QMRGMILDEVQRFRQNVRTVPGQSGGGLQGQGVPVPLPQGNGWTEDPRPQEYAGHGNTGLE
QDLQGGLDASRR

>gi|326431521|gb|EGD77091.1| MAP kinase [Salpingoeca sp. ATCC 50818]

MMEAQPMMTGEEQQQQQQQQQHPHHDQQHLHAHSDSIIPRGVGAPHQDPIIKGEPFRAGPRY
ANIRFIGEGAYGVVCSAVDLATQEQVAIKKICPFEHQTYCQRTLREIKILTRFKHENVRNTCACCCSCA
LDLLEKMLIFNPDKRITVEMALSHPYFEQYYDPSDEPEAEEPFTFECDVDDIGKEALKELIFQEVQASR
AREAQELAAM

>gi|325095837|gb|EGC49147.1| MAP kinase [Ajellomyces capsulatus H88]

MPDKPHRTVHWEGQVRRSSKWLLSSCRPRGRGNEFLDRFCDSQLVSYSDRAKRRRHVGEFILYRG
PQILISPCRLDTREWTVDRDVMAASSFQAFCVCLVKSKARLNTSSKNNVRIPLYAAFPQLLVSTKIAGL
QDAFLSFGGNFILITRGCDLQITGLDHSRIHGERVTIDHVYDNANQCYQAPELMLDAQTYHPAMD
MWAAGCVLAEMINGCPLFSEERCTNQLYAIIKLLGYAPGDLMDGLSSGNIIGYLSPARDWKPLRKHI
STSDNEALDLLEQLLDFDPAIRYPATQALEHVYVSLYHDLADELISDKTWSVADLDYAEWPVNDWKT
LMYVMRIHHRPVQPPIMTSLPAFPCPLPPGHVRNTPHRFPCMALSSYEMADFANGSPASTGLLSG
V

>gi|325090433|gb|EGC43743.1| MAP kinase [Ajellomyces capsulatus H88]

MYALSATGMPLNRKANSGNRSHQLNVPSRDRQDALSSGPPTATLHNPQPRDSGQANEYLVGGM
TVQEADERWPLDRVLQWLAQNGFSNHWQETFRVLNLYGASFVELGSRANGRKDLGKMHNVVYP
QNECAKSGTGWDRAKEREEGKRMRKLIRRIADQASSETANLGARYYEGHMLPSASTEDGLENSPNI
RRDSFTNFSSGTAESSPGQQYARTTPNSAQKQHSGQRSEFPTQDSRSDFSRNVFGMLDGRRHPSA
SSDNGIPLPSEDNPQSSSPGRHMVTMAHQEYVPYSAENTGRPEKRHSSDSLLSRGFASQSLFGAHG
ASRQNDSKKNGSGPSPQDQCTRQVLGESLPKEHGKGFFHKLKWKKGPDSIHAGSDENASPTSPAG
ARHLPPTSAFMRQGYDGSDMPLNERPPSSVSDYDWLQSRSRKVTTNVPQRRFALATPDGWNYRLI
DLTDVDAADTLRATICHSLGIEDPGSALIYLTELGQITHEEPLSDTMLVVNRTKSAQATLKLFVHLTTPS
ATVPVTQPTGLGLSLAERARLGRNMVSDEARNYVGTVSPSHRSQPGMKPNTNKFSPYDPRSSGEN
GNDIDLDLESREASILAAHEEYRREAERKQKAYLQSRQEHQQQESPQSIRRDGVIDFDSPRLSPYEDK
KPDNLVPLRKPPSAPSESSTLSKVNSLSRKPGDRPPRGYDTDRSKRSSAEQISEERREKPWTPTPNTPS
SGVGDGFVGAALASIGKVSSAIGKPFPSPITVSRSPRESEPVSGKGCSLQSVDLNDRDGRRNSPSSPK
LPFFSRGKGTSNFKAPHEGDGRGKILVLPDNMNLLRTDLDSSASASPSSAKISSTLAENRKSIGPDFDF
QETEVSFAKAPAAEDDSDEDSEGLFAILASAKSVMLTKMNKLSTNNGSAIQGRSAKPALTVNTGRR
GAKGMSVSFKSPIIRETSNTPPTRSTDKEIGGENEHLSNENDSLDSQEASKFNRPESIVRDDIWACRP
PVEGMIERLDDYFDVDLDEPAAHSNLDSIMSQDNTDSFGSAESTLKAKGTANTIAQRNVTRSQGGG
LNRMKSIREVAKGAHQVHRNQSIIASNARSGALLRRKSTKMFGAKIMQVKPGSRLSEHPVPLPQNP
GSQNKLPRQATFRIIGQLIGKGTYGRVYLGINADNGEILAVKQVEVNQKAAGHDKDKMKEMVSAL
DQEIDTMQHLEHPNIVQYLGCERGELSISIYLEYIPGGSIGSCLRKHGKFEENIVKSLTHQVLSGLAYHD
QGILHRDKADNILLDLDGTCKISDFGISKKTDNIYGNDVTNSMQGSVFWMAPEVVQSQGQGYSAK
VDIWSLGCVVLEMFAGRRPWSKEEAIGAIFKLGSLNQAPPIPDDVSVAITPEALAFIDTERPTAETLLS
HPFCKPDPHYNFLDTELHAKIRHVL

>gi|325090027|gb|EGC43337.1| MAP kinase [Ajellomyces capsulatus H88]

MDRPDSTSTPDTEASRSGGYFSSHPPYAVPEREYANGRQQPEGIQTTETPRSSNAGFSSVPVPASQS
AYSSWSPILTRPRGSSGSGGSMNGLETPLPPDMPAINDRDVRPQRPSGPARTPSNTYAPAPPQFTP
LSSNNQIPVATKRPSRRDPDARYRAQEKAYVQRVRQGRNEWFNFETQIPGLNFTPDSEPEEESPSSE
SQFDNDPFDPDTHLVLEDDDAQPTLEELQDPKNKERLEWYSMLASVLKGDVIREQRLIGTMEQKSR
EVWNLEIFVGARAARFGRPIPLQKKFVECQISNLGPLIEDIISFEIKGETEVGKPPLKQVEDVVEKIEKCE

SLYPSRRILQAEHPRAASEEFQESCEAIIAWHNTTMSINTELILRWVGNEELDFAKPMTMPSHAADL
SDEGSFLDRIMKEDGLKTLQSTENIYDNDKKKEPSILDGIGGVIKKAKITLIENAEAFAKRHLPPYIEELL
TLINFPSRLIQEVIRLRLSYARKMKDPALQSPILVDQMIVQFQILVAVDIKQRYLVISDPEPGWDLPPC
VDENFDNIVVDGLKYYFKLLNWKLSANKNTFKEAEILEGEWEFSNEIGRQLENGDIEVAEQFSTLTAK
SLQRLMIHFERELHSRPEEDAIETEKRYKQIFDSRRQRKLFRFSRLLRQRFENATEFNLREDMVETLSE
ALLASGHFLVTSNDSVGQKGVHLIGSPSLYGRPKDIQSILGTSFRSEDSPEDPSNPYILVVRPEKGFSW
NGKRMEVDLLEHPTDVRYGKLRVAGSQQRLQNARLALTRHTGLQLDITIEQRANLGRVNVELNKIK
KTAYKLSTGIIDSVEIIRRQSKNADNHELIQSCFAFATEFGKRSLMYMDASRRSLNHSKLINLALDWVS
FICDDCDAADRKTKWAAALEFAMIVTHGQNVLAISNEDYCHLRLKVAGCMSLLISHFDIMGARSSLA
AQAEQQHADPSGQGFRKLDLSRITDDAQASQEVQERREQLFAEIDLARIEADAKRQALGKVLEGVN
EADRSVFLSSATNITMRWQQGQFIGGGASGSVYAAIDLDTSYLMAVKEIRLQEPSLIPGAAQQIRDE
MGVLEVLDHPNIISYYGIEVHRDKVYIFMEYCSGGSLANLLEHGRIEDETVIMVYTLQMLEGLAYHQ
AGIHRDIKPANILLDHNGVIKYVDFGAAMVIARQGKTLAAMDHYSSHARDGKGHVKDASGQRKNH
KSVTGTPMYMSPELVRGEVGHTSGRHGCMDIWSLGCVILEMATGNRPWAGVDNEWAIMYIAQG
NQQLPTPDQLSLEGIDFIKRCFEIDPVKRPSATELLQHEWIVNIRQQVVAEPQTPSSDGWSTSGSLPP
SGATTRQNSSNLL

>gi|325089591|gb|EGC42901.1| MAP kinase [Ajellomyces capsulatus H88]

MGDSFKARTLKRKNVKGLALNSAGPKAGSNTSDGDAQIPGGFGNQDGNRTDTLEIGLEFKLDLRSE
DLVVLKELGAGNGGTVSKVMHASTKVIMARKIIRVDVKENVRKQIVRELQVGHDCNSPYIVYGAFQ
NEARDIVLCMEYMDCGSLDRISKDFGPVRVDVLGKIAESILAGLVYLYEVHRIMHRDIKPSNVLINSR
GNIKLCDFGVATETVNSIADTFVGTSTYMAPERIQGGAYTVRSDVWSVGLTVMLVGRFPFDATDSA
AGDRASAGPMGILDLLQQIVHEPAPKLPKSDAFPPILDEFVAKCLLKKPEERPTPRELYDKDAFLQAA
KRTPVNLREWAISMMEQHNRKSYLAPPAPKAITRDGSRDSISHSRAESPRARYTPTSGEIPLNIAREP
TSNNSSAGQMYGDPMSAIEPSSTMGFEHLSLGSATHHHPDYNHNPLQHLTSNGNGHSNNNSSIP
HSSRQYPSHPHIDTSVPQYASPMSASATTARAPIQSATLSRPPPPSGPLPAPPGSAGPGGWRTQSH
RV

>gi|325087700|gb|EGC41010.1| MAP kinase [Ajellomyces capsulatus H88]

MSSPAPLLKIPTPGANRKQAPRLKLGIPGSPKLNIANSNGAGTNPAPDVPQLSQPIPARPAPPQLRLA
TPKGSKGTPQEVSSLNNGRPSMQIVTGVSATSYNGDYGNRSRSGSFNTYDGRVSGPTSASNYSALS
FAIGLRQPPGGTPDPTSAISSVYSDRGDGGLSVERDNSMNGLLPDLEKLSLEKGRPLDVEDLDDEGW
LAASSQKKIIELDSLGEGAGGAVTRCMLKGGKTVFALKIITTDPNPDVKKQIRLNFNKDCASEHICRYY
GAFMDKSTSTISIVMEFCEGGSLDSVYREVKKLGGRTGEKVLGKVAEGVLNGLTYLHGRKIIHRDIKPS
NILLCRNGQVKLCDFGVSGEFGTKGDANTFIGTSYYMAPEITQSYTITSDVWSLGVTLLEVAQHRFPF
PADGTEMQPRAGATKTSNTVAHGGSSLDARNEKQEGQHGTFSETGVGLARLEVLDNYKALTACIR
HFTPHTVLVIIKIHQYCSNL

>gi|62858891|ref|NP_001017127.1| mitogen-activated protein kinase 1 [Xenopus (Silurana) tropicalis]

MAAAGASSNPGGGPEMVRGQAFDVGPRYTNLSYIGEGAYGMVCSAYDNVNKVRVAIKKISPFEH
QTYCQRTLREIKILLRFKHENIIGINDIIRAPTIEQMKDVYIVQDLMETDLYKLLKTQHLSNDCYFLYQIL
RGLKYIHSANVLHRDLKPSNLLLNTTCDLKICDFGLARVADPDHDHTGFLTEYVATRWYRAPEIMLN
SKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGILGSPSQEDLCINLKARNYLLSLPHKNKV
PWNRLFPNADPKALDLLDKMLTFNPHKRIEVEAALAHPYLEQYYDPSDEPVAEAPFKFEMELDDLPK
ETLKELIFEETARFQPGY

>gi|53830383|gb|AAU95083.1| MAP kinase [Apium graveolens Dulce Group]

GNSIPPIMPIGRGAYGIVCSIMNTETNEMVAIKKIANAFDNYMDAKRTLREIKLLRHLDHENIIALTDV
IPPPVRRNFSDVYIATELMDTDLHQIIRSNQVLSEEHCQYFLYQLLRGLKYIHSANIIDLKPSNLLLNSN
CDLKICDFGLARPNTDDEFMTEYVVTRWYRAPELLLNSSDYTAAIDVWSVG

>gi|47551261|ref|NP_999813.1| MAP kinase [Strongylocentrotus purpuratus]

MADQGGAKTKRTNEEKPETVRGQVFDVGPRYVTLNYIGEGAYGMVCSAVDTRHGGKVAIKKISPF
EHQTYCQRTLREIKILTRFNHENIINIQDIIKADTIEAMRDVYIVQSLMETDLYKLLKTQPLDHICYFLYQ
ILRGLKYIHSANVLHRDLKPSNLLLNTTCDLKICDFGLARIADPGHDHTGFLTEYVATRWYRAPEIMLN
SKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGVLGSPSQDKCIINEKARAYLQGLPFKSKI
PLKSLFPKADNKALDFLERMLSFNPDKRITVEEALAHPYLEQYYDPDDEPVKEEPFTFVTELDDLPKEK
LKEMIFEEASKFNPSPSPNTS

>gi|320591785|gb|EFX04224.1| map kinase [Grosmannia clavigera kw1407]

MAEFIRTQIFGTTFEITSRYSDLQPVGMGAFGLVCSARDQLTNQNVAIKKIMKPFSTPVLAKRTFREL
KLLKHLRHENVISLSDIFISPLEDIYFVTELLGTDLHRLLTSRPLEKQFIQYFLYQIMRKYVHSAGVVHRD
LKPSNILVNENCDLKICDFGLARIQDPQMTGYVSTRYYRAPEIMLTWQKYDVEVDIWSAGCIFAEML
DGKPLFPGKDHVNQFSIITELLGTPPDDVINTIASENTLRFVKSLPKEQSLRDRFKNAEDPAIDVLEKM
LVFDPKKRITATEALLHEYLAPYHDPTDEPVAEEKFDWSFNDADLPVDSWKIMMYSEILDYHNIETTE
PVVT

>gi|320582283|gb|EFW96500.1| MAP kinase [Ogataea parapolymorpha DL-1]

MSPTSKDKPSDEETHQEDSETLRSLSKLKLQIPSQGVLLSPRGTPLSSPHNTGTYTADQMLKIQTDLN
NGVPVEAIGKLDTAPEQLPTKKSVKSSPDEQPQRTPLLKTPSFHYITNGTGPISSRSSRNNYQKLRTLF
SNQSNGSSGPMSATIEGVRPHSSILRSNLNTKYSQQYQQQEMLYLNGINKFKNRYKVNDDYYNKSV
DIEDDDDPAEVTVDEDPEALKIQDKLEEFQEDLSQDDSKEFKALKALSQQGTSNEWEKPSEYRLDST
VLLDILNQSDDIQLKHTDDNAAILERLEWQSLLQSVLTGDVLTGEKTKLIKPLNEVEGESYLRASYKED
LWIGIRSKLFGRTEEDQKRLVQYHRGLVDEILDEIMNFRLMPDIQNSPYITQVKFGFDKVNDLLNRYE
RCQELWRTQKEMENEKPLCGTPEFTSRLHALIAWTSITCAIQRESDVLRKWVGNDDLDILRSPGPSS
ANSELPELESQDDQDHSDSETSSSRNKNGNIKEDSFVERIMKEKDIEDLFNKRLFASCAHWTFKAKES
YLEYQQYFEKLNLPSYVDSLLVLAMFPSKLMKELVNTRLSYAKKLRNPTMMMIDQVLEDFKLYITLAL
EIRTSFLEYCSPREGWISSLDQDADDNAILECVHHYLLLLNRKLLDSPKSSKSFRTFKEPEELEREWSFL
QNLGFYIEGGSAEVATQFSILTSKLVARLHQYMQHQFQGPPYDGTPLDKHKMVRWYTSMMENFG
QLKRKFFRFHAILFYFQNILYNLNGARMKKFLDMLKESNHVLYHNAQLAEEGVYVFASESIASKPYEV
SRILKSSHLGVDFSKIPKRHMEAAENYTYYAEPIYAEAEHFGENQNEFDESYDYVLVVYPAKAMMW
DGIVLLDLTSLIGNLDKGKVLLISKGGSSSKVDDCANWFKECVGNTIGSAVGKRCSLPKVQRELQVISK
QFFRMSCFVIDAVPSVRNQCRGIADTQELANTVFTYIRDSGRDFLRTFDNARKSVLILKLLQAIEWLSF
VDDCIPTDPKTFRWCVSALEFAMDITTGFNILTLDSEKFYRLKDKVAGCMSLLISHFDIMGARTKEM
QKKRMLNYHSISEKDLFTLDDESLSSLREHIMYQIGRLEEERRLLQVEQQSVRVLDDTDTNQFLTYLA
SSFSSVSIRWQKGKFLGGGTFGSVYASINLDTGGALAVKEIRFQDRQSIKSIVPAIKGEMTVLEMLSH
PNIVQFFGVEVHRDRVYIFMEYCSGGSLASLLEYGRIEDESVQLYTLQMLELAYLHQFGIVHRDIKPE
NILLDHMGVIKFVDFGSAKVIAMAAHGNTSNTTGGSSSSGGNGSGSGTATLNSILHSGRKTQALTG
TPMYMSPETIRGETIGKFGAIDIWSLGCCLLEMAGRRPWANLDNFAVMYHIAAGHLPQFPTNDQL
SIQGQHFLAKCLDIDPTKRLTAVELLQDPWIQAIRNEAFSDSSNSSTTELAGEHTPV

>gi|320580965|gb|EFW95187.1| MAP kinase [Ogataea parapolymorpha DL-1]

MGDNSDLSSKLQDLSIHNRGLNPNAQAKLLAFQAKRQQQHSSEELFSPARNASPILSSPSTPRTEDA
GAPGTPNLDTEEKTDSQSAEGLMRRTSFRIPKKQSETDEKALSDSRSRSHSFKTMKDPVEFGGHATK
SSDAVPSQDKPLPELPDLALSDKLDAIVRNEINQAASTEAKPPQRKQSLSQRRGMKLDFNSLTDPQS
QTSSNKSMNKLKLNMLPQRGVPSVPHNSAPAPIGGARSKPNLRLPQAQPKPAMANYAKYVDIKSG
SLNFAGKASVHSKGVDFSNGSSFRISHDDLQFLEELGRGNYGIVSKVLHRPTGIIMAMKEVRLELDDS
KFRQILMELEVLHSCVSDCIVDFYGAFFVEGAVYMCMEYMQGGSLKIGNGLNEPELAYATKCVVKG
LKQLKDDHNIIHRDVKPTNILVGDSGKVKLCDFGVSGNLVASLARTNIGCQSYMAPERIKSSTPDDAT
YTVQSDIWSLGLSILEIAKGSYPYPQETYDNIFSQLSIVDEPPTLPDDRFSKEARDFVNLCLNKNPNKRP
VYAELLSHPWLNKYDDATCQQLMAEVVADALERKREQNESSPNTSEPHVMPPLHKTQLNR

>gi|320580501|gb|EFW94723.1| MAP kinase [Ogataea parapolymorpha DL-1]

MSHSNIYKDLPPLPRHLEKDNLSSRSSSADNAIRRPALTLPIRPVTSAQVSASSVDTVDSSGGSSSGRR
PPPLFSHVSLPESSRVVQQQESTPFVSSLNIPNKPPTPFLESKSLKRKNVMKLTLATPSVSSHPSSSGM
GNVNSSASSIEQSGFKDPDKKASTDELIANIQTLELGLEYQLSIKAEELVMLKKLGSGNSGTVSKVLHL
PTQKTMARKTIHIDAKEVIQSQIIRELRIMHECDSPFIIGFYGAFLEDVVICMEYVDCGSLDKIFKLTGP
FPDFMLKHIAYSVLSGLVYLYDNHRIIHRDVKPSNVLLDSKGNIKLCDFGVSRELINSMADTFVGTSTY
MSPERIQGGVYNIKGDVWSLGLMLYELASGKFAGGPGGAAPGVSGLKGDPQIKTPDSILDLLQRIV
NERPPSLKESDGYTPELCEFVELCLKKEKDRPDPHELLKHKFLADFPEPDSLKVSAKYRSDIKKWAKNV
RRVQKGKPTK

>gi|298705650|emb|CBJ28898.1| MAP kinase [Ectocarpus siliculosus]

MAGWRSHSQRAGRETFHTDVRYSNFEPIGDGSYGFVCSADDRATGKRVAMKKVKDIFRDLGDAK
RILRELKLLRHFRPHENVVTILDIMVHPENSLDFRDVYIVTNLMESDLQKIISSTQPLTDQHFFLYQLLR
GLKYIHSANVLHRDLKPSNLVLNANCDLAICDFGLSRGVEQEGGETLTEYVQTRWYRAPELLCYSSTY
DTAVDMWSVGCIFAELLGRKPFFRGKNPMHQLQMIVDVLGCPSEEDMSFIQKARAVVLQHARQA
VTRRGTGGVRPLAVYFPTDTSPLALDLLAKMLVFNPRRRIGVVEALEHPYLADLHAQMIGKEPKCEKI
FDFDFEKEGGGSSDRLVPKKQRVIPRGELKALVLEELLVYRPSAQENLAVAKQAAEGERQQRLRQSA
SPGSWSNSPGLDAMDASGYEALSPAAQMSLGGLSPMDGVGPGMITPTPGVHGYSGAVSYGSAV
PPQDNSRGQSRAAKT

>gi|51860134|gb|AAU11317.1| MAP kinase [Alternaria brassicicola]

MGDLANRKVFKVFNQEFIVDERYNVTKELGQGAYGIVCAATNNQTGEGVAIKKVTNVFSKKILAKR
ALREIKLLQHFRGHRNITCLYDMDIPRPDNFNECYLYEELMECDLAAIIRSGQPLTDAHFQIYQILCGL
KYIHSANVLHRDLKPGNLLVNADCELKICDFGLARGFSMDPEENAGYMTEYVATRWYRAPEIMLSF
QSYTKAIDVWSVGCILAELLGGKPFFKGRDYVDQLNQILHYLGTPNEETLSRGPRAQDYVRNLPYM
QKISFQSLFKNANPDALDLLDRMLAFDPSSRISVEEALEHRYLQIWHDASDEPSCPTTFDFQFEVVEEI
PEMKKMILDEVSRFRQMVRVQPGAGAGANQAPQVPIPNNYDRAYEPRPQEAFNQGGWNGSDL
ERDLQGLDGRMR

>gi|210160945|gb|ACJ09359.1| MAP kinase [Phytophthora sojae]

MAIEPSRYGPDFHCVTVSRDVFEVRSHYVNLRPVGGGSYGIVCSAEDTLRGRKVAIKKITDVFDDLTD
AKRILREMKLLRHLGVHENIINILDVILIPPNVMDFHDIYIVTDLMESDLERIISSSQPDAHFQYFLYQIL
RGMKFVHSGNVLHRDLKPSNLLVNSNCDLSICDFGLARGVETAHNEDLTEYVVTRWYRAPELLTDC
QNYNDAVDVWAIGCIFAEMLRRRPFFTGRDPSDQLHMIIRVLGSPTEEEMSFVPHEAAKRAILQHG

FYPKRPLIEFFPDANPLAVDLLSQMLKFNPAERISVVQALAHPYLAQLQNPADEPVCAEPFNFDFERE
SLDLGVEMPKEELQRLVFQECMSIHQLHHMQ

>gi|89242511|gb|ABD64614.1| MAP kinase [Emericella nidulans]

MAEFIRSDILGTTFETTSRYANLQPVGLGTAGVVCSAYDLISEQVVAIKKMMKPFHSTSVAKRTYREV
KLLRHLRHDNLINMSDIFISPLEDVYLVTELLGTDLHRLLNGKPLESKFAQYFTYQILRKYIHSAGVIHRD
LKPGNLLINENCDLKICDFGLARVQEPQMTGYVSTRYYRAPEIMLTWQRYGSKVDLWSVGCILAEM
LLGRPLFPGTDHINQFWLITDLLGNPPDEVIDRITTNNTRRVVKSMAKNRPLKEILPAAEDAALNLLD
NLLVFDPDRRISAEQGLMHPWMAPYHDPTDEPVATEQFDWSFNDADLPLDTWKIMIYSEVLDFF
QLTTNAEPSGEQSQNQSQSQSQAFTSSQDLQLASMLNLGEGELPFAATIDPNKFGSVDYLMDGQS
LDPNSFS

>gi|538517|gb|AAB59325.1| MAP kinase [Saccharomyces cerevisiae]

MNCTLTDNTRAINVASNLGAPQQRTIFAKERISIPGYYEIIQFLGKGAYGTVCSVKFKGRSPAARIAVK
KISNIFNKEILLKRAIRELKFMNFFKGHKNIVNLIDLEIVTSSPYDGLYCYQELIDYDKVIHSSVQLSEFHIK
YFLYQILCGLKYIHSADVIHRDLKPGNILCTLNGCLKICDFGLARGIHAGFFKCHSTVQPHITNYVATR
WYRAPELLLSNQPYSKSVDIWAVGCILAEFYARKPVFMGRDSHIFEIIKVLGTPDKDILIKFGTIKAWN
LGKNSNNPVYKKIPWSNIFPFASHEAINLIESLLHWDSTHRLNVEQAISHPFLNEVRKPDDEPVCLQG
PFDFTYESELNSMSKLRDYLVEEVKNFKTDLSSL

>gi|302845375|ref|XP_002954226.1| MAP kinase [Volvox carteri f. nagariensis]

MPPPLLPSGFIRPGKGAYGTVYSAVDGQTGETVAIKVIPVTDQDREELTQIQKEIRFLADCNHPNVV
RYLGSYRHPNELWIVMEYCGGGSVSDLLSATSEPLSEDLIAYVCGEALKGLAYLHGLGKVDIKCGNILL
TTGGEVKIADFGVSAQLTATMSKRNTFIGTPHWMAPEVIQESRYDGKVDVWALGISAIEMAELRPP
RWNVHPLRVIFMIGRDPPPRLSQLDKWSPVFQDFVSQALLKVKVYVCMYVCYCTYV

>gi|302813316|ref|XP_002988344.1| MAP kinase [Selaginella moellendorffii]

MRGFASNRRALRVAVPRQDTNISDFLTASGTFQDGDILLNRDGLRVVTQEPTTSPVDGQIALTDLEA
VKVIGKGSSGVVQLVRHKWTGQVFALKAIQMNIQETMRKQIVQEIKINQSSQCPYVVVCYFYNNG
VISIVFEYMDGGSLLDVIKEVNALPEPYLAAICKQVLKGLVYLHLDRRIIHRDIKPSNLLVNHKGEVKITD
FGVSAVLANSMGQRDTFVGTYTYMSPERISGGAYGFESDIWSLGLTLLECTRFPYLPPGQENGYLNF
YELLETIVEQPAPVASPEMFSAEFCSLISACIQKEPKDRMTAAELLKHPFIQKYENEDINLAVLVPRLPP
GA

>gi|302801482|ref|XP_002982497.1| MAP kinase [Selaginella moellendorffii]

MKCSLASVIKESNGLDESKLRVYTRQILSGLEYLHRMNIVHRDVKCGNILLDPNGKAKLADFGLAKKI
DYSVAKSCKGTFVYMAPEVLLTEGTYGLAADVWSLGCTVIEMACGKPPWSGFGMMPFYERDGCS
PPIPPKMSTEAVSFINLCLTRDPRRRPSAAALLSHSFFQKCKI

>gi|302798523|ref|XP_002981021.1| MAP kinase [Selaginella moellendorffii]

MTHQSPYPAYCPSPRPRVVLCEKLGCGSYSVVYRGENTQTGQQVAVKVLHDDERLSPKEVSVLSRL
DHEHIVKYIGTTTLGDGRAGILLELMKCSLASVIKESNGLDESKLRVYTRQILSGLEYLHRIVHRDVKCG
NILLDPNGKAKLADFGLAKKIDY

SVAKSCKGTFVYMAPEVLLTEGTYGLAADVWSLGCTVIEMACGKPPWSGFGMMPFYERMRDGCS
PPIPPKMSTEAVSFIKLCLTRDPRRRPSAAALLSHPFFQERSLKV

>gi|302797897|ref|XP_002980709.1| MAP kinase [Selaginella moellendorffii]

MDCSASSSPIVLLREGYSNEDINDYEIDSREVECGAGSYGSVRLGVYRGQAVAVKSYNRGVSESSIRR
EVEVMRSLKGESRVVQFLGRVQTGLDDDRCIVMELAYNLSLRALLDASGQSLSGRLKVVRDLCGGL
CSLHGRGIAHEDVKSDNVLLDFGLRAKLCDFGTARQMGDNDFGEVLGTPAFMAPEKRAAPPGSM
YHRLASDIYSLGLVLQELLGDVEIVVQCLASCPLERPSCDEVLDALDHLYSSDDRFSFKGLLDHAIGEAE
RVNLACYWTDISSARAGCFSINNNTRRHLTCSPRLKAQWPSCFWVS

>gi|302794971|ref|XP_002979249.1| MAP kinase [Selaginella moellendorffii]

MFSCLDFVSRSRPEVPAPRAHRIWILWRCLPCHRLPGFAHCGSQMVFFQRVGDVLCCPLLAKRVLR
EVCIMRRLSHRYVITLTDVFISMSMEVSGGIDLYIATEFADGGDMYHLREPLTPEHVKFLMLLTGMSY
IHSCRVWHRDLKSENILLMADMSVKICDFGLSRSAEEVVTPSYRAPEVIMSRGQYSSSIDIWSLGCIF
WVSVSSNDITILNLDVIFNVIGTPGWSDIESVPSESWRSYLKHLPGRVRNLELLGYVDQEALDLLFRM
LAFNPGRRCTAEEALSHIYVSNRLYFAFSYKYSM

>gi|302792360|ref|XP_002977946.1| MAP kinase [Selaginella moellendorffii]

MEARKPYPVAASDYRVLEEIGHGRNATVHRALCVPRGEIVSIKSIDLEKCRSDLDEVRREAQTLSLIDH
PNVVAALALFIVGQRLWVVMPYMAAGSCLTIMRVARPYGLDELLVATVLRECLKALDYFHGHIHRD
VKAGNILVDQHGGVKLGDFGVSACLFDCYNRQIARRTTFAGTPCWMAPEVLDPVCGYDCSADIWS
LGITALELAQGHAPLSDLPPMKMVLVELSSPPPTLEPERAKVFSKSFKDFVACLKEASKRPTAGKLLKH
GFFKHAQSGEYLVEHLLRELPPLWEQVRELRNRDVAELGKKISLPEGEQQKQQEVVSEWNFCVADS
SSSSSTSGKGEAKPEEEEKK

>gi|302790403|ref|XP_002976969.1| MAP kinase [Selaginella moellendorffii]

MRSLKGESRVVQFLGRVQTGLDDDRCIVMELAYNLSLRALLDASGQSLSGRLKVVIARDLCGGLCSL
HGRGIAHEDVKSDNVLLDFGLRAKLCDFGTARQMGDEKRAAPPGSMYHRLASDIYSLGLVELCLAS
CPLERPSCDEVLDALDHLYSSDDRDFDSFKGLLDHAIGEAERVNLACYWTDAFMDPFSVVAGVVGL
VASIDSIINLLNRVKGLLERLDQEDYARMVLAVEIYKELRSV

>gi|58271510|ref|XP_572911.1| MAP kinase [Cryptococcus neoformans var. neoformans JEC21]

MTSPSAQPMIPRSQPPRPSHTQSSPAINSTGIKPNGPPSVIRRAPSVPVNPSTAAASGSLSSLLKSEN
TAQAVSRSSPPTEPNDLPRPIEPTPMLPITGLPNSSSSSSNARHGSSSSISRGPSVTGTPATTALGAPIE
PTPPQTGASKMAAAAKRGLDGSAGNNVKVYEEGHPLNEETLKQRGYQTLNILNHPFHLPDRWKLL
RPLGQGAYGLVIQVQDAETEIPIAVKCVTRVFDKVILARRALREITLLRHGHDNLTGLVDMDNVWD
GYNEIYLYMEPMEADLHQIIRSGQPLGNAHIQFFIYQLLRGMKYIHSANVIHRDLKPGNLLVNSGCEL
KICDFGLARGFNPVKGEEPQGEEGKLTEYVATRWYRAPEIMLNRYTTAIDVWSIGCILAELLGLKPVF
KGKDYIEQMTLILETLGTPDEETMARVASEKALTFLKTLPTYEKKDLGSIFPDADPLAVDLTDKLLEFDP
TRRIDVPSALTHAYVERYHDPEDEPSCDKIDKWEVESLSTIEELKEAITREIQGFREEVRMAAEEDDED
EEWAEGEYLDDENVFHDSPGPALASTLEKFTYPDHIAPTGSAPRTREHSPTTTFITSAEDYFTAQHGF
GGPNGRASRRSSSHSTSGRPASFFSPFGAGMTQIVPTPNAYPRSHAQASPELTTAEKTPRDRRSSGL
WRTRSRAQSQSGNLVLERLSSLEINDHKDGEKNRIDALHAVVGLGGDGEVPPMTVSPSDAPPSEVP
KSFGY

>gi|58271314|ref|XP_572813.1| MAP kinase [Cryptococcus neoformans var. neoformans JEC21]

MDNTPRHLFQTPNNVYILQQPWQFVKELGQGAYGCVSSARNSSTGETCAVKKVTNVFQKKILTKR
CLRELRLLHHFRGHKNITCLYDMDIVFDPPGSGQFREVYLYEELMEADLHAIIRSGQPLSDAQSFLYQ
TLCGLKYIHSANVLHRDLKPGNLLVNADCELKICDFGLARGFQPGAVQTDQGQAGFMTEYVATRW
YRAPEIMLSFANYTSSIDMWSVGCILAELLGGKPIFKGEDYVDQLNKILNLLGTPETLRRVGSPRAQD
YIRSLPIKPRVKFETLYPNASPLALDLLSKLLTFDPAKRYGCEEALEHQYLAVWHDPADEPLCEVPFDFS
FEEEDSVSGMRDLILEEVRSFRYLVRQQSMPPARKDSHELPPAPAQHPGAGVGPAFHERANSEGD
MEEHPGSALEKQLERQKLS

>gi|300260431|gb|EFJ44650.1| MAP kinase [Volvox carteri f. nagariensis]

MPPPLLPSGFIRPGKGAYGTVYSAVDGQTGETVAIKVIPVTDQDREELTQIQKEIRFLADCNHPNVV
RYLGSYRHPNELWIVMEYCGGGSVSDLLSATSEPLSEDLIAYVCGEALKGLAYLHGLGKVDIKCGNILL
TTGGEVKIADFGVSAQLTATMSKRNTFIGTPHWMAPEVIQESRYDGKVDVWALGISAIEMAELRPP
RWNVHPLRVIFMIGRDPPPRLSQLDKWSPVFQDFVSQALLKVKVYVCMYVCYCTYV

>gi|46849992|gb|AAT02418.1| MAP kinase [Schistosoma japonicum]

MVRVLVKNQVFEVSPRYTDLNYIGEGAYGMVVDAFDTLKGEKVAIKKTSPFEHQTFCQRTYRELKIL
LGFSHENIIDIKNIILVGNTLEDMKDVYIIQTLMDTDLYKLLKTQELSGEHICYFLYQVLLKYIHSANVLH
RDLKPSNLLLNATCDLKICDFGLARVNDPEHDHMGMLTEYVATRWYRAPEIMLSSKSYTKAIDIWSV
GCIFGEMLNRRPLFPGKHYIEQLTLILGVLGTPSREDQVWIVNDKARGVKFKYSPRKSWKEIYSSADA
KTIDLLDRLLTFNPTTRITVEEALAHPYFEHYYDPSDEPVARKPFSFEEELDNLPVRQLKKMIFQEVNQ
FREPD

>gi|531125|gb|AAA20888.1| MAP kinase [Mus musculus]

MSQERPTFYRQELNKTIWEVPERYQNLSPVGSGAYGSVCAAFDTKTGHRVAVKKLSRPFQSIIHAKR
TYRELRLLKHMKHENVIGLLDVFTPARSLEEFNDVYLVTHLMGADLNNIVKCQKLTDDHVLIYQILRG
LKYIHSADIIHRDLKPSNLAVNEDCELKILDFGLARHTDDEMTGYVATRWYRAPEIMLNWMHYNQT
VDIWSVGCIMAELLTGRTLFPGTDHIDQLKLILRLVGTPGAELLKKISSESANIQSLAQMPKMNFANV
FIGANPLAVDLLEKMLVLDSDKRITAAQALAHAYFAQYHDPDDEPVADPYDQSFESRDLLIDEWKSL
TYDEVISFVPPPLDQEEMES

>gi|529040|gb|AAA74301.1| MAP kinase [Homo sapiens]

MSQERPTFYRQELNKTIWEVPERYQNLSPVGSGAYGSVCAAFDTKTGLRVAVKKLSRPFQSIIHAKR
TYRELRLLKHMKHENVIGLLDVFTPARSLEEFNDVYLVTHLMGADLNNIVKCQKLTDDHVLIYQILRG
LKYIHSADIIHRDLKPSNLAVNEDCELKILDFGLARHTDDEMTGYVATRWYRAPEIMLNWMHYNQT
VDIWSVGCIMAELLTGRTLFPGTDHIDQLKLILRLVGTPGAELLKKISSESANIQSLTQMPKMNFANV
FIGANPLAVDLLEKMLVLDSDKRITAAQALAHAYFAQYHDPDDEPVADPYDQSFESRDLLIDEWKSL
TYDEVISFVPPPLDQEEMES

>gi|485755|gb|AAA28677.1| MAP kinase [Drosophila melanogaster]

MEEFNSSGSVVNGTGSTEVPQSNAEVIRGQIFEVGPRYIKLAYIGEGAYGMVVSADDTLTNQRVAIK
KISPFEHQTYCQRTLREITILTRFKHENIIDIRDILRVDSIDQMRDVYIVQCLMETDLYKKTQRLSNDHIC
YFLYQILRGLKYIHSANVLHRDLKPSNLLLNKTCDLKICDFGLARIADPEHDHTGFLTEYVATRWYRAP

EIMLNSKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGVLGSPSRDDLECIINEKARNYLES
LPFKPNVPWAKLFPNADALALDLLGKMLTFNPHKRIPVEEALAHPYLEQYYDPGDEPVAEVPFRINM
ENDDISRDALKSLIFEETLKFKERQNAP

>gi|468151|gb|AAC50101.1| MAP kinase [Homo sapiens]

MSLHFLYYCSEPTLDVKIAFCQGFDKQVDVSYIAKHYNMSKSKVDNQFYSVEVGDSTFTVLKRYQNL
KPIGSGAQGIVCAAYDAVLDRNVAIKKLSRPFQNQTHAKRAYRELVLMKCVNHKNIISLLFTPQKTLE
EFQDVYLVMELMDANLCQVIQMELDHERMSYLLYQMLCGIKHLHSAGIIHRDLKPSNIVVKSDCTL
KILDFGLARTAGTSFMMTPYVVTRYYRAPEVILGMGYKENVDIWSVGCIMGEVHKILFPGRDYIDQ
WNKVIEQLGTPCPEFMKKLQPTVRNYVENRPKYAGLTFPKLFPDSLFPADSEHNKLKASQARDLLSK
MLVIDPAKRISVDDALQHPYINVWYDPAEVEAPPPQIYDKQLDERHTEEWKELIYKEVMNSEEKTK
NGVVKGQPSPSAQVQQ

>gi|289125|gb|AAB41548.1| MAP kinase [Medicago sativa]

MEGGGAPPADTVMSDAAPAPPQMGIENIPAVLSHGGRFIQYNIFGNIFEVTAKYKPPIMPIGKGAY
GIVCSAHNSETNEHVAVKKIANAFDNKIDAKRTLREIKLLRHMDHENVVAIRDIVPPPQRENDVYIAY
ELMDTDLHQIIRSNQALSEEHCQYFLYQILRGLKYIHSANVLHRDLKPSNLLLNANCDLKICDFGLARV
TSETDFMTEYVVTRWYRAPELLLNSSDYTAAIDVWSVGCIFMELMDRKPLPRDHVHQLRLLMELIG
TPSEDDLGFLNENAKRYIRQLPPYRRQSFQEKFPHVHPEAIDLVEKMLTFDPRKRITVEDALAHPYLTS
LHDISDEPVCMTPFSFDFEQHALTEEQMKELIYREALAFNPYQ

>gi|258470|gb|AAA11604.1| extracellular-signal-regulated kinase 1 [Rattus norvegicus]

MAAAAAAPGGGGGEPRGTAGVVPVVPGEVEVVKGQPFDVGPRYTQLQYIGEGAYGMVSSAYDH
VRKTRVAIKKISPFEHQTYCQRTLREIQILLGFRHENVIGIRDILRAPTLEAMRDVYIVQDLMELYKLLKS
QQLSNDHICYFLYQILRGLKYIHSANVLHRDLKPSNLLINTTCDLKICDFGLARIADPEHDHTGFLTEYV
ATRWYRAPEIMLNSKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLHLGILGSPSQEDLNCIINM
KARNYLQSLPSKTKVAWAKLFPKSDSKALDLLDRMLTFNPNKRITVEEALAHPYLEQYYDPTDEPVAE
EPFTFDMELDDLPKERLKELIFQETARFQPGAPEAP

>gi|297816426|ref|XP_002876096.1| map kinase [Arabidopsis lyrata subsp. lyrata]

MEISSASDDSIPYVETDPSGRYGRFREVLGKGAMKTVYKAFDQVLGMEVAWNQVKLNEVFRSPEPL
QRLYSEVHLLKNLNHESIIRYCTSWIDVNRRTFNFITELFTSGTLREYRRKYQKVDIRAIKARQILNGLAY
LHGHDPPVIHRDLKCDNIFVNGHLGQVKIGDLGLAAILRGSQNAHSVIGTPEFMAPELYEEDYNELV
DIYSFGMCVLEMLTGEYPYSECTNPAQIYKKVTSGKLPDSFHLIQHTEARVGKCLETVSRRLPAKELLG
DPFLAATDERDLAPLCRLPQQLAIQNLASNGTVVQHLPSTTDPTRTTDMSITGKMNSEDHTIFLQVQ
ILDGDGHMRNIQFPFNILSDTPLEVALEMVKELEIVDWDLEAAMIENEISLLVPNWRANDSSIRHQG
FGHEDDEDNGEAEGRTRLFSSASSSHDSHVAVRENNDDSSNDVIPDMDDGNKSSNRLLDSSTYHYS
PAIDDDQSQQQRRRVRLQQKMRSLVDTRTQVLRSLELINKRRGRGFDPNANELQPQPSSTDFIRRC

>gi|297321934|gb|EFH52355.1| map kinase [Arabidopsis lyrata subsp. lyrata]

MEISSASDDSIPYVETDPSGRYGRFREVLGKGAMKTVYKAFDQVLGMEVAWNQVKLNEVFRSPEPL
QRLYSEVHLLKNLNHESIIRYCTSWIDVNRRTFNFITELFTSGTLREYRRKYQKVDIRAIKARQILNGLAY
LHGHDPPVIHRDLKCDNIFVNGHLGQVKIGDLGLAAILRGSQNAHSVIGTPEFMAPELYEEDYNELV
DIYSFGMCVLEMLTGEYPYSECTNPAQIYKKVTSGKLPDSFHLIQHTEARVGKCLETVSRRLPAKELLG
DPFLAATDERDLAPLCRLPQQLAIQNLASNGTVVQHLPSTTDPTRTTDMSITGKMNSEDHTIFLQVQ

ILDGDGHMRNIQFPFNILSDTPLEVALEMVKELEIVDWDLEAAMIENEISLLVPNWRANDSSIRHQG
FGHEDDEDNGEAEGRTRLFSSASSSHDSHVAVRENNDDSSNDVIPDMDDGNKSSNRLLDSSTYHYS
PAIDDDQSQQQRRRVRLQQKMRSLVDTRTQVLHRSLMELINKRRGRGFNANELQPQPSSTDFIRR
C

>gi|123187081|gb|ABM69251.1| MAP kinase [Candida glabrata]

AKTEAFRNRIDTLDSWLNFKRNFEEKIHYIRNWVVGTKDPETQVVVDINDDDAIFRHYAHEFADQM
IKEKDIEAIFQKRIFFPLAPWILKAKLFFLKNRDTLNELNLMYLNDQLEMLLMFPMRLVKDQLRLSYAK
KLQKPTMMMIDQMIDDFNSYIRVAVQMKFTVISYCQGWQFTVNIDPQFDDTVVEAIRHLFILLELK
LLDGGGKSTNAFKEPDILLKYWDGLKNCGHYIDGAGKVIAIEFTKLTLRLVHLSYLLQQQNSPPKLTNE
AEAEKWLVQLFETLGSMKRKLNRFTNVLMKAFQNSVTYRIDDHAQLMNGLKDTGHFLVYTGGKLE
KQGIYLIASPELLGCPENEILKVLYNSDSGCDLIPKLEIENSLTYNVAEKWDLSTSIVQGVGKDGLPRYYL
QNGNVDAQFRPPNLNSGKSHVAEMYNDDRDPDADILELEMKLNSLGYILVLCPQEPMLWSGEVF
NLSEFTTEEINDLDFKTRPDTIKLMCQSSSYALEYCDRLQSASDCVTFLEKRCSFEVVENNLQKLNKAY
FRC

>gi|290992997|ref|XP_002679120.1| map kinase [Naegleria gruberi]

MESQQQLINNKSSDESLASLATMIDSTLNIKKEDDLDMKPMKDEKVKKKKKKKSSSCSTSSEEQMYK
NQPVVIDSEGQCSKNRTIIGGFNGHKYEIGKVISFQKSNVNGHPTIYSNRPIKVLGSIGVVNERSSRRV
GQDRLNTYGVEIGTNKYAWVTETVIDEFECNREKNPVAATSSMDITTTPSSFIGSSDSSSNSSFPPLLV
NDNNSSDDANDPMAKKRKRDLFTQPLSSMVPKMDMSFLQPFPNFPPFGTPKAHLPQPELKLQLLS
MSPSRAHSKISTHFVIYVSLNENDLLMKSSLITHLFSPFSLPTTICFIEKANPSNVYNITRKHILTPLQEGL
RHDLEIFSYTPIIKENNLECIVKLMYGHHEILTCDNGLDQFFGEENSIGLGQNASLQEVRDEDNFLDDL
DELTSGVLENQSSVNEMDSMNLFDQFEMSPMDSTEKFEEFKLKRDYNGHSLLHHFSAREMYNQV
YELLKLGYNPMERDKMGFNVLDWCKYYNLEMYEIQNFIAHRSFESPTVTPNSVEMNLPSEIENSSAY
LTDYLDSLLHSDFTLEDVNSFMLKLLKKVSNSFPNNLLLNPDTNLLISKQRHDTEVLVDFTDLENNNN
LELLPRLSLRYWAPEILLMMCNALVERNISSIISKQNIWTIGVILTELMYLSRKENKERNSIFGLIVSEHL
LPLNQFKVLGKCDELRKLIEDISIPRQPHSPLFSFSNMEGINEKEKERIIFEMNERTLQSKRNSFSFALDS
CSEVADLISRFTWNPAERITIEQIIEHPYWLENSESNKMNAIKESIMKQKLLAQVEYFSPLADISILTHH

>gi|290986280|ref|XP_002675852.1| map kinase [Naegleria gruberi]

MPQDNPFEIPATSSSDVGLTRDSTFMNQQDPSPSTTTTTTNLLLSKTPSSLKTKKVKSRQLGLSITAPS
SDQYPEEDPAGMGDEIPSFLLDEQSAAIVQPGKVISTIGTLPTSSSSPIPVRLLSNLSDKRPSSSVSSPSS
SIADNFNNIANNTTTSVQVTPLRMSRKGTSDVKKKKGPMLKLEVPVKTKLANEFTVSHSGTWKAED
ILIGRGGLISEKLDSATTTPSSSENLSVSELHSANSSSSITPLSGTSASPIGEVTRGSKKIAYEDLKIYKTKL
GEGASGKVYRAHLKNDKTQQFALKVIDIYAENVTPKQILSEIKSLCDSVQCDNIVKFYEAYHREGSIRIL
MEYMNCGALDDIYRTTGSIPEDVLSEISFQLKLAYLAEKGVIHRDIKPANVLLNKNGVTKLTDFGMSN
QNLKSKDFKTFQGTFYYMSPERLKGLTHSVDSDIWSVGVLIAECAIGGLPFTKGAEVSVWTLLKHVQ
SNPEVVTIKPGEVSDEFFDFIKCMEEPINRPSAKQLLNHPYIKKYIKDQDNFKPVRTAKWLKEVYLPKK
KEKEEQKNLDFNTLSDIVTNSFQLKQ

>gi|284092735|gb|EFC46376.1| map kinase [Naegleria gruberi]

MESQQQLINNKSSDESLASLATMIDSTLNIKKEDDLDMKPMKDEKVKKKKKKKSSSCSTSSEEQMYK
NQPVVIDSEGQCSKNRTIIGGFNGHKYEIGKVISFQKSNVNGHPTIYSNRPIKVLGSIGVVNERSSRRV
GQDRLNTYGVEIGTNKYAWVTETVIDEFECNREKNPVAATSSMDITTTPSSFIGSSDSSSNSSFPPLLV

NDNNSSDDANDPMAKKRKRDLFTQPLSSMVPKMDMSFLQPFPNFPPFGTPKAHLPQPELKLQLLS
MSPSRAHSKISTHFVIYVSLNENDLLMKSSLITHLFSPFSLPTTICFIEKANPSNVYNITRKHILTPLQEGL
RHDLEIFSYTPIIKENNLECIVKLMYGHHEILTCDNGGLDFQFFGEENSIGLGQNASLQEVRDEDNFLD
DLDELTSGVLENQSSVNEMDSMNLFDQFEMSPMDEKFEEFKLKRDYNGHSLLHHFSAREMYNQV
YELLKLGYNPMERDKMGFNVLDWCKYYNLETMYELIQNFIAHRSFESPTVTPNSVEMNLPSEIENSS
AYLTDYLDSLLHSDFTLEDVNSFMLKLLKVNSFPNNLLLNPDTNLLISKQRHDTEVLVDFTDLENNNN
LELLPRLSLRYWAPEILLMMCTNALVPERNISSIISKQNIWTIGVILTELMYLSRKENKERNSIFGLIVSE
HLLPLNQFKVLGKCDERKIEDISIPRQPHSPLFSFSNMEGINEKEKERIIFEMNERTLQSKRNSFSFALD
SCSEVALDLISRIFTWNPAERITIEQIIEHPYWLENSESNKMNAIKESIMKQKLLAQVEYFSPLADISILT
H

>gi|284089451|gb|EFC43108.1| map kinase [Naegleria gruberi]

MPQDNPFEIPATSSSDVGLTRDSTFMNQQDPSPSTTTTTTNLLLSKTPSSLKTKKVKSRQLGLSITAPS
SDQYPEEDPAGMGDEIPSFLLDEQSAAIVQPGKVISTIGTLPTSSSSPIPVRLLSNLSDKRPSSSVSSPSS
SIADNFNNIANNTTTSVQVTPLRMSRKGTSDVKKKKGPMLKLEVPVKTKLANEFTVSHSGTWKAED
ILIGRGGLISEKLDSATTTPSSSENLSVSELHSANSSSSITPLSGTSASPIGEVTRGSKKIAYEDLKIYKTKL
GEGASGKVYRAHLKNDKTQQFALKVIDIYAENVTPKQILSEIKSLCDSVQCDNIVKFYEAYHREGSIRIL
MEYMNCGALDDIYRTTGSIPEDVLSEISFQLKLAYLAEKGVIHRDIKPANVLLNKNGVTKLTDFGMSN
QNLKSKDFKTFQGTFYYMSPERLKGLTHSVDSDIWSVGVLIAECAIGGLPFTKGAEVSVWTLLKHVQ
SNPEVVTIKPGEVSDEFFDFIKCMEEPINRPSAKQLLNHPYIKKYIKDQDNFKPVRTAKWLKEVYLPKK
KEKEEQKNLDFNTLSDIVTNSFQLKQ

>gi|35384078|gb|AAQ84550.1| MAP kinase [Trichoderma atroviride]

MADLQGRKVFKVFNQDFVVDERYTVTKELGQGAYGIVCAAVNGQTNEGVAIKKVTNVFSKKILAKR
ALREIKLLQHFRGHRNITCLYDMDIPRPDNFNETYLYEELMECDLAAIIRSGQPLTDAHFQIYQILCGL
KYIHSANVLHRDLKPGNLLVNADCELKICDFGLARGFSVDPEENAGYMTEYVATRWYRAPEIMLSFQ
SYTKAMDVWSVGCILAELLGGRPFFKGRDYVDQLNQILHILGTPNEETLRRGPRAQEYVRNLPFMP
KKPFPALFPDANPDALDLLDKMLAFDPSQRISVEQALEHPYLHIWHDASDEPDCPTTFNFDFEVVED
VGDMRKMILDEVLRFRQLVRTAPASGNQAAAQQIQVPMPQAGGQTADPRPQEYMGHANGLEQ
DLAAGMDIRR

>gi|24286498|gb|AAN46679.1| MAP kinase [Strongylocentrotus purpuratus]

MADQGGAKTKRTNEEKPETVRGQVFDVGPRYVTLNYIGEGAYGMVCSAVDTRHGGKVAIKKISPF
EHQTYCQRTLREIKILTRFNHENIINIQDIIKADTIEAMRDVYIVQSLMETDLYKLLKTQPLDHICYFLYQ
ILRGLKYIHSANVLHRDLKPSNLLLNTTCDLKICDFGLARIADPGHDHTGFLTEYVATRWYRAPEIMLN
SKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGVLGSPSQDKCIINEKARAYLQGLPFKSKI
PLKSLFPKADNKALDFLERMLSFNPDKRITVEEALAHPYLEQYYDPDDEPVKEEPFTFVTELDDLPKEK
LKEMIFEEASKFNPSPSPNTS

>gi|19852119|gb|AAM00014.1|AF493611_1 MAP-kinase [Acetabularia acetabulum]

DCFYVLLSDSYQVKLADFGMSKMKEDTYFSETMVKGTPAYIAPEAFKGESVDEKCDIYALGLIMWE
MVAKQRPWQDLNLPVVIMARVAIKGERPPIPNGNTF

>gi|15076937|gb|AAK82989.1|AF284814_1 MAP kinase [Blumeria graminis]

LCDFGLARGFSVDPEENAGYMTEYVATRWYRAPEIMLSFQSYTKAIDVWSVGCI

>gi|15076935|gb|AAK82988.1|AF284813_1 MAP kinase [Blumeria graminis]

LHRDFKPSNLLLNANCDLRVCDFGLARSAASQEDCSGFMTEYVATRWYRAPEIMLTFKEYTKAIDV
WSVGCI

>gi|13430383|gb|AAK25816.1|AF348490_1 MAP kinase [Neurospora crassa]

MSSAQRGGARKISFNVSEQYDIQDVVGEGAYGVVCSAVHKPSGQKVAIKKITPFDHSMFCLRTLRE
MKLLRYFNHENIISILDIQKPRSYETFNEVYLIQELMETDMHRVIRTQELSDDHCQYFIYQRALKAMH
SANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNSGFMTEYVATRWYRAPEIMLTFKEYTK
AIDVWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYYGIKSRRAEIRSLPFKKKVPFRTL
FPNTSELALDLLEKLLAFNPVKRITVEEALKHPYLEPYHDPDDEPTAPPIPEEFFDFDKHKDNLSKEQLK
QLIYQEIMR

>gi|10798897|gb|AAG23132.1|AF205375_1 MAP kinase [Botryotinia fuckeliana]

MTARAPNPASGSRKISFNVSEQYDIQDVVGEGAYGVVCSALHKPSGQKVAIKKITPFDHSMFCLRTL
REMKLLRYFNHENIISILDIQKPRNYESFTEVYLIQELMETDMHRVIRTQDLSDDHCQYFQTLRALKA
MHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNSGFMTEYVATRWYRAPEIMLTFKE
YTKAIDVWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYYGIKSRREYIRSLPFKKKVPF
KTMFPKTSDLALDLLEKLLAFNPVKRITVEEALKHPYLEPYHDPEDEPTANPIPEEFFDFDKNKDNLTK
EQLKKLIYDEIMR

>gi|7385125|gb|AAF61706.1|AF226711_1 MAP kinase [Kluyveromyces lactis]

MNEYDAVDRHTFKVFNQDFTVDKRFQLIKEIGHGSYGIVCSARFTEAADETTVAIKKVTNVFSKTLLC
KRSLRELKLLRHFRGHKNITCLYDMDIVFQPDGMFNGLYLYEELMECDMHQIVKSGQPLAHYQSFIY
QILCGLKYIHSADVLHRDLKPGNLLVNADCQLKICDFGLARGYSENPVENNQFLTEYVATRWYRAPEI
MLSYQGYTKAIDVWSCGCILAELLGGKPIFKGKDYVDQLNRILQVLGTPPELKRIGSKNVQDYIHQLG
YIPKIPFSTLYPNANPDALNLLEGMLSFDPQLRITVDDALQHPYLSIWHDPADEPICTEKFDFSFESVN
EIEQLKQMVIDEVTDFRQYVRLPLLHEQQQQQGKTDGGFDQREDQRTFQAQLEEQVNNGRTASN
VPSFDEPFSSQMMGSASQQDPLVGIHSDNLPSHELDFPPRPSENVLDSPMGLSHQQTHNGSPECQ
DINDLLGLERELEFGLDRQFNETVWYIASSTLFVEHLLLFCYT

>gi|5007038|gb|AAD37790.1|AF149424_1 MAP kinase [Ipomoea batatas]

MVGGGDFLAVQTHGGQYVQYDIFGNLFEVTSKYAPPITPIGRGAYGIVCSALNAETNEMVAIKKIAD
AFDNYMDAKRTLREIKLLRHLEHENVIAIKDVIPPPLRREFNDVYIATELMDTDLHQIIRQGLSEEHCQ
YFLYQILRGLKYIHSANVIHRDLKPSNLLLNSNCDLKICDFGLARTNLDNEFMTEYVVTRWYRAPELLL
NSSDYTAAIDVWSVGCIFMELMNRKPLFQGKDHVHQMRLITELLGTPTSLGSIQNENARRYIRQLPL
RPRQQLANGFPHVHPLAIDLMDKMLTFNPSKRITVEEALAHPYLAQLHDKSDEPICPVPFTDFEKQA
YGEEQIKDMIYQEALAMNPGYA

>gi|2795859|gb|AAB97138.1| MAP kinase [Drosophila melanogaster]

MSVSITKKFYKLDINRTEWEIPDIYQGLQPVGSGAYGQVSKAVVRGTNMHVAIKKLARPFQSAVHA
KRTYRELRLLKHMAHENVIGLLDIFHPHPANGSLENFQQVYLVTHLMDADLNNIIRMQHLSHVQFL
VYQILRGLKYIHSAGVIHRDLKPSNIAVNEDCELRILDFGLARPTENEMTGYVATRWYRAPEIMLNW
MHYDQTVDIWSVGCIMAELITRRTLFPGTDHIHQLNLIMEMLGTPPAEFLKKISEARSYIQSLPPMK

GRSFKNVFKNANPLAIDLLEKMLELDAEKRITAEEALSHPYLEKYAEPSVEQTSPPYDHSFEDMDLPV
DKWKELIYKEVTNFKPPPSYAQVLKDVK

>gi|2191146|gb|AAB61033.1| MAP Kinase [Arabidopsis thaliana]

MSAESCFGSSGDQSSSKGVATHGGSYVQYNVYGNLFEVSRNAATNSETGEEVAIKKIGNAFDNIIDA
KRTLREIKLLKHMDHENVIAVKDIIKPPQRENFNDVYIVYELMDTDLHQIIRSNQPLTDDRLLRGLKYV
HSANVLHRDLKPSNLLLNANCDLKLGDFGLARTKSETDFMTEYVVTRWYRAPELLLNCSEYTAAIDI
WSVGCILGETMTREPLFPGKDYVHQLRLITELIGSPDDSSLGFLRSDNARYRQLPQYPRQNFAARFP
NMSAGAVDLLEKMLVFDPSRRITVDEALCHPYLAPLHDINEEPVCVRPFNFDFEQPTLTEENIKELIYR
ETVKFNPQDSV

>gi|66810219|ref|XP_638833.1| extracellular response kinase [Dictyostelium discoideum AX4]

MSSEDIDKHVLRKYEVLQKIGKGAYGIVWKAIDKKTKQTVALKKIFDAFQNATDAQRTFREIMFLQE
LHGHENIIKLLNVIKADNDRDIYLVFEHMETDLHAVIRAKILEEIHKQYTIYQLLKALKYSANVLHRDIKP
SNLLLNSECLVKVADFGLARSITSLESIAEANPVLTEYVATRWYRAPEILLGSTKYTKGVDMWSIGCIL
GELLGEKAMFPGNSTMNQLDLIIEVTGRPSAEDIEAIKSPFAGTMLSPPSNPRSLSDMYPSASVDAL
DLLKKLLQFNPDKRITAEEALAHPFVTQFHNPAEEPHFDRIIKISIDDGQKFPIAEYRNRLYNDIIKKKKE
ERKKQTNPTKPDTTAPTLST

>gi|285005033|emb|CBG37782.1| MAP kinase [Pisum sativum]

ALAHPYLTSLHDISDEPVCTTPFSFDFEQHALTEEQMKELIYREALAFNPE

>gi|257222594|gb|ACV52575.1| MAP kinase [Nicotiana benthamiana]

PPIMPIGKGAYGIVCSALNSETNEHVAIKKIANTFDNKIDAKRTLREIKLLRHMDHENIVAIRDIIPPPQ
REAFNDVYIAYELMDTDLHQIIRSNQGLSEEHCQYFLYQILRGLKYIHSANVLHRDLSNLLLNANCDLK
ICDFGLARVTSETDFMTEYVVTRWYRPPELLLNSSDYTAAIDVW

>gi|106640241|gb|ABF82263.1| MAP kinase [Cicer arietinum]

MAGVNQNGVAEFVAVPTHGGQFVQYNVFGNLFEVTAKYRPPIMPIGRGAYGIVCSLLNTETNELV
AVKKIANAFDNHMDAKRTLREIKLLRHLDHENVIGLRDVIPPPLRREFMMSTLPPNSWILIFSFAPIKI
CQMNTASTFCIKFFVGLRYIHSANIIHRGLKPSNLLLNANCDLKIIDFGLARPTMESDFMTEYVVTRW
YRAPELLLNSSDYTSAIDVWSVGCIFMELMNKKPLFPGKDHVHQMRLLTELGPTDADIGLVKNEDA
RRYIRQLPQYPRQPLNRVFPHVHPLAIDLVDKMLTVDPTRRITVEEALAHPYLEKLHDVADEPVCTEP
FSFEFEQQHLDEEQIKEMIYREALALNPEYA

>gi|33150458|gb|AAP97127.1| MAP kinase [Oreochromis mossambicus]

CQRTLREIKILLRFKHENIIGINDIIRAPTIEQMKDVYIVQDLMETDLYKLLKTQHLSNDHICYFLYQILR
GLKYIHSANVLHRDLKPSNLLLNTTCDLKICDFGLARVADPDHDHTGFLTEYVATRRAPEIMLNSKGY
TKSIDIWSVGCILAEMLSNRPIFPGKHYFDQ

>gi|5802574|gb|AAD51717.1| MAP kinase [Ipomoea batatas]

YFLYQILRGLKYIHSANVIHRDLKPSNLLLNANCDLKICDFGLARPNIENEFMTEYVVTRWYRAPELLL
NSSDYTGAIDVWSVGCIYMELMNRKPLFPGKDHVHQMRLLTE

>gi|1110512|gb|AAA83210.1| MAP kinase [Aplysia californica]

EIVRGQTFEVAPRYTNLTYIGEGAYGMVVSATDNQTKQKVAIKKISPFEHQTYCQRTLREIKILTRFKH
ENIIDIRDILRAPTVEDMKDVYIVQCLMETDMYKLLKTQQLSNDHVCYFLYQILRGLKHSANVLHRDL
KPSNLLLNTTCDLKICDFGLARVADPDHDHTGFLTEYVATRWYRAPEIMLNSKGYTKSIDVWSVGCIL
AEMLANRPLFPGKHYLDQLNHILGVLGSPSQEDLQCIINDKARGYIQSPKPKVPWNKLYPNADVKAL
DLLEKMLTFNPNKRITVEQALAHPYLEQYYDPADEPVAEEPFTFEMELDDLPKERLKELIFQETLQIQD
KNLEHS

>gi|60467416|gb|EAL65439.1| extracellular response kinase [Dictyostelium discoideum AX4]

MSSEDIDKHVLRKYEVLQKIGKGAYGIVWKAIDKKTKQTVALKKIFDAFQNATDAQRTFREIMFLQE
LHGHENIIKLLNVIKADNDRDIYLVFEHMETDLHAVIRAKILEEIHKQYTIYQLLKALKYSANVLHRDIKP
SNLLLNSECLVKVADFGLARSITSLESIAEANPVLTEYVATRWYRAPEILLGSTKYTKGVDMWSIGCIL
GELLGEKAMFPGNSTMNQLDLIIEVTGRPSAEDIEAIKSPFAGTMLSPPSNPRSLSDMYPSASVDAL
DLLKKLLQFNPDKRITAEEALAHPFVTQFHNPAEEPHFDRIIKISIDDGQKFPIAEYRNRLYNDIIKKKKE
ERKKQTNPTKPDTTAPTLST

>gi|60466138|gb|EAL64201.1| extracellular signal-regulated protein kinase [Dictyostelium discoideum AX4]

MEPEFDHFQSQMDSDNTHQSTMFNVQDNNAILMSGMENVLQSPRQLQAAAQAQQQAAAQA
QQQQVQAQQVQAQQAQQQQQQQQQNQQQQQQQQNQQNQQQQQNQQQQSQQMTQQQL
QQLMPPPPTSDTFNDNISYFVYGSQFTVPRRYSIVKCIGHGAYGVVCSAKDNLTGEKVAIKKISKAFD
NLKDTKRTLREIHLLRHFKHENLISIKDILKPNSKEQFEDVYIVSELMDTDLHQIITSPQPLSDDHCQYFY
MLRGLKHIHSANVLHRDLKPSNLLINEDCLLKICDLGLARVEDATHQGFMTEYVATRWYRAPEVILS
WNKYTKAIDIWSVGCIFAELLGRKPLFQGKDYIHQITLIIETIGSPSEEDICNIANEQRQIRNMGNQPK
VNFANMFPKANPDAIDLLERMLYFDPSKRLTVEEALAHPYFQSLHDPSDEPICLHKFSLNFEAWDLN
RDLLKELIYNEMLAYHPEDPQAPYYTDLNNPNFNLSRIQSSSELFNLLQQKQIHQQVNQQSIKN

>gi|254566023|ref|XP_002490122.1| MAP kinase [Komagataella pastoris GS115]

MGNKDNSTNIPIRTVSSQKYADLEIKQFSPTYETSTIQENEGKGGRSTTRKQVTSTTIPSTTKMTPELL
NPQSTKTFQAKTLKRKNLKKLQLENNIHADDGDTEIISSNDLVHSFQNLELGLEYQLSHDDLLTLKLLG
SGNSGSVSKVLHIPSKKTMARKVIHVETKKTVLTQIVRELRIMYECNSPYIINFYGAFLHEGDVTICME
YVDCGSLDRVLKLVGPFEEFILAHVAFSTLCGLNYLYDSHKIIHRDKSNVLLNSKGGVKLCDFGVSRELI
NSIAQTFVGTSTYMSPERIQGGKYSVKGDVWSLGLMLIELATGKFPFGDNSSMGPDSILDLLQRVV
NEKPPSLDPEKFSSQLCDFVNLCLKKESERPNPIELRHFLKDCKQENTKAKVKRWATNVRRILKGKD
MGNKVRNTKQ

>gi|254265812|emb|CAQ86894.1| MAP Kinase [Acremonium chrysogenum]

LGQGAYGIVCAAVNNQTNEGVAIKKITNVFSKKILAKRALREIKLLQHFRGHRNITCLYDMDIPRPDN
FNETYLYEELMECDLAAIIRSGQPLTDAHFQSFIYQILCGLKYIHSANVLHRDLKPGNLNADCELKIADF
GLARGFSIDPEENAGYMTEYVATRWYRAPEIMLSFQSYTKAIDVWSVGCILAELLGGRPFFKGRDYV
DQLNQILHILGTPNEETLFSHRIPPRPRNTFVTWATCPRSPSPGSFPKQR

>gi|224009836|ref|XP_002293876.1| map kinase [Thalassiosira pseudonana CCMP1335]

MADVVDPHVLRHCDVGKKLGQGAYGIVWKAINRTSGATVALKKCFEAFRCNTDAQRTYREVMYL
RALSDHENIVKIESVINADNDRDLYIVFADYMETDLNQVIRARILEEIHIRFIVYQLLKALKYTAKILHRDI
KPSNLLIDASCRVKVCDFGLCRSIADDDEQPSESLLMTDYVATRWYRSPEVLMGSKKYTEGLDLWSV
GCILGEMFRSRPLLSGTSTMNQLEKIFELTGNPTAKDVKSWQSSFATTILDNVQAKSQVKLGELCPEL
PKGAKHLMKSLIKLDPRGTAESALEHEYLADFHDPESEPSFPRGPIKVSRRKYLSRIHELFMAYQRTPS
FDHCFLLKLGINDKTKLSADQYRLQIYASIVKEKRGEVLLKGKIVKQKEAKRSSTIKDTTPPSSTPEVPSS
LYRSDTTDTVASTVSYA

>gi|238029918|emb|CAY67841.1| MAP kinase [Komagataella pastoris GS115]

MGNKDNSTNIPIRTVSSQKYADLEIKQFSPTYETSTIQENEGKGGRSTTRKQVTSTTIPSTTKMTPELL
NPQSTKTFQAKTLKRKNLKKLQLENNIHADDGDTEIISSNDLVHSFQNLELGLEYQLSHDDLLTLKLLG
SGNSGSVSKVLHIPSKKTMARKVIHVETKKTVLTQIVRELRIMYECNSPYIINFYGAFLHEGDVTICME
YVDCGSLDRVLKLVGPFEEFILAHVAFSTLCGLNYLYDSHKIIHRDKSNVLLNSKGGVKLCDFGVSRELI
NSIAQTFVGTSTYMSPERIQGGKYSVKGDVWSLGLMLIELATGKFPFGDNSSMGPDSILDLLQRVV
NEKPPSLDPEKFSSQLCDFVNLCLKKESERPNPIELRHFLKDCKQENTKAKVKRWATNVRRILKGKD
MGNKVRNTKQ

>gi|225560024|gb|EEH08306.1| MAP kinase [Ajellomyces capsulatus G186AR]

MDRPDSTSTPDTEASRSGGYFSSHPPYAVPEREYANGRQQPEGIQTTETPRSSNAGFSSVPVPASQS
AYSSWSPILTRPRGSSGSGASMNGLETPLPPDMPAINDRDVRPQRPSGPARTPSNTYAPAPPQFTP
LPSNNQIPVATKRPSRRDPDARYRAQEKAYVQRVRQGPNEWFNFETQIPGLNFTPDSEPEEESPSSE
SQFDNDPFDPDTHLVLEDDDAQPTLEELQDPKNKERLEWYSMLASVLKGDVIREQRLIGTMEQKSR
EVWNLEIFVGARAARFGRPIPLQKKFVECQISNLGPLIEDIISFEIKGETEVGKPPLKQVEDVVEKIEKCE
SLYPSRRILQAEHPRAASEEFQESCEAIIAWHNTTMSINTELILRWVGNEELDFAKPMTMPSHAADL
SDEGSFLDRIMKEDGLKTLQSTENIYDNDKKKEPSILDGIGGVIKKAKITLIENAEAFAKRHLPPYIEELL
TLINFPSRLIQEVIRLRLSYARKMKDPALQPILDQMIVQFQILLKVAVDIKQRYLVISDPEPGWDLPPC
VDENFDNIVVDGLKYYFKLLNWKLSANKNTFKEAEILEGEWEFSNEIGRQLENGDIEVAEQFSTLTAK
SLQRLMIHFERELHSRPEEAVETKRYKQIFDSVRVRQRKLFRFSRLLRQRFENATEFNLREDMVETLSE
ALLASGHFLVTSNDSVGQKGVHLIGSPSLYGRPKDIQSILGTSFRSEDSPEDPSNPYILVVRPEKGFSW
NGKRMEVLLEHPDVRYGKLRLVADGSQQRLQNARLALTRHTGLQLDITIEQRANLGRVNVELNKIK
KTAYKLSTGIIDSVEIIRRQSKNADNHELIQSCFAFATEFGKRSLMYMDASRRSLNHSKLINLALDWSFI
CDDDAADRKTFKWAVAALEFAMIVTHGQNVLAISNEDYCHLRLKVAGCMSLLISHFDIMGARSSLA
AQAEQQHADPSGQGFRKLDLSRITDDAQASQEVQERREQLFAEIDLARIEADAKRQAGKVLEGVEA
DRSVTFLSSSATNITMRWQQGQFIGGGASGSVYAAIDLDTSYLMAVKEIRLQEPSLIPGAAQQIRDE
MGVLEVLDHPNIISYYGIEVHRDKVYIFMEYCSGGSLANLLEHGRIEDETIMVYTLQMEGLAYLHQA
GIVHRDIKPANILLDHNGVIKYVDFGAAMVIARQGKTLAAMDHYSSHARDGKGHVKDASGQRKNH
KSVTGTPMYMSPELVRGEVGHTSGRHGCMDIWSLGCVILEMATGRPWAGVDNEAIMYKIAQGS
QPQLPTPDQLSLEGIDFIKRCFEIDPVKRPSATELLQHEWIVNIRQQVVAEPQTPSSDGWSTSGSLPP
SGVTTRQNSSNLL

>gi|225559588|gb|EEH07870.1| MAP kinase [Ajellomyces capsulatus G186AR]

MGDSFKARTLKRKNVKGLALNSAGPKAGSNTSDGDAQIPGGFGNQDGNRTDTLEIGLEFKLDLRSE
DLVVLKELGAGNGGTVSKVMHASTKVIMARKVGHDCNSPYIVTVYGAFQNEARDIVLCMEYCGSL

DRISKDFGPVRVDVLGKIAESILAGLVYLYEVHRIMHRDIKPSNVLINSRGNIKLCDFGVATETVNSIAD
TFVGTSTYMAPERIQGGAYTVRSDVWSVGLTVMELAVGRFPFDATDSAAGDRSGPMGILDLLQQI
VHEPAPKLPKSDAFPPILDEFVAKCLLKKPEERPTPRELYDKDAFLQAAKRTPVNLREWAISMMEQH
NRKSYLAPPAPKAITRDGSRDSISHSRNAEASPRARYTPTSGEIPLIAEPTSNNSSAGQMYGDPMSAI
EPSSTMGFEHLSLGSATHHHPDYNHNPLQHLTSNGNGHSNNNSSIPHSSRQYPSHPHIDTSVPQYA
SPMSASATTARAPIQSATLPSRPAPPPSGPLPAPPGSAPGGRTQSHRV

>gi|225557849|gb|EEH06134.1| MAP kinase [Ajellomyces capsulatus G186AR]

MLSSQPQYSAGLPLHTPSQLPSSISTPYMSLPSHKSGLPTATRDGPFSSPTESEFSDGYDGLDSVRSW
DEKQVIDWLHSIRCGQYEALFKANHFNGDNLLDCDQKILQEMGIKKIGDRVRIFVAIKQNKNVSNRK
KRNRASLAALDSAQYTPPSSESPRPANSRQQAAGNRRWSRQVDLPSLTGYNTSYTTSGRTSSRPSSP
PADSDRGLRSYRYPGVSPMENSRREQGEVPQTARTVMHIRQNPSMDGITMSLPNSPVIRVIHSGG
QTKVLNIKHCKTPEDIFICVLRKLLLPESHYRNYCFYVLDGLDPNPGNCRRLTDSELLKICDGLHRSERG
RLILRKIHAGEPEPEELQRAAQIALDESQTAHLNALSGTNVRQILQKLTGESWHNIRQPLSPLSATDR
NREEFQRPTPSERHQSAKLRSFFGARPPSEMIIHELTSYFPSHQKEDIEKTMRLSVRRSQRMSRAASR
LSVVSNLSYASSLKDAPPIPSIADTWLAGNNGARPRPLSVSKFNLTQTSFRDSIASSLQPLQEESPIEPN
RKSYVSFDSGSDHTPGETDRQTFLDETISLSATDGAGSINERLSIIVAEDGEEQDDGLTAFLAGDNFG
NKNWMKGSLIGEGSFGSVFLLHSIGELMAVKQVELPSATKGTEFDQRKNSMVTALKHEIDLLQGLQ
HPNIVQYLGTSTDEQHLNIFLEYVPGGSIAMMLKQYNTFQEPLIKNFVRQILAGLSYLHSRDIIHRDIK
GANVLVDNKGGKISDFISKRVEASTVLGSGANLGGGGHIHRPSLQGSVYWMAPEVVRQTAHTKKA
DIWSLGCLVVEMFIGAHPFPDCSQLQAIFAIGSNQARPPPPENASKEAMAFLDMTFEINHEKRPSA
DELLSSFLSQTI

>gi|225556692|gb|EEH04980.1| MAP kinase [Ajellomyces capsulatus G186AR]

MSSPAPLLKIPTPGANRKQAPRLKLGIPGSPKLNIANSNGAGTNPAPDVPQLSQPIPARPAPPQLRLA
TPKGSKGTPQEVSSLNNGRPSMQIVTGVSATSYNGDYGNRSRSGSFNTYDGRVSGPTSASNYSALS
FAIGLRQPPGGTPDPTSAISSVYSDRGDGGLSVERDNSMNGLLPDLEKLSLEKGRPLDVEDLDDEGW
LAASSQKKIIELDSLGEGAGGAVTRCMLKGGKTVFALKIITTDPNPDVKKQIRLNFNKDCASEYGAFM
DKSTSTISIVMEFCEGGSLDSVYREVKKLGGRTGEKVLGKVAEGVLNGLTYLHGRKIIHRDIKPSNILLC
RNGQVKLCDFGVSGEFGTKGDANTFIGTSYYMAPERITGQYTTSDVWSLGVTLLEVAQHRFPFPAD
GTEMQPRAGLIDLLTYIVRQPIPQLKDEPDNGIKWSENFKYFIECCLEKEPRRRATPWRMADHPWM
LEMKSKKVNMAHFLKQVWGWQD

>gi|220970548|gb|EED88885.1| map kinase [Thalassiosira pseudonana CCMP1335]

MADVVDPHVLRHCDVGKKLGQGAYGIVWKAINRTSGATVALKKCFEAFRCNTDAQRTYREVMYL
RALSDHENIVKIESVINADNDRDLYIVFADYMETDLNQVIRARILEEIHIRFIVYQLLKALKYTAKILHRDI
KPSNLLIDASCRVKVCDFGLCRSIADDDEQPSESLLMTDYVATRWYRSPEVLMGSKKYTEGLDLWSV
GCILGEMFRSRPLLSGTSTMNQLEKIFELTGNPTAKDVKSWQSSFATTILNQAKSQVKLGELCPELPK
GAKHLMKSLIKLDPNKRGTAESALEHEYLADFHDPESEPSFPRGPIKVSRRKYLSRIHELFMAYQRTPS
FDHCFLLKLGINDKTKLSADQYRLQIYASIVKEKRGEVLKGIVKQKEAKRSSTIKDTTPPSSTPEVPSSLY
HRRSDTTDTVASTVSYA

>gi|222354892|gb|ACM48257.1| MAP kinase [Phytophthora infestans]

MSSQDGAGRASEDKNGDGVYVTKNRSLFSMWLHGKAIPSRSGPAVVFRSADVIQEGYLLKQGLRL
KMWSRRYFILRLEERHMTLGYYTSKDSLTLCSETPIGPGHLLGHVNTTKYPRRLELRCGTKVLEAEDQ

KSYEAWKNALQEAIRWNHAMVPSKDGSFVTYGKQATEDIKQEERSRAEAAKKLREKQRADEAAAA
ANAANKPKYLPATRPGTQCFMTSNTRFEIPSHFEYVKTIGSGAYGVVISATSSQTTVAIKNIQRAFDD
LTDAKRIVREIKLMRHLNHKCVLGVEDIFEPVALSKFEDVYIVSQLMATDLHRVIYSRHALSDEHIAFF
MYQMLCAMKYVHSANVIHRDLKPSNVLVNANCELKICDFGLARGFPEELELTEYVVTRWYRAPEIM
LGCMKYTREVDVWSMGCIFAEMMSRKPLFPGQDYIDQLHLIMNALGAPNDQDLYFLSNARARKF
MNAEFQKRGPNPTKPLAHMFADSPPDALDLLQKMLVIDPNRISDEALAHPYLAAIRNVEDETTATS
SFDFDFENEKLTKPVLQRLIWDEMRHFHPEVGDETATEGDDSSVATTQASITPVTPVTPATVEQDTT
ETTSDSSDAPVKVSTPTASEEAKPEDEDGEQHSTNSDKIHRTDKLTDAQTRQEAGEPAREVA

>gi|222354890|gb|ACM48256.1| MAP kinase [Phytophthora ramorum]

MSSRGSQDAGRASEDKAGDGVYVTKNRSLFSMWLHGKAVPSRTNPAVVFRSADVIQEGYLLKQGL
RLKMWTRRYFILRLEERHMTLGYYTSKDSLTLCSETPIGPGHVLGHVNSAKFPRRIELRCGTMILDAE
DQKSFEAWKNALQEAIRWNHAMVPTKDGSFVTYGKQASEDLKQEERSRAEAAKKLREKQRADEA
AAAANAANKPKYLPATRPGTQCFMTSNTRFEIPSTFEYVKTIGSGAYGVVISATDSTKTLAVKNIQRA
FDDLTDAKRIVREIKLMRHLNHKCVLGVEDIFEPLALSKFEDVYIVSQLMATDLHRVIYSRHALSDEHI
AFFMYQMLCAMKYVHSANVIHRDLKPSNVLVNANCELKICDFGLAGVPEEELELTEYVVTRWYRAP
EIMLGCMKYTREVDVWSMGCIFAEMMSRKPLFPGQDYIDQLHLIMNALGAPNDQELYFLTNARA
RKFMNAEFQKRGPNPTKPLAHMFTDSPPDALDLLQKMLVIDNKRSVDEALAHPYMASIRNVEDET
TATSSFDFDFENEKLTKPVLQKLIWDEMRHFHPEVGDEAAASANSGEGENDSFATTQASNTPVTPV
TPATAEEDSAATSEITEITATAVEVSTPATEEAKPEDGDGQQSATSDQKLDRTSVDVGKLPTDAQTR
QEAGEPAREVA

>gi|222144621|gb|ACM46122.1| MAP kinase [Hyaloperonospora parasitica]

MSALNSSPAAEEKTGDGVYVTKNRSLFSMWLHGKSVPSRAHPAVVFRSADVIQEGYLLKQGLRLKL
WTRRYFILRLEERHMTFGYYTSKDSLTLCTETPIGPGHLLGQVNTTKYPRRLELRCGTKVMEAEDQRS
FEAWRNALQEAIRWNHAMVPTKDGSFVTYGKQASEDLKQEERSRAEAAKKLREKQRVDEAAAAA
NAASKPKYLPATRPGTQCFMTSNTKFEIPSSFEYVKTIGSGAYGVVISATDAKTGTAVKNIQRAFDDL
TDAKRIVREIKLMRHLNHKCVLGVEDIFEPVALSKFEDVYIVSQLMATDLHRVIYSRHGLSDEHIAFFM
YQMLCAMKYVHSANVIHRDLKPSNVLVNANCELKICDFGLARGVPEELELTEYVVTRWYRAPEIML
GCMKYKCEVDVWSMGCIFAEMMSRKPLFPGQDYIDQLHLIMNALGAPNDQELYFLSNARARKFM
NAEFQKRGPNPTKPLAQMFADAPPDALDLLQKMLVIDPNKITVDALAHPYLASIRNVEDETTAISSF
DFDFENETLTKPVLQKLIWDDMRHFHPEVCEGSSASGNSDERGSNSLATTQTSITPVTPPTHGTAEG
DKSESTETSARATDTDVQGSMPATEEEVTQEDAAAANVDEKRRSAGDRKTIRTSIDAGKPTDALTE
QEAGEPAREVA

>gi|222144619|gb|ACM46121.1| MAP kinase [Phytophthora capsici]

MSAQDEDKNGDGVYVTKSRSLFSMWLHGKAAPSKAHPAVVFRSADVIQEGYLLKQGLRLKMWTR
RYFILRLEERHMTLGYYTSKDSLTLCSETPIGPGHVLGQVNSKFPRRLELRWGTKMMILEAEDTYEA
WRNALQEAIRWNHAMVPTKDGSFVTYGKQASEDQKQEERSRAEAAKKLRDKQRADEAAAAANA
ANKPKYLPATRPGTQCFMTSNTRFEIPSNFEYVKTIGSGAYGVVISATDSKSGKTVAIKIRAFDDLTDA
KRIVREIKLMRHLNHKCVLGVEDIFEPVALSKFEDVYIVSQLMATDLHRVIYSRHALSDEHIAFFMYQ
MLCAMKYVHSANVIHRDLKPSNVLVNANCELKICDFGLARGVFPEEELLTYVVTRWYRAPEIMLGC
MKYTREVDVWSMGCIFAEMMSRKPLFPGQDYIDQLHLIMNALGAPNDQELYFLTNARARKFMNA
EFQKRGPNPTKPLAHMFTDSPPDALDLLQKMLVIDPNKRISVDDLAHYLASIRNVDDETTATSSFDF
DFENEKLTKPVLQRLIWDEMRQFHPEVGDTNEGDNDSVATTQASITPVTPATSATEQEDSARSETV
VKVSTPATEEAKPEDDAPTTEPSSNSDKDQRTSINGKTDAQRQEAGEPAREVS

>gi|157874981|ref|XP_001685899.1| map kinase; mitogen activated protein kinase [Leishmania major strain Friedlin]

MPATKSLAELQAEVRRLDDRYLLERIIGAGSYGVVIRARDTKSDNRLVAMKRVNKEIFEEVILAKRILR
EIKLLAHFNDDNIIGLRNILTPKDPENFDHFYIVMDIMETDLKQVLRSGQELTEAHIQIYQALRALHIIH
SAGVIHRDITPANILVNTNCDLKICDFGLAKEENDQGEYMTDYVTMRWYRAPELVMEDKDYSVQID
VWGIGCILGELLGSRPLFQGKDRVNQLDKIVDVIGTPSEEDINSVGSSAAQKYLKKKSHRPQADWRQ
RYPKASPEALDLLRHMLVFKRRITVLQAMRHPFLEQLHDDADDNLSYTLFRFDENEQKTIMDVKRAI
YKESVKFHNEHPSSMRATTMYSAFNTPSVAAPSVATEGEGRSAQQTIEKNIPEDVAEGNFDREQV

>gi|157871574|ref|XP_001684336.1| map kinase; mitogen-activated protein kinase [Leishmania major strain Friedlin]

MDNYDVLEVIGEGTYGVVFKCRDKRTNRIVAVKQFKNFQTNAYVRVAMLRELRVEQLLKSEPNVTQ
LLETFKQKNRVYLVMEYIPRSLLDVLEEVQHGLPEDSLVVLLFTILLGIRSCHRNGIIHRDPENILVRDD
GAASLCDFGFCRPLPRQLQPQAPPSSHQLSISSHDIGSSASPMVESGSFGLRPLPPPNNAPQMCNA
ASVSSENSAMLSELVLADHQAIMTNYVATRWYRSPEMLLGMSSYTYAVDMWVAIMAEAIDGEPLL
PGKTELEQLSLIQTRIGDFPAAYEAAVRKQNGGMLRLRSLNPLAAPPQQLRTKSMQQKSRRASDVR
DAAQKRTESKQSTSSYLTERYGGRIAKAGLNLLHGLLRIDAAERITEELGHPYFDSVRGRFDATANGA
RRVCNSNGACDEAADMRPTTAETAESMLMPLTTAASRQAPLPPLTATGAVDCTSPFLSTSDAAGG
GSSPCLVAAAPPLVEVPFSLVDRVGAGADDDGGGPLQMPGAESPRVTTVAWGASSSSPGSRAPCG
VAGSNSSASDSSSLSLWTASDTSAEVDPPTDVTAAKDHVSFPGLSSVLVSLHPESPKPTETDGHHAA
AAACNRAAEGSNSTPRQLAPEEDNNDDQPVLRRAASEANTRAIQRDASMHSYDCSSTSLFQSRQR
QHSPRDARQLRHRTSSLESGGSVTALRGSDSSRTNTAAQEASGAGGAVSATAASGMDVPASLSVL
QSRRTAQRRSGSVVNSRLSSSKISAASACTASPPLLAKSYSFKSIPTSRSKALAPAEVQSTSKYDLMQS
VPEDHTEKRRRPSGPASSPRCQDSRGSVEKRAAANSKGAHTCSSSSMTFNALRSARGDPGCTGGLG
SATKERHSSVGRRIDGHGLHVPAAPSVNATTPGSSCRATAQEPVEVSSLRRRSTAKSRPPQQPGRRT
STPTARAGIANGTLHSPALTKPLFVRSSPEASASLSVSDARVGGGKKRGLSRFVSPNVPREVRPLPAP
ERVTLLQEIESGFLVGTPAVEVLAPVVAAPVSHTPRHAESKTDAGGGARGRNEGDTRASAIARADHL
VRASQPPEMLDNDVQPDGHRGGGNSTSLLTLGETRRQCSGTASSRASAAKRGTAASGETSAFVEG
AASSEEDHGRQQNQRPPHPCGSTGGRPPRTDVNSLSGNTSTHSANATTVGSSRAAPSLIFRSARTA
SSPLKLATIHPSSFAVQGEGELRELSTSGCHAKTSASTGMSFTAPSNSVDSPPTCRLAPALLRHHPTTA
VGACSQAYASLGPDPVFGSSAFSAHSPLVAKGSARSPTLSPNPQKRSDADARRVSMESPIVSLSGKR
QQRRLSDIPIELSLSEELFADSAACGPRGGRRRHENTTPLSTTPPITMPDDLETVLMGTPSASRRDQR
PQDEVPCTATWSSARSGTTAMMSSNMPGNSTPFRGLDGDSDGLSAPFEGKGSAAKTEAVDITART
TRHGVAPSLFAAVPKGVPALNEDDVRSVCETPSLPIRGSLEACGAGNSSTSSRKIPGPSAPPQPLLGG
ASVLSAQQLHAGGGRRKSRLVL

>gi|157868084|ref|XP_001682595.1| map kinase; mitogen activated protein kinase [Leishmania major strain Friedlin]

MERYTVMGQLGDGSFGTVSKAQNTSTGEIVAVKKMKQRFHSWEECLQLREIQSLRKVQHPNLVKL
KEVVREKTELFMIFEYCEKNIFQIQRQRADEMSGTVAFSDKEIRSIMCQTLLGVQAIHKAGFRDLKPE
NLLISGDLVKVADFGLAKEIRSRPPFTEYVSTRWYRAPELVLHSTHYNSPVDIWACAVIFAELYLCRPLF
PGTSESDQLFKICSVLGSPAPNEWDEGYQLARRMNMRFPTVAPTPLRHILTPPAAVDLMAQMLRF
NPAERPTATQCLQHPYFTGSGGSSALYAGIATGQPHNPFQMAASSAVAAQSMSNVGLTSNSSPPP
TTSNASLFKYANLFNQGNRSPLSVSSTSAPFSGSSALQGSVTSSNIRSTTQRKTSVPNAADSDDEFNF

>gi|154343978|ref|XP_001567933.1| map kinase [Leishmania braziliensis MHOM/BR/75/M2904]

MPATKSLAELQAEVCRLDDRYRLERIIGAGSYGIVIRARDIKSDNCLVAIKRVNKEIFDEVVLAKRILREI
KLLAHFNDENIIGLRNILTPEDPENFEHFYIVMDIMETDLKQVLRSGQELTEAHIQIYQVLRALHIIHSA
GVIHRDITPANILVNTNCDLKICDFGLAKEENDQGEYMTDYVTMRWYRAPELVMEGKDYSVQIDV
WGIGCILGELLGSRPLFQGKDRVNQLDKIVDLIGTPSDEDISSVGSAAAQKYLKKKGYRPRPDWRQR
YPNASVQALDLLRRMLVFNQRITVLQAMRHPFLDQLHDDADDSITYTPFHFDEQKQKTVLDVKRAI
YEESVKFHKAHQSSMQTTSMNNTFNSISMPAPSVATEGEGRSAQQTIEKDIPESTTDGNFDRDQA

>gi|154340271|ref|XP_001566092.1| Map kinase [Leishmania braziliensis MHOM/BR/75/M2904]

MDHYDVLEVIGEGTYGVVFKCRDKRTNRIVAVKQFKSFQSNAYVRVAMLRELRVEQLLKGEPNVTQ
LLETFKQKNRLYLVMEYIPRSLLDLLEEARHGLPEDSLMVLLFTILLGIRSCHRNGIIHRDPENILVRND
GTASLCDFGFCRPLPRELQPQPQQQPHQHSTSSKDVGSLASPMTGNGSFGQGSLQSPYSTPQVRN
GASASTANSAVLSELVLADHQAIMTNYVATRWYRSPEMLLGMPSYTYAVDMWVAIMAEAIGGEP
LLPGKTELEQLSLIQTRIGDFPAAYEAAVRKRNGGMLRTKSTQQKSRRPRDARGGAQENVEAKQGT
SLYLTNHYGGRITMAGMDLLHRLLRVDAAERIAVEDALEHPYFDDIRGFDAVNGDHAAFSSQDACH
KTTEMQATTAHQEPFPPLTATRAIHSTSPFFCTPGVAGGGGSPCLEAVAPPLVEVPISLLDKSTEVQD
DGGSPLPMPCRAARSPRLTSVAWEASASSSASRAACVVATDSSVNSSSFSLWTSSDTSAKVAPPTD
VTAEEGHDPLPQLSSVLIPLALESPKVNETITDCAAAARDRAAGDGNSPPLRLVLEEVKSGGRVVPRS
QAAREGTNARAVQHDASVIIEDCSSTSLFQSRSHHSRDVRLLRRRTSSLKDSARVRALTRAGSLPMN
AFAQEPGGAGGAACEDVVGDMDFSTPLSLPKTRRATKKERDDVMKTRPLPHRGTAANAFRTKSPS
SLLAQSCSFKSMLASRSKPQEQSLAPVVEPPKHRLTHSAREGHAEKLRHLSGAMSAPRSQGSRGGV
DKSTAATSNGARPCNNNSGTSIALPSTRGGTGRSGGLASVAKERRSRTGKGRDRSVGRVFPAAPSC
VSETALASSFRAAAQGLAEIVQRHQGPNLHPSPQRRRRTCTPTGRAGTANGNPYSLALSKPLFARSP
PEVSAALAVSNTRGGGSKSPGHLRYASPQLPCEVRPLPVQERVTLLREIESLSISVGTPSAVEVLAPVA
AVPASHRPKYEWDIDSSDVHGRNQGGTTDFPITSAEPVVPTSQPPNQLGNGVRPDEDHCSGDADS
LLTLFETEKQFSAMTVKRDTVASGATSAPGKRTADSKPEDDGWEKCLQRPPHSGGSTSGCSPRMES
SSLAGASTHTANVTGGSCRVARSLIFRSYRTASSPLRLAAIHPFSPTNQREGLPSELSISNHHESFSAST
GMSFKTPPNTTNSAHTRRLAPALLRHHHFTTAAGDYSLQTPIALGPDPVFGRSSFSAQSPCVSSSAR
SPFSPAPQQLSGVDGQHALIESQLLSLSGARQQRRLSNPIELSLSGELLEDSAAGVPRGGYRGHENST
LLSSTPPTTTHDDLETVVLMETPPAHRHTNQQRQHRVHSSGSWSPTRTGMRVMSCSMPDNSTSR
GLDREADESPAHRERKGSVATADVVDTPAGATRHNTVPELFPAAPTRLLGCDEDDVISISNTSPLSM
RGSLNAFGTVNDISRSSRERVGLSLAPPQPLLGGSSVLSAQQLHAGGRRKSRLML

>gi|154335818|ref|XP_001564145.1| Map kinase [Leishmania braziliensis MHOM/BR/75/M2904]

MERYTVMGQLGDGSFGTVSKAQNTSTGEIVAVKKMKQRFHSWEECLQLREIQSLRKVQHLNLVKL
KEVVREKTELFLIFEYCEKNIFQIQRQRADQMSGTIAFSDKEIRSIMCQTLLGVQAIHKAGFRDLKPEN
LLISGDVVKVADFGLAKEIRSRPPFTEYVSTRWYRAPEIVLHSTHYNSPIDIWACAVIFAELYLCRPLFP
GTSESDQLFKICSVLGSPAPNEWDEGYQLARRMNMRFPTVAPTPLRQILTPPAAVDLMEQMLRFN
PAERLTATQCLQHPYFTGIGGSSALYAGIATGQPHNPFQIASSGVSASQSISNVGLTSNSSPPPTTSN
VSLFKYANLFNQGNRSPLSVSSTSAPFSGSSALQGNLNSSNIRSPAQRKISVTNTADSDDEFNF

>gi|124087404|ref|XP_001346842.1| MAP kinase [Paramecium tetraurelia strain d4-2]

MSKEEDHSEVEDHILRRFDLQEYKGKGAYGIVWKAYDTKTKQIVALKKVFDAFQNSTDAQRTYREV
VFLKQLNNHDNIVKLISVIRADNNKDLYMVFEYMETDLHRVIRAELLNNMHIQYVMYQILKKYIHSG
QLVHRDLKPANILINADCHIKVADFGLSRCLSETENNNEIPIMTEYVATRWYRAPEILFGSHYYSTAVD
MWSVGCILGEMILGKACFAGTSTLDQIDKIIQLIGKPTLSDLESINAPMGYIEQMDSKKQFSYHQFFP
KANDLQIDFIKKLLVYNPKKRLTAEQALDHPYLKDFKQTEPEILLDQYITIPFNDNKKLKLQDYRDALYK
GLITKKSNNLVASNYSSYLTNKMSRNEPNPNSIVVKSDTQYFKQPTNQQQQVRCKSRLDQRSESVSK
KIAQTQYFNTQDIMRIQRQTDKSKSFHIDEEMPTVHKSITKQQLLDQQVPTTTHQKQQEKSYNRMK
PSNGSKLSESKENSRINSVEGTINNHLLAQAQYNFHKRLQKKKQVSEGQPHPGQQNQKPKQIPKKS
KTPDLKNYQMVHSRSLSQNKNISVSRSSSKPKTRGSPYYSEGKVLNSQPDMNCSFSKSKQQSVYSIV
NSNLPLYAKILSKHQNIVKFNQQKLRYESLKK

>gi|71407603|ref|XP_806259.1| MAP kinase [Trypanosoma cruzi strain CL Brener]

MMDQTQCVPNDFSRCGPFEEDKGEFASNSFGAGGLILPRPQVPLRVYTPFFATVPFPSVLNGSHVE
YFLVALKQLSHLVHEVAVGLLPGKDDVCDVKRTFLIFHISHFVDVSFADTVFMESLTPVRPTAISEYIGL
IQWLGDRFVTRWREATEQKTLCSSMSASNSFRRLWIAVKNTADAISSHTVLQGEIFDRICIRLPKRRL
LEFYITEGNIPSCFCIGCLVWSSLTAFAFVILVWMARGSFSQWCSLAITLVINFSGFLCFLYALVLRQSR
LQWLSELLAENHLAGSIASQSTRTSSRVGKDVVFTIRSKEDVAFTLAIKSCVLNRQIILIGIVNTKSLVICS
WNRAAHMATGIAPEQVIGKSLEAVMEAKSIATARLMELRDKPRQQQRLLLNNARKNFPVTIKATAT
IAHVDGIPIGMFAGTVVDDEQQAMMSYFSRVDTYAALRALRYSGCASSILHTLVLSNEWDALKRRT
TNAMRSWCLVTLEEFLRPLKEIPESSLMHVESTPKQFQCDYNGIKEFLAKLKQWFFPEDDSCLELMV
ACVTCGIEGYLALQFDVTVPDDSIVSLRLKDETLELLSLIGCLTLNSSTHFQFFIPIALRPFDMTLDSEGR
NGHSGKHPFMCTFLLEPVVYRRHFYGICDESRHRIFPVSSLSSLKNLLSNFLNEVTAVILSAASPDFGS
MLSYCREKGQFVLVVREGSERSNDGTPDPSADGPPSDVVKDGDYILHRPLCEERWGYFLEYLYDTR
NPECNVPHAPMLTVIRQIGRGSCSFVDLVQDKLTGGYMACKTVFISHERTLDALREEVDIMRQCSSP
FIVKCIVASHSPSTAEFRMILQFCPDSLERHARRKRIKLSQLPLYAFQLLSAVQHLHENGIAHRDKPANI
LMNEKHLKLADFGSAQRKKLKEGSVYGVTAQFMAPERLLFLPEEEEIVWRETPMDGLFAEDIWSVG
LTLLDIIGIYPLVLKSLNNVKDFLGFYMQLRDSGDELPFELPKEDSTDSHERLCAYDFIRGMQLQPKRR
PRASELLQHLFLRGAKNECDFNGELVVPGSNLWLDPVSWSSHHLNDSLLPSQHSFFTASASDEEPED
GFSEEAFRSVVNLDGVCL

>gi|126697468|gb|ABO26691.1| map kinase [Haliotis discus discus]

MAAPAHQQKSGGKTAGELVRGQIFEVGPRYTSLNYIGEGAYGMVVSAIDTETKSKVAIKKISPFEHQ
TYCQRTLREIKILTRFKHENIINISDILRAPSIEEMKDVYIVQCLMETDMYKLLKTQQLSHVCYFLYQILR
GLKYIHSANVLHRDLKPSNLLLNTTCDLKICDFGLARVADPDHDHTGFLTEYVATRWYRAPEIMLNSK
GYTKSIDVWSVGCILAEMLSNRPLFPGKHYLDQLNHILGVLGS

>gi|193784669|dbj|BAG50821.1| MAP kinase [Nicotiana benthamiana]

MDGPAHQADTVMSDAAAAQQPAPPPQPVSGIDNIPATLSHGGRFIQYNIFGNIFEVTAKYKPPIMP
IGKGAYGIVCSALNSETNEHVAIKKIANAFDNKIDAKRTLREIKLLRHMDHENIVAIRDIIPQREAFNDV
YIAYELMDTDLHQIIRSNQGLSEEHCQYFLYQILRGLKYIHSANVLHRDLKPSNLLLNANCDLKICDFGL
ARVTSETDFMTEYVVTRWYRPPELLLNSSDYTAAIDVWSVGCIFMELDKPLFPGRDHVHQLRLLME
LIGTPSEAEMEFLNENAKRYIRQLPLYRRQSFVEKFPHVNPAAIDLVEKMLTFDPRRRITVEDALAHPY
LTSLHDISDEPVCMTPFNFDFEQHALTEEQMKELIYRELANPEYQHM

>gi|193784667|dbj|BAG50820.1| MAP kinase [Nicotiana benthamiana]

MDGSGQQTDTMMSDAGAEQPPPAAQPVAGMDNIPATLSHGGRFIQYNIFGNIFEVTAKYKPPILP
IGKGAYGIVCSALNSETIENVAIKKIANAFDNKIDAKRTLREIKLLRHMDHENIVAIRDIIPQREAFNDV
YIAYELMDTDLHQIIRSNQGLSEEHCQYFLYQILRGLKYIHSANVLHRDLKPSNLLLNANCDLKICDFGL
ARVTSETDFMTEYVVTRWYRPPELLLNSSDYTAAIDVWSVGCIFMELMRPLFPGRDHVHQLRLIME
LIGTPSEAEMEFLNENAKRYIRQLPLYRRQSFTEKFPHVHPDAIDLVETMLTFDPRRRITVEGALAHPY
LNSLHDISDEPICMTPFSFDFEQHALTEEQMKELIYRESAFPEYQHM

>gi|187761609|dbj|BAG31943.1| MAP kinase [Nicotiana benthamiana]

MKTTKPLKELKLSVPAQDTPISSFLTASGTFHDGDLLLNQKGLRLISEENESPASETKEIDLQFSLEDLET
IKVIGKGSGGVVQLVRHKWIGTLFALKVIQMTIQEDIRKQIVQELKINQSSQCSHVCYHSFYHNGAIS
LVLEYMDRGSLADVIRQLKTILEPYLAVVCKQVLQGLVYLHNERHVIHRDIKPSNLLXNHKGEVKITDF
GVSAMLASSMGQRDTFVGTYNYMAPERISGSTYDYKSDIWSLGMVLCAIGRFPYIQSEDQQAWPS
FYELLEAIVSSPPPSAPADQFSPEFCSFVSACIQKDPRDRSSALDLLSHPFIKKFEDKDIDFGILVSSLEPP
VNFPR

>gi|187761607|dbj|BAG31942.1| MAP kinase [Nicotiana benthamiana]

MENETNEKLEIKGVPTHEGKYVEYNVLGNFFEVTSKYIPPIQPVGRGAYGMVCCATNSETKEEVAIKK
IGNAFENRIDAKRTLREIKLLSHMDHENIIKIKDIVRPPDREEFNDVYIVYELMDTDLHIRSSQALTDDH
CQYFLYQLLRGLKYVHSANVLHRDLKPSNLLLNANCDLKICDFGLARTTSETDFMTEYVVTRWYRAP
ELLLNCTEYTAAIDIWSVGCILMELVKREPLFPGRDYAQQLGLIIELLSEDSDLGFLRSDNARKYVKHLP
RVPRQPFSQKFSDVSPLALDLAERMLVFDPAKRITVEDALNHPFLISLHEINEEPVCDSPFNFDFEQAS
LSEDDIKELIWNEALKFDPNTMK

>gi|190406935|gb|EDV10202.1| MAP kinase [Saccharomyces cerevisiae RM11-1a]

MARTITFDIPSQYKLVDLIGEGAYGTVCSAIHKPSGIKVAIKKIQPFSKKLFVTRTIREIKLLRYFHEHENII
SILDKVRPVSIDKLNAVYLVEELMETDLQKVINNQNSGFSTLSDDHVQYFTYQIALKSIHSAQVIHRDI
KPSNLLLNSNCDLKVCDFGLARCLASSSDSRETLVGFMTEYVATRWYRAPEIMLTFQEYTTAMDIWS
CGCILAEMVSGKPLFPGRDYHHQLWLILEVLGTPSFEDFNQIKSRKEYIANLPMRPPLPWETVWSKT
DLNPDMIDLLDKMLQFNPDKRISAAEALRHPYLAMYHDPSDEPEYPPLNLDDEFWKLDNKIMRPEE
EEEVPIEMLKDMLYDELMKTME

>gi|190406146|gb|EDV09413.1| MAP kinase [Saccharomyces cerevisiae RM11-1a]

MTTNEEFIRTQIFGTVFEITNRYNDLNPVGMGAFGLVCSATDTLTSQPVAIKKIMKPFSTAVLAKRTY
RELKLLKHLRHENLICLQDIFLSPLEDIYFVTELQGTDLHRLLQTRPLEKQFVQYFLYQRGLKYVHSAGV
IHRDLKPSNILINENCDLKICDFGLARIQDPQMTGYVSTRYYRAPEIMLTWQKYDVEVDIWSAGCIFA
EMIEGKPLFPGKDHVHQFSIITDLLGSPPKDVINTICSENTLKFVTSPRDPIPFSERFKTVEPDAVDLLEK
MLVFDPKKRITAADALAHPYSAPYHDPTDEPVADAKFDWHFNDADLPVDTWRVMMYSEILDFHKI
GGSDGQIDISATFDDQVAAATAAAAQAQAQAQAQVQLMAHSHNGAGTTGNDHSDIAGGNKVS
DHVAANDTITDYGNQAIQYANEFQQ

>gi|183584854|gb|ACC63895.1| MAP kinase [Gossypium raimondii]

MQQNQLKKELKEMDFFTEYGDANRYKILEVIGKGSYGVVCAALDTHTGEKVAIKKIQDVFEHMSDA
IRILREVKLVRLLRHPDIVEIKRIMLPPSKREFKDLFVVFELMESDLHQVIKANDDLTREHFFLYQMLRA

MKYMHTANVYHRDLKPKNILANANCKLKVCDFGLARVAFNDTPTTVFWTDYVATRWYRAPELCG
SFFSKYTPAIDIWSIGCIFAEVLTGKPLFPGKSVVHQLELITDLIGTPSLETIGRNDKARKYLSEMRKKKP
VPFSQKFPNADPLAVRLLQRLLAFDPKDRPTAEEALADPYFKGLSKIEREPSCQPISKLEFEFERRRVTK
EDVRELIYREALEYHPQLLKDYLNGHEGSNFLYPSPVG

>gi|169600893|ref|XP_001793869.1| MAP kinase [Phaeosphaeria nodorum SN15]

MPPAGSGSSRKISFNVSEQYDIQDVVGEGAYGVVCSALHKPSGQKVAIKKITPFDHSMFCLRTLREM
KLLRYFNHENIISILDIQKPRNYETFTEVYLIQELMETDMHRVIRTQELSDDHCQYFIYQRALKAMHSA
NVLHRDLKPSNLLLNANCDLKVCDFGLARSAASTEDNSGFMTEYVATRWYRAPEIMLTFKEYTKAID
VWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYYGIKSRRAREYIRSLPFKKKIPWKAM
FPKTNDLALDLLERLFNPVKRITVEEALKHPYLEPYHDPDDEPTADPIPEEFFDFDKNKDNLTKEQLKL
LIYQEIMR

>gi|157868358|ref|XP_001682732.1| map kinase; mitogen-activated protein kinase [Leishmania major]

MAQLVPLAELPSGKKIYSVRGQRFEVDREYDLVKVVGFGACGTVCSAVANGSGERVAIKRLSRVFG
DLREGKRILREMEIMTSLKHNNLIRLHHFMRPQSKETFEDIYLVMDLYDTDLNRIIRSRQKDEHLQYF
MIQAFRGLHYLHSAKVMHRDLKPSNLLVNADCALAICDFGLARDDQVMSSSDLTQYVVTRWYRPP
EVLGMGSNQYTSAVDVWSLGLIFAELMVGRALLPGTDYIGQLVMIVNLLGSPSIDEFLSSEAKAFILS
QPHRPALSFRDLFSMATEEATDLLSKLLVFHPARRLTAKQVMEHPYFSKYRDAAEEADAPDPFVWN
HSHIETKEQLREDLWRVVEAHSQLNE

>gi|154336056|ref|XP_001564264.1| map kinase [Leishmania braziliensis MHOM/BR/75/M2904]

MTQLVPLAELPSGKKIYSVRGQGFEVDREYDLVKIIGFGAYGTVCSAVANRSGERVAIKRLSRVFGDL
REGKRILREMEIMTSLKHSNLIRLHHFLRPHSKETFEDIYFVMDLYDTDLNRIIRSRQKDEHLQYFMIQ
AFRGLHYLHSAKVMHRDLKPSNLLVNADCALAICDFGLARDDQVMSSSDLTQYVVTRWYRPPEVL
GMGFNQYTSAVDVWSLGLIFAELMVGRTLLPGTDYIEQLVMIVNLLGSPSIDEFLSSEARAFILSQPH
RPALPFRDLFPMATEEATDLLSKLLVFHPARRLTAKQVMEHPYFSKYRDPAEEADAPNPFVWNHSH
IETKAQLREDLWRVVEAYSHSNE

>gi|53792602|dbj|BAD53617.1| MAP kinase [Oryza sativa Japonica Group]

MEFFTEYGEASQYQIQEVIGKGSYGVVAAAVDTRTGERVAIKKINDVFEHVSDATRILREIKLLRLLRH
PDIVEIKHIMLPPSRREFQDIYVVFELMESDLHQVIRANDDLTPEHYQFFLYQLLRALIHAANVFHRDL
KPKNILANSDCKLKICDFGLARASFNDAPSAIFWTDYVATRWYRAPELCGSFFSKYTPAIDIWSIGCIF
AELLTGRPLFPGKNVVHQLDIITDLLGTPSSETLSRIRNEKARRYLTRKKHAVPFSQKFRNTDPLALRLL
ERLLAFDPKDRSSAEEALADPYFASLANVEREPSRHPISKLEFEFERRKLTKDDVRELIYREILEYHPQM
LQEYMKGGEQISFLYPSGVDRFKRQFAHLEENSKERGSPLQRKHASLPRERVGVSKDGYNQQNTND
QERSADSVARTTVSPPMSQDAQQHGSAGQNGVTSTDLSSRSYLKSASISASKCVAVKDNKEPEDDY
ISEEMEGSVDGLSEQVSRMHS

>gi|457406|dbj|BAA04870.1| MAP kinase [Arabidopsis thaliana]

MAMLVEPPNGIKQQGKHYYSMWQTLFEIDTKYVPIKPIGRGAYGVVCSSINRETNERVAIKKIHNVF
ENRVDALRTLRELKLLRHVRHENVIALKDVMLPANRTSFKDVYLVYELMDTDLHQIIKSSLSDDHCKY
FLFQLLRGLKYLHSANILHRDLKPGNLLVNANCDLKICDFGLARTSQGNEQFMTEYVVTRWYRAPEL

LLCCDNYGTSIDVWSVGCIFAEILGRKPIFPGTECLNQLKLIINVVGSQQEDRFIDNPKARRFIKSLPYS
RGTHLSNLYPQANPLAIDLLQRMLVFEPTKRISVTDALLHPYMAGLFEPGTNPPAHVPISLDIDENME
EPVIREMMWNEMLYYHPEAEILNA

>gi|457404|dbj|BAA04869.1| MAP kinase [Arabidopsis thaliana]

MDGGSGQPAADTEMTEAPGGFPAAAPSPQMPGIENIPATLSHGGRFIQYNIFGNIFEVTAKYKPPI
MPIGKGAYGIVCSAMNSETNESVAIKKIANAFDNKIDAKRTLREIKLLRHMDHENIVAIRDPPPLRNA
FNDVYIAYELMDTDLHQIIRSNQALSEEHCQYFLYQILRGLKYIHSANVLHRDLKPSNLLLNANCDLKI
CDFGLARVTSESDFMTEYVVTRWYRAPELLLNSSDYTAAIDVWSVGCIFMLDRKPLFPGRDHVHQL
RLLMELIGTPSEEELEFLNENAKRYIRQLPPYPRQSITDKFPTVHPLAIDLIEKMLTFDPRRRITVLDALA
HPYLNSLHDISDEPECTIPFNFDFENHALSEEQMKELIYEAAFNPEYQQ

>gi|457402|dbj|BAA04868.1| MAP kinase [Arabidopsis thaliana]

MAKEIESATDLGDTNIKGVLVHGGRYFQYNVYGNLFEVSNKYVPPIRPIGRGAYGFVCPAVDSETHE
EIAIKKIGKAFDNKVDAKRTLREIKLLRHLEHENVVVIKDIIRPPKKEDFVDVYIVFELMDLHQIIRSNQS
LNDDHCQYFLYQILRGLKYIHSANVLHRDLKPSNLLLNSNCDLKITDFGLARTTSETEYMTEYVVTRW
YRAPELLLNSSEYTSAIDVWSVGCIFAEIMTREPLFPGKDYVHQLKLTLIGSPDGASLEFLRSANGGKY
VKELPKFPRQNFSARFPSMNSTAIDLLEKMLVFDPVKRITVEEALCYPYLSALHDLNDEPVCSNHFSF
HFEDPSSTEEEIKELVWLESVKFNPLPSI

>gi|457400|dbj|BAA04867.1| MAP kinase [Arabidopsis thaliana]

MSAESCFGSSGDQSSSKGVATHGGSYVQYNVYGNLFEVSRKYVPPLRPIGRGAYGIVCAATNSETGE
EVAIKKIGNAFDNIIDAKRTLREIKLLKHMDHENVIAVKDIIKPPQRENFNDVYIVYELMDLHQIIRSNQ
PLTDDHCRFFLYQLLRGLKYVHSANVLHRDLKPSNLLLNANCDLKLGDFGLARTKSETDFMTEYVVT
RWYRAPELLLNCSEYTAAIDIWSVGCILGETMTREPLFPGKDYVHQLRLTLIGSPDDSSLGFLRSDNA
RRYVRQLPQYPRQNFAARFPNMSAGAVDLLEKMLVFEPSRRITVDEALCHPYLAPLHDINEEPVCVR
PFNFDFEQPTLTEENIKELIYRETVKFNPQDSV

>gi|457398|dbj|BAA04866.1| MAP kinase [Arabidopsis thaliana]

MNTGGGQYTDFPAVDTHGGQFISYDIFGSLFEITSKYRPPIIPIGRGAYGIVCSVLDTETNELVAMKKI
ANAFDNHMDAKRTLREIKLLRHLDHENIIAIRDVVPPPLRRQFSDVYISTELMDTDLHIRSNQSLSEEH
CQYFLYQLLRGLKYIHSANIIHRDLKPSNLLLNANCDLKICDFGLARPTSENDFMTEYVVTRWYRAPEL
LLNSSDYTAAIDVWSVGCIFMELMNRKPLFPGKDHVHQMRLLTELLTTESDLGFTHNEDAKRYIRQL
PNFPRQPLAKLFSHVNPMAIDLVDRMLTFDPNRRITVEQALNHQYLAKLHDPNDEPICQKPFSFEFE
QQPLDEEQIKEMIYQEAIALNPTYG

>gi|111068910|gb|EAT90030.1| MAP kinase [Phaeosphaeria nodorum SN15]

MPPAGSGSSRKISFNVSEQYDIQDVVGEGAYGVVCSALHKPSGQKVAIKKITPFDHSMFCLRTLREM
KLLRYFNHENIISILDIQKPRNYETFTEVYLIQELMETDMHRVIRTQELSDDHCQYFIYQRALKAMHSA
NVLHRDLKPSNLLLNANCDLKVCDFGLARSAASTEDNSGFMTEYVATRWYRAPEIMLTFKEYTKAID
VWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYYGIKSRRAEIRSLPFKKKIPWKAMFP
KTNDLALDLLERLLAFNPVKRITVEEALKHPYLEPYHDPDDEPTADPIPEEFFDFDKNKDNLTKEQLKL
LIYQEIMR

>gi|155029052|emb|CAM58448.1| MAP kinase [Caenorhabditis elegans]

MSSAVKLADRYLMTKRLGDGTFGEVMLAKKIDTGDRVAIKRMKKKFYSWEEAMSLREVKSLKKLN
HPNIIKLREVIRENDILYFVFEFMQENLYELMKDRDRYFPESVIRNIIYQVLQGLAFMHKNGHRDMKP
ENIMCNGTELVKIADFGLAREIRSKPPYTDYVSTRWYRAPEILLRSTSYNSPIDMWALGCIMAELYILR
PLFPGTSEMDQLFKIISILGTPNKDEWPEGYQLASAMNFRFQQVVATPMEQVTISKEGMKLMMD
MMLWNPEKRPNANQSLRYKYFQVAEKLGAPVVSQPAPGSIRKTSAASVKSDTKAMTAKAAKKDYI
GSENVSPQQPAKVIDRHINRNLPLNKETLFEKSDNKPLGPTKSNEAKPAKIYLSKSKYVPGQVSKDTH
QNQIMTTNGLTGTTKTTTFSAKKEGRTAVQTRFEYAYGSSFCSSHKSLFLFVFLLPFGACLSSQYS

>gi|151384858|gb|ABS11090.1| MAP kinase [Triticum aestivum]

MDGAPVAEFRPTMTHGGRFLLYNIFGNQFEITAKYQPPIMPIGRGAYGIVCSVMNFETREMVAIKKI
ANAFDNNMDAKRTLREIKLLRHLDHENIVGLRDVIPPAIPQSFNDVYIATELMDTDLHHISNQELSEE
HCQYFLYQLLRGLKYIHSANVIHRDLKPSNLLLNANCDLKICDFGLARPSSESDMMTEYVVTRWYRA
PELLLNSTDYSAAIDVWSVGCIFMELINRAPLFPGRDHMHQMRLITEVIGTPTDDDLGFIRNEDARR
YMRHLPQFPRRSFPGQKVQPAALDLIERMLTFNPLQRITVEEALEHPYLERLHDVADEPICTDPFSFD
FEQHPLTEDQMKQLIFNEALELNPNFRY

>gi|83764024|emb|CAJ44437.1| MAP kinase [Echinococcus multilocularis]

MSGDISDPYTIKGQVFDIGPRFTNLNYIGEGAYGMVISAFDHQRNERVAIKRITPFEHQTYCQRTYRE
IRILSRLDHENIIPLYDVFTTSNFEDMKEVYIVEKYMETDLYKFLKVQQLSREHTCYFLMLRGLKYIHSA
NVLHRDLKPSNILLNRMCDLRICDFGLARIADPQCDQAGLLTEYVATRWYRAPEIMLTSKVYTKAIDL
WSIGCILAEMYSNRVLFPGKHYIDQLKMILEVLGSPHQEDINSISNTATYLEQLPKRKKIPWQQLFPF
ADPKGLDLLDRLLCFAPSRRITVEEALAHPYLAQYYDPSDEPTCPHPFAHEADDLPKERLKVLVWEEI
QHLKGDEQAEPIDAG

>gi|24430320|emb|CAC87145.1| MAP kinase [Claviceps purpurea]

MTDIPGRRAFKCFNQEFVVDERYTVTKELGQGAYGIVCAAVNNQTKESVAVKKVTNVFSKKILAKRA
LREIKLLQHFRGHRNITCLYDMDIPRPDVFNETYLYEELMECDLAAIIRSGQPLTDAHFQIYQILSGLKY
IHSANVLHRDLKPGNLLVNADCELKICDFGLARGFSADPEQNAGYMTEYVATRWYRAPEIMLSFQS
YTKAIDVWSVGCILAELLGSRPFFKGRDYVDQLNQILHVLGTPNEETLSRGPRAQEYVRNLPVMPKK
NFATLFPQANPHALDLLDKMLAFDPSSRISVEQALEHPYLQVWHDPADEPNCPTIFNFDFEVLDDV
GEMRKVILDEVIRFRQMVRTASSAEPTTGQAQTAAAGQVPMPQGGWKAEDPRPQENTPQGNGL
EQDLQAGLDAA

>gi|20451671|emb|CAD30671.1| MAP kinase [Drosophila mauritiana]

ADDTLTSQRVAIKKISPFEHQTYCQRTLREITILTRFKHENIIDIRDILRVDSID

>gi|20451669|emb|CAD30670.1| MAP kinase [Drosophila simulans]

ADDTLTSQRVAIKKISPFEHQTYCQRTLREITILTRFKHENIIDIRDILRVDSID

>gi|20451667|emb|CAD30669.1| MAP kinase [Drosophila sechellia]

ADDTLTSQRVAIKKISPFEHQTYCQRTLREITILTRFKHENIIDIRDILRVDSID

>gi|7267832|emb|CAB81234.1| MAP kinase [Arabidopsis thaliana]

MAKEIESATDLGDTNIKGVLVHGGRYFQYNVYGNLFEVSNKYVPPIRPIGRGASVLSVDSETHEEIAIK
KIGKAFDNKVDAKRTLREIKLLRHLEHENVVVIKDIIRPPKKEDFVDVYIVFELMDTDQIIRSNQSLNDD
HCQYFLYQILRGLKYIHSANVLHRDLKPSNLLLNSNCDLKITDFGLARTTSETEYMTEYVVTRWYRAPE
LLLNSSEYTSAIDVWSVGCIFAEIMTREPLFPGKDYVHQLKLITEISPDGASLEFLRSANARKYVKELPK
FPRQNFSARFPSMNSTAIDLLEKMLVFDPVKRITVEEALCYPYLSALHDLNDEPVCSNHFSFHFEDPS
STEEEIKELVWLESVKFNPLPSI

>gi|6580145|emb|CAB63149.1| MAP kinase [Arabidopsis thaliana]

MEISSASDDSIAYVETDPSGRYGRFREVLGKGAMKTVYKAFDQVLGMEVAWNQVKLNEVFRSPEP
LQRLYSEVHLLKNLNHESIIRYCTSWIDVNRRTFNFITELFTSGTLREYRRKYQKVDIRAIKARQILNGLA
YLHGHDPPVIHRDLKCDNIFVNGHLGQVKIGDLGLAAILRGSQNAHSVIGTPEFMAPELYEEDYNEL
VDIYSFGMCVLEMLTGEYPYSECTNPAQIYKKVTSGKLPDSFHLIQHTEARVGKCLETVSRRLPAKELL
ADPFLAATDERDLAPLFRLPQQLAIQNLAANGTVVEHLPSTTDPTRTTDMSITGKMNSEDHTIFLQV
QILDGDGHMRNIQFPFNILSDTPLEVALEMVKELEITDWDPLEIAAMIENEISLLVPNWRANDSSIRH
ESFGHEDDEDNGDTEGRTRLFSSASSSHDSPVAVRENDSSNDVIPDMDDGNRSSNRLLNSSTYHYS
PAIDDDQNQQQRRRVRLQQKMRSLVDTRTQVLHRSLMELINKRRGRGFDPNTNELQPQPSSTDFI
RRC

>gi|5596479|emb|CAB51417.1| MAP kinase [Arabidopsis thaliana]

MAKEIESATDLGDTNIKGVLVHGGRYFQYNVYGNLFEVSNKYVPPIRPIGRGASVLSVDSETHEEIAIK
KIGKAFDNKVDAKRTLREIKLLRHLEHENVVVIKDIIRPPKKEDFVDVYIVFELMDTDQIIRSNQSLNDD
HCQYFLYQILRGLKYIHSANVLHRDLKPSNLLLNSNCDLKITDFGLARTTSETEYMTEYVVTRWYRAPE
LLLNSSEYTSAIDVWSVGCIFAEIMTREPLFPGKDYVHQLKLITEISPDGASLEFLRSANARKYVKELPK
FPRQNFSARFPSMNSTAIDLLEKMLVFDPVKRITVEEALCYPYLSALHDLNDEPVCSNHFSFHFEDPS
STEEEIKELVWLESVKFNPLPSI

>gi|89242509|gb|ABD64613.1| MAP kinase [Aspergillus fumigatus]

MAEFVRAEVLGTKFEYTTRYVNPQPIGMGSFGLVCSAFDQITQQPVALKKIMKPFDSSSLAKRTYREI
RLLKYLRHENLICMRDIFISPLEDIYIATELLGTDLGRLLSIKPLDSKFSQYFIYQILRKYIHSANVIHRDLKP
TNILINENCDLKICDFGLARLQEPQMTGYVATRYYRAQEIMLTWQRYGVQVDVWSAGCILAEMLR
RKPLFPGKDHVHQFHLITNILGNPPDAVIEKITSKNTVNFVKSLPSERDLSTVVPKDTDFDAIDLLKKM
LVIDPDTRISAQDALRYPYLAPYHDPTDEPVASGPFDWSFDSADFPKETWKIMIYSEVLDYLNVDNP
ADPAPFDPSTPFDPSALEREFSEFLSDSGQI

>gi|4456682|emb|CAB37188.1| MAP kinase [Medicago sativa]

MENKNPESEKANSKGTLIHDGKYIQYNVLGNLFEVYSNYIPPLQPVGRGAYGIVCCATNSDTNEGVA
IKKIGDAFDNRIDAKRTLREIKLLCHMDHDNVIKIKDIIKPADKEKFNDVYIVYELMDTDQIIQSNQALT
DEHCQYFLYQLLRGLKYIHSANVLHRDLKPSNLLLKANCDLKICDFGLARTTSETDFMTEYVVTRWYR
APELLLNCSEYTAAIDVWSVGCILMEIIRREPLFPGKDYVQQLALITELSPNEEDLGFLRSDNAKKYVK
QLPHVDKQPFAERFPDMSPLALDLAEKMLVFDPSKRITVEEALNHPYMSSLHEINEEPVCPSPFVFD
FEQATLNEDDIKELIWRESLNFCKEQILE

>gi|8777336|dbj|BAA96926.1| MAP kinase [Arabidopsis thaliana]

MNMNQVAEYVETDPTGRYGRFAEILGRGAMKTVYKAIDEKLGIEVAWSQVKLKEVLRSSVDLQRLY
SEVHLLSTLNHKSIIRFYTSWIDVHNHTLNFITELFTSGTLRQYKNKYLRIDIRAIKSWARLEGLVYLHEH
DPPVIHRDLKCDNIFVNGHLGQVKIGDLGLARMLRDCHSAHSIIGTPEFMAPELYEENYNELIDVYSF
GMCFLEMITSEFPYSECNHPAQIYKKVVGGKLPGAFYRVGDIEAQRFIKLVSASKRVSAKELLQDPFL
ASDESWMVYTSGAGNPKPFLNENEMDTLKLEDDELRTEMSIAGKLGAEDNKIDLEVQIAYDNGLA
NNVFFPFDIMNDTSIDVAKEMVKELEIIDWEPVEIAKMIDGISLVSDWKYEEDDETPHDHHRHRTDS
FHSSSSHASSSQASLSNYMARGLQDWVQDDLHDETYSQSSSHSGSYSNLNYIAVDEYSSQSPVMSR
THNMTRFCPEESSHLQSGQANAYAASSSTNRSLADNRLTRNRSLVDVQRQLLHRSPGEEARKRRLF
KTVGDVETVGFQSPYAVSRKPPSSRR

>gi|110739420|dbj|BAF01620.1| MAP kinase [Arabidopsis thaliana]

MAMLVEPPNGIKQQGKHYYSMWQTLFEIDTKYVPIKPIGRGAYGVVCSSINRETNERVAIKKIHNVF
ENRVDALRTLRELKLLRHVRHENVIALKDVMLPANRSSFKDVYLVYELMDTDLHQIIKSSLSDDHCKY
FLFQLLRGLKYLHSANILHRDLKPGNLLVNANCDLKICDFGLARTSQGNEQFMTEYVVTRWYRAPEL
LLCCDNYGTSIDVWSVGCIFAEILGRKPIFPGTECLNQLKLIINVVGSQQESDIRFIDNPKARRFIKSLPY
SRGTHLSNLYPQANPLAIDLLQRMLVFDPTKRISVTDALLHPYMAGLFDPGSNPPAHVPISLDIDEN
MEEPVIREMMWNEMLYYHPEAEISN

>gi|82706044|ref|XP_727218.1| MAP kinase [Plasmodium yoelii yoelii 17XNL]

MDKHNLIHIYFSQICLGIKNLHEHNVAHRDLKPDNILVTNKLININLDTPDINVEICDLGSAKKVEKNII
SIPYICSRWYRAPELLCGSMYYTTDVDLWSLGCIIFELINLCPLFPGKFKKDEYSEEQIINLIEVLGSPNM
DPNERLKIDEVLDNSYFSTLHI

>gi|82491930|gb|ABB77845.1| MAP kinase [Phycomyces blakesleeanus]

MAARLENFNAGDDYKIVDVIGEGAYGVVCSAIQQSTGRKVAIKRILPFDHAMFCLRTLREIKLLKYFQ
HENIVSILDIVKPATLEDFTEV

>gi|82491927|gb|ABB77843.1| MAP kinase [Phycomyces blakesleeanus]

MTQPSRRNDMSRLQQFDAGEQYSIVDIVGEGAYGVVCSAVHKPTGQTVAIKRILPFDHAMFCLRTL
REIKLLKYFNHENIISILDIVKPKSYDEFTEVYLIQELMETDLHRVIRTQDLSDDHCQYFTTLRALKAMHS
ANVLHRDLKPSNLLLNANCDLKICDLGLARSANSADENSGFMTEYVATRWYRAPEIMLTFKEYTKAI
DVWSVGCILAEMLSGKPLFPGRDYHHQLTLILDVLGTPTMDDFYGIKSRADYIRSLPFKKRIPFARLFP
EATVDLLEKLLSFNPDRRITVEEALKHPYLEAYHDPDDEPNATPIHESFFDFDKYKDQLTKEQLKRKFF
FHIIKRKKERLTQNIYINMYITEMLYEEITQ

>gi|73761699|gb|AAZ83349.1| MAP kinase [Gossypium hirsutum]

IKRIMLPPSKREFKDLFVVFELMESDLHQVIKANDDLTREHHQFFLYQMLRAMKYMHTANVYHRDL
KPKNILANANCKLKVCDFGLARVAFNDTPTTVFWTDYVATRWYRAPELCGSFFSKYTPAIDSIGCIFA
EVLTGKPLFPGKSVIHQLELITDLIGTPSLETISGVRNDKARKYLSEMRKKKPVPFSQKFPNADPLAVRL
LQRLLAFDPKDRPTAEEALADPYFKGLSKIEREPSCQPISKLEFEFERRVKEDVRELIYREALEYHPQLLK
DYLNGHEGSNFLYPSPVGQFKKQFAYLEENGGRSAPVFPLERKHVSLPRSTVHSNGITPNTQSTSVSY
ENRQDREADARKAMDVISSKPKPTRPPPRVPSEVLSPYKPGRVVGSVVPYEDVKNIKDGYHAKNFY

RNAVPPQNVSPHCFLLNQEKSGTQTDRNLQTKPQQQFSMVAKPSPGTAFDMNSNPYYRTQAKTE
RRLPIDAKLLQAQSQFGAVGAAAVAVAAHRNATVHGLS

>gi|62516666|gb|AAX63387.1| MAP kinase [Phaeosphaeria nodorum]

MPPAGSGSSRKISFNVSEQYDIQDVVGEGAYGVVCSALHKPSGQKVAIKKITPFDHSMFCLRTLREM
KLLRYFNHENIISILDIQKPRNYETFTEVYLIQELMETDMHRVIRTQELSDDHCQYFIYQRALKAMHSA
NVLHRDLKPSNLLLNANCDLKVCDFGLARSAASTEDNSGFMTEYVATRWYRAPEIMLTFKEYTKAID
VWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYYGIKSRRAEIRSLPFKKKIPWKAMFP
KTNDLALDLLERLLAFNPVKRITVEEALKHPYLEPYHDPDDEPTADPIPEEFFDFDKNKDNLTKEQLKL
LIYQEIMR

>gi|62321752|dbj|BAD95376.1| MAP kinase [Arabidopsis thaliana]

MGLSNKGNITTPCGKHCSKSIQSMFRLNPLEEELMVWFVLLSIVRLMREFAIKKIHNVFENRVDALR
TLRELKLLRHVRHENVIALKDVMLPANRSSFKDVYLVYELMDTDLHQIIKSSQSLSDDHCFLFQLLRGL
KYLHSANILHRDLKPGNLLVNANCDLKICDFGLARTSQGNEQFMTEYVVTRWYRAPELLLCCDNYG
TSIDVWSVGCIFAEILGRKPIFPGTECLNQLKLIINVVGSQQESDIRFIDNKRRFIKSLPYSRGTHLSNLY
PQANPLAIDLLQRMLVFDPTKRISVTDALLHPYMAGLFDPGSNPPAHVPISLDIDENMEEPVIREM
MWNEMLYYHPEAEISNA

>gi|74355985|dbj|BAE44363.1| MAP kinase [Solanum tuberosum]

MVDANMGGAQFPDFPKIVTHGGQYVQYDIFGNYFEITNKYRPPIMPIGRGAYGIVCSVFNAELNE
MVAVKKIANAFDNYMDAKRTLREIKLLRHLDHENVIGLRDVIPPPLRREFSDVYIATELMDTHQIIRS
NQGLSEDHCQYFMYQLLRGLKYIHSAHVIHRDLKPSNLLLNANCDLKICDFGLARPNLENENMTEYV
VTRWYRAPELLLNSSDYTAAIDVWSVGCIFMELMNRKPLFAGKDHVHQIRLLTLGTPXESDLSFLRN
EDAKRYVRQLPQHPRQQLATVFPHVNPLAIDLVDKMLTLDPTRRITVEEALAHPYLXKLHDAADEPV
CPIPFSFDFEQQGIGEEQIKDMIYQEALALNPEYA

>gi|56627|emb|CAA46318.1| MAP kinase [Rattus norvegicus]

MAAAAAAPGGGGGEPRGTAGVVPVVPGEVEVVKGQPFDVGPRYTQLQYIGEGAYGMVSSAYDH
VRKTRVAIKKISPFEHQTYCQRTLREIQILLGFRHENVIGIRDILRAPTLEAMRDVYIVQDLMELYKLLKS
QQLSNDHICYFLYQILRGLKYIHSANVLHRDLKPSNLLINTTCDLKICDFGLARIADPEHDHTGFLTEYV
ATRWYRAPEIMLNSKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLHLGILGSPSQEDLNCIINM
KARNYLQSLPSKTKVAWAKLFPKSDSKALDLLDRMLTFNPNKRITVEEALAHPYLEQYYDPTDEPVAE
EPFTFDMELDDLPKERLKELIFQETARFQPGAPEAP

>gi|897810|emb|CAA61537.1| MAP kinase [Schizosaccharomyces pombe]

MAEFIRTQIFGTCFEITTRYSDLQPIGMGAFGLVCSAKDQLTGMNVAVKKIMKPFSTPVLAKRTYREL
KLLKHLRHENIISLSDIFISPFEDIYFVTELLGTDLHRLLTSRPLETQFIQYFLYQILRKFVHSAGVIHRDLK
PSNILINENCDLKICDFGLARIQDPQMTGYVSTRYYRAPEIMLTWQKYNVEVDIWSAGCIFAEMIEG
KPLFPGRDHVNQFSIITELLGTPPMEVIETICSKNTLRFVQSLPQEVPFAEKFKNADPDAIDLLEKMLV
FDPRKRISAADALAHNYLAPYHDPTDEPVADEVFDWSFQDNDLPVETWKVMMYSEVLSFHNMD
NELQS

>gi|871984|emb|CAA56314.1| MAP KINASE [Avena sativa]

MDGAPVAEFRPTMTHGGRFLLYNIFGNQFEITSKYQPPIMPIGRGAYGIVCSVMNFETREMVAIKKI
ANAFDNNMDAKRTLREIKLLRHLDHENIVGLRDVIPPSIPQSFNDVYIATELMDTDLHHISNQELSEE
HCQYFLYQLLRGLKYIHSANVIHRDLKPSNLLLNANCDLKICDFGLARPSSESDMMTEYVVTRWYRA
PELLLNSTDYSAAIDVWSVGCIFMELINRAPLFPGRDHMHQMRLITEVIGTTDDLGFIRNEDARRYM
RHLPQFPRRPFPGQFPKVQPAALDLIERMLTFNPLQRITVEEALEHPYLERLHDVADEPICTDPFSFDF
EQHPLTEDQMKQLIFNEALELNPNFRY

>gi|557680|emb|CAA56727.1| MAP kinase [Xenopus laevis]

MSSNQSYVFYRQELNKTLWEVPDRYQNLTPVGSGAYGSVCSSFDTRTALRIAVKKLSRPFQSIIHAKR
TYRELRLLKHMKHENVIGLLDVFSPAKSFEEFNDVYLVTHLMGADLNNIVKCQKLTDDHFLIYQILRG
LKYIHSAGIIHRDLKPSNLAVNEDCELKILDFGLARHTDEEMTGYVATRWYRAPEIMLNWMHYNQT
VDIWSVGCIMAELLTGRTLFPGTDHIDQLKLILRLVGTPEPELLQKISSEARYIQSLPYMPKMNFEDVF
LGANPQAVDLLEKMLVLDTDKRITAAEALAHSYFAQYHDPDDEPIAEPYDQSFESRELDIEEWKRLTY
EEVTCFVPPPLDSEEMES

>gi|298019|emb|CAA47099.1| MAP Kinase [Medicago sativa]

MEGGGAPPADTVMSDAAPAPPQMGIENIPAVLSHGGRFIQYNIFGNIFEVTAKYKPPIMPIGKGAY
GIVCSAHNSETNEHVAVKKIANAFDNKIDAKRTLREIKLLRHMDHENVVAIRDIVPPPQRENDVYIAY
ELMDTDLHQIIRSNQALSEEHCQYFLYQILRGLKYIHSANVLHRDLKPSNLLLNANCDLKICDFGLARV
TSETDFMTEYVVTRWYRAPELLLNSSDYTAAIDVWSVGCIFMELMDRKPLFPGRDHVHQLRLLMEL
IGTPSEDDLGFLNENAKRYIRQLPPYRRQSFQEKFPHVHPEAIDLVEKMLTFDPRKRITVEDALAHPYL
TSLHDISDEPVCMTPFSFDFEQHALTQMKELIYREALAFNPEYQQ

>gi|64894|emb|CAA42482.1| MAP kinase [Xenopus laevis]

MAAAGAASNPGGGPEMVRGQAFDVGPRYINLAYIGEGAYGMVCSAHDNVNKVRVAIKKISPFEH
QTYCQRTLREIKILLRFKHENIIGINDIIRAPTIEQMKDVYIVQDLMETDLYKLLKTQHLSNDCYFLYQIL
RGLKYIHSANVLHRDLKPSNLLLNTTCDLKICDFGLARVADPDHDHTGFLTEYVATRWYRAPEIMLN
SKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGILGSPSQEDLCINLKARNYLLSLPHKNKV
PWNRLFPNADPKALDLLDKMLTFNPHKRIEVEAALAHPYLEQYYDPSDEPVAEAPFKFEMELDDLPK
ETLKELIFEETARFQPGY

>gi|30348584|emb|CAD43731.1| MAP kinase [Ustilago maydis]

MSIANASSSTASHDLDAADADPCPSACTSVSALCNMSTLPSPRPFGYRPTYVPAMVASGVSAVTVT
TNSHRPPSKSHSISSVDSLASVSSNAPSTPTHDADDVRFEMAVIPKLVRASADAYLDRVGKPPSPAP
QIVATSATTKTNAQAARSVAAAAAAAAAAAAVPPSHSALRNENHKNAISFRVGSKYKVCEIIGEGAY
GVVCSAIHRATGQKVAIKKIQPFEHQMFALRTLRELKLLRFFQECDVSENIISLIIKPSTYEAFTEVYLVQ
ELMETDLHRVIRTQELSDDHCQYFTYQTLRALKPMHCADVIHRDLKPSNVLLNANCDLKVCDFGLA
RSVLTADQDTGFMTEYVATRWYRAPEIMLTFKQYTKAIDAWAGCLAEMLTGRPLFPGRDYHQQLS
LILDVLGTPTLEEFQNINSRRSRDYIRSMPFRKRREFRTLFPKASPEAIDFLQKTLTFDPRNRLTVEECL
QHPYLSAYHDPDDEPGAPRLDPDFFYFDMQKESTKELRKELWYQVQEFQPLLR

>gi|27884252|emb|CAD61274.1| MAP Kinase [Catharanthus roseus]

RTLRELKLLRHMDHENVVAIRDIIPPPQRESFNDVYIAYELMDTDLHQIIRSNQALSEEHCQYFLYQIL
RGLKYIHSANVLHRDLKPSNLLLNANCDLKICDFGLARVTSETDFMTEYVVTRWYRAPLLNSSDYTTA
IDVWSVG

>gi|20975736|emb|CAD31224.1| MAP Kinase [Oryza sativa Japonica Group]

MDGAPVAEFRPTMTHGGRYLLYDIFGNKFEVTNKYQPPIMPIGRGAYGIVCSVMNFETREMVAIKK
IANAFNNDMDAKRTLREIKLLRHLDHENIIGIRDVIPPPIPQAFNDVYIATELMDTDLHHISNQELSEE
HCQYFLYQILRGLKYIHSANVIHRDLKPSNLLLNANCDLKICDFGLARPSSESDMMTEYVVTRWYRAP
ELLLNSTDYSAAIDVWSVGCIFMELINRQPLFPGRDHMHQMRLITEVIGTTDELGFIRNEDARKYMR
HLPQYPRRTFASMFPRVQPAALDLIERMLTFNPLQRITVEEALDHPYLERLHDIADEPICLEPFSFDFE
QKALNEDQMKQLIFNEAIEMNPNIRY

>gi|9757944|dbj|BAB08432.1| MAP kinase [Arabidopsis thaliana]

MEGFNRIKEKRRNHDGRRDREIGKSEMMGISFAAKLRFRSRFRTSSIDSYCFARQISSMEEADFAEK
DPSGRYIRYDDVLGRGAFKTVYKAFDEVDGIEVAWNLVSIEDVMQMPGQLERLYSEVHLLLKHENII
KLFYSWVDEKNKTINMITELFTSGSLRVYRKKHRKVDPKAIKNWARQILKGLNYLHSQNPPVIHRDLK
CDNIFVNGNTGEVKIGDLGLATVLQQPTARSVIGTPEFMAPELYEEEYNELDYSFGMCMLEMVTCE
YPYNECRNQAQIYKKVTSNIKPQSLGKVDDPQVRQFIEKCLLPASSRPTALELSKDPFLARDGGKDSA
LLASSSTSSKYVRPPQLEHLPMDVDHNENKSVSSNEDYPWSQTELRIAENKEFRLRGERSDDVTASM
VLRIADPSGKCRIVHFAFYLESDTATAIAEEMVEELHLTSQEVVVIADMIDDFIMQLLSDRTSSHHNQ
NSPRLTHEDHEAANQQTVNSKDEEAAGQSMKSDIADYFPYSANDGNAAMEAGRDAESMSSYLDS
CSMMSTIYNLSISDNDYPEDLKTELNLIESQFNQSFQDLLKLKEDAIENAKRKWITKKQKAVNIS

>gi|9294249|dbj|BAB02151.1| MAP kinase [Arabidopsis thaliana]

MDDVAGLQEAAGARFSQIELIGRGSFGDVYKAFDKDLNKEVAIKVIDLEESEDEIEDIQKEISVLSQCR
CPYITEYYGSYLHQTKLWIIMEYMAGGSVADLLQSNNPLDETSIACITRDLLHAVEYLEGKIHRDIKAA
NILLSENGDVKVADFGVSAQLTRTISRRKTFVGTPFWMAPEVIQNSEGYNEKADIWSLGITVIEMAK
GEPPLADLHPMRVLFIIPRETPPQLDEHFSRQVKEFVSLCLKKAPAERSKELIKHRFIKNARKSPKLLERI
RERPKYQVKEDEETPRNGAKAPVESSGTVRIARDERSQGAPGYSFQGNTVKNAGWDFTVGGSQSI
GTVRALKPPQARERRQEVSPNRISQRTTRPSGNQWSSAGSISEASEGGFVRRHPFQNDHEDGFHEE
DDSSLSGSGTVVIRTPRSSQSSSVFREPSSGSSGRYAAFDDASASGTVVVRGQYDDSGSPRTPKSRLG
IQERTSSASEDSNANLAEAKAALDAGFRRGARELGMGNNNNDGKVNRRREQMADDSDYSRNSG
DKSSKQKVVPRSEQVSDEEDDSIWESLPASLSVLLIPSLKEALGDDSKESTVRTVSRSLVMMEREKPG
SCEAFVAKLIELLGSSKEASVKELHMAVCFAKTTPDNAENKMKQANKEFSSNTNVSPLGRFLLSRWL
GQSSRDL

>gi|9294059|dbj|BAB02016.1| MAP kinase [Arabidopsis thaliana]

MGASHSTNVNNHPHSRNASNHPLTNSNSTSSRHSASSSDRLSVSNLRSQLTTIYRNQEEEEEEEEEE
EEEEEGGKEKRAEEEAKSFSLVRDFDLSGLNCIRVSRRNYILMDPHKKVALETEFFTEYGSRYQIQEVI
GKGSYGVVASAIDTHSGEKVAIKKINDVFEHVSDATRILREIKLLRLLRHPDIVEIKHVMLPPSRREFRD
IYVVFELMESDLHQVIKANDDLTPEHYQFFLYQLLRGLKFIHTANVFRLKPKNILANSDCKLKICDFGL
ARVSFNDAPSAIFWTDYVATRWYRAPELCGSFFSKYTPAIDIWSIGCIFAEMLTGKPLFPGKNVVHQ
LDIMTDLLGTPPPEAIARIRNEKARRYLGNMRRKPPVFTKFPHVDPLALRLLHRLLAFDPKDRPSAEE
ALADPYFYGLANVDREPSTQPIPKLEFEFERRKITKEDVRELIYREILEYHPQMLQEYLRGGEQTSFMY

PSGVDRFKRQFAHLEENYGKGEKGSPQRQASLPRERVPAPKKENGSHNHDIENRSIASLVTTLESPP
TSQHEGSDYRNGTSQTGYSARSLLKSASISASKCIGMKPRNKSEYGESNNDTVDALSQKVAALHT

>gi|9293876|dbj|BAB01779.1| MAP kinase [Arabidopsis thaliana]

MVLVKCDWVRSLTSCLLIIVTRRRRVMNGEESFVEDCSVFVEIDPSGRYGRYDEILGKGASKTVYRAF
DEYEGIEVAWNQVKLRNFTRNPEELEKFFREIHLLKTLNHQNIMKFYTSWVDTNNLSINTELFTSGTL
RQYRLRHRRVNIRAVKQWCKQILKGLLYLHSRSPPIIHRDLKCDNIFINGNQGEVKIGDLGLAAILRKS
HAVRCVGTPEFMAPEVYDEEYNELVDVYAFGMCVLEMVTFDYPYSECTPQIYKKVTSGKKPEAFYL
VKDPEVREFVEKCLANVTCRLTALELLQDPFLQGYDETGVFLRHPLIDDPLYHDQFESSQICEIDLFAN
DDEDHVDISIKGKRNGDDGIFLRLRISDAEGRIRNIYFPETIDTAWSVAVEMVSELDITNQDVAKIAE
MIDAEIAALVPDWKNDTESSQNVNNNKNNNTAGFCGECASNGYIQETVSSGEKSHHNHHEFDSSE
DKSCSSVHGRFADMWGLRESYSDDGEKQSSRKRSGWSENEMRRELRWLKARHKIQLMKMRGQT
ICETPIEISLTPGTSVSLPLLYRAISLPVDAVDM

>gi|40645549|dbj|BAD06585.1| MAP kinase [Candida tropicalis]

MMNIDQHHQQLQQQSQAQAQAQAQAQAQAQAQAQAQAQAQAQAQAAAAAVAASSQRQVSFNVS
DHYQILEIVGEGAYGIVCSAIHKPSNQKVAIKKIEPFERSMLCLRTLRELKLLKHFNHENIISILAIQLNFE
SFNEIYLIQELMETDLHRVIRTQNLTDDHIQYFIYQTLRALKAMHSANVLHRDLKPSNLLLNSNCDLKV
CDFGLARSIASQEDNYGFMTEYVATRWYRAPEIMLTFQEYTTAIDVWSVGCILELSGRPLFPGRDYH
NQLWLIMEVLGTPNMEDYYNIKSKRAREYIRSLPFCKKIPFQELFSNKPGINPLALDLLEKLLIFNPAKR
ITVEDALKHPYLQLYHDPNDEPISDKIPEDFFDFDKKKDSLTEDKKMLYEEIMKPL

>gi|12331300|emb|CAC24705.1| MAP kinase [Nicotiana tabacum]

MKTTKPLKELKLSVPAQDTPISSFLTASGTFHDGDLLLNQKGLRLISEENESPASETKEIDLQFSLEDLET
IKVIGKGSGGVVQLVRHKWVGTLFALKVIQMTIQEDIRKQIVQELKINQASQCSHVCYHSFYHNGAI
SLVLEYMDRGSLADVIRQLKTILEPYLAVVCKQVLQGLVYLHNERHVIHRDIKPSNLLVNHKGEVKITD
FXVSAMLASSMGQRDTFVGTYNYMAPERISGSTYDYKSDIWSLGMVLCAIGRFPYIQSEDQQAWP
SFYELLEAIVSSPPPSAPAVQFSPEFCSFVSACIQKDPRDRSSALDLLSHPFIKKFEDKDIDFGILVSSLEP
PVNFPR

>gi|4902476|emb|CAB43520.1| MAP kinase [Arabidopsis thaliana]

MYMEISSASDDSIAYVETDPSGRYGRFREVLGKGAMKTVYKAFDQVLGMEVAWNQVKLNEVFRSP
EPLQRLYSEVHLLKNLNHESIIRYCTSWIDVNRRTFNFITELFTSGTLREYRRKYQKVDIRASWARQILN
GLAYLHGHDPPVIHRDLKCDNIFVNGHLGQVKIGDLGLAAILRGSQNAHSVIGTPEFMAPELYEEDY
NELVDIYSFGMCVLEMLTGEYPYSECTNPAQIYKKVTSGKLPDSFHLIQHTARFVGKCLETVSRRLPA
KELLADPFLAATDERDLAPLFRLPQQLAIQNLAANGTVVEHLPSTTDPTRTTDMSITGKMNSEDHTIF
LQVQILDGDGHMRNIQFPFNILSDTPLEVALEMVKELEITDDPEIAAMIENEISLLVPNWRANDSSIR
HESFGHEDDEDNGDTEGRTRLFSSASSSHDSPVAVRENNDDSSNDVIPDMDDGNRSSNRLLNSSTY
HYSPAIDDDQNQQQRRRVRLQQKMRSLVDTRTQLHRLMELINKRRGRGFDPNTNELQPQPSSTDF
IRRC

>gi|121489749|emb|CAK18846.1| MAP kinase precursor [Phillyrea latifolia]

TRNEDARKYIRQLPRHPRQPLAKVFPHVNPLAIDLIDKMLTINPRKRITVEEALEHPYLAKLHDTADEP
VCPEPFSFDFEQQILSEEQIKEMIYQEALTLNPEYA

>gi|150035860|sp| ABR67244| MAP Kinase

MSRSNPPNAAGSRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKITPFDHSMFCLRTL
REMKLLRYFNHEIISILDIQKPRNYESFNEVYLIQELMETDMHRVIRTQDLSDDHCQYFITLRALKAMH
SANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNSGFMTEYVATRWYRAPEIMLTFKEYTK
AIDVWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYY

>gi|164427078|sp| XP_959713| MAP Kinase

MSSAQRGGARKISFNVSEQYDIQDVVGEGAYGVVCSAVHKPSGQKVAIKKITPFDHSMFCLRTLRE
MKLLRYFNHENIISILDIQKPRSYETFNEVYLIQELMETDMHRVIRTQELSDDHCQYFIYQRALKAMH
SANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNSGFMTEYVATRWYRAPEIMLTFKEYTK
AIDVWSVGCILAEMLSGKPLFPGKDCMYHHQLTLILDVLGTPTMEDYYGIKSRAEYIRSLPFKKKVPF
RTLFPNTSELALDLLEKLLAFNPVKRITVEEALKHPYLEPYHDPDDEPTAPPIPEEFFDFDKHKDNLSKE
QLKQLIYQEIMR

>gi|10798897|sp| AAG23132| MAP Kinase

MTARAPNPASGSRKISFNVSEQYDIQDVVGEGAYGVVCSALHKPSGQKVAIKKITPFDHSMFCLRTL
REMKLLRYFNHENIISILDIQKPRNYESFTEVYLIQELMETDMHRVIRTQDLSDDHCQYFQTLRALKA
MHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNSGFMTEYVATRWYRAPEIMLTFKE
YTKAIDVWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYYGIKSRREYIRSLPFKKKVPF
KTMFPKTSDLALDLLEKLLAFNPVKRITVEEALKHPYLEPYHDPEDEPTANPIPEEFFDFDKNKDNLTK
EQLKKLIYDEIMR

>gi|156039459|sp| XP_001586837| MAP Kinase

MASRAPNPSSGSRKISFNVSEQYDIQDVVGEGAYGVVCSALHKPSGQKVAIKKITPFDHSMFCLRTL
REMKLLRYFNHENIISILDIQKPRNYESFTEVYLIQELMETDMHRVIRTQDLSDDHCQYFQTLRALKA
MHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNSGFMTEYVATRWYRAPEIMLTFKE
YTKAIDVWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYYGIKSRREYIRSLPFKKKVPF
KTMFPKTSDLALDLLEKLLAFNPVKRITVEEALKHPYLEPYHDPEDEPTANPIPEEFFDFDKNKDNLTK
EQLKQLIYEEIMR

>gi|21636306|sp| AAM69918| MAP Kinase

MSRSTAPNASASRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKITPFDHSMFCLRTLR
EMKLLRYFNHENIISILDIQKPRSYDSFNEVYLIQELMETDMHRVIRTQDLSDDHCQYFQTLRALKAM
HSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNSGFMTEYVATRWYRAPEIMLTFKEYT
KAIDVWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYYGIKSRREYIRSLPFKKKVPFRT
LFPKTSDLALDLLEKLLAFNPVKRITVEDALKHPYLEPYHDPEDEPTAPPIPEEFFDFDKHKDTLSKEQL
KQLIYQEIMR

>gi|18479080|sp| AAL73403| MAP Kinase

MSRANPPNAAGSRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKITPFDHSMFCLRTL
REMKLLRYFNHENIISILDIQKPRSYESFQEVYLIQELMETDMHRVIRTQDLSDDHCQYFQTLRALKA
MHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNSGFMTEYVATRWYRAPEIMLTFKE
YTKAIDVWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYYGIKSRREYIRSLPFKKKVPF

RTLFPKTSDLALDLLEKLLAFNPVKRITVEEALKHPYLEPYHDPEDEPTAPPIPEEFFDFDKHKDNLSKE
QLKQLIYQVIMW

>gi|30313609|sp| AAO46014| MAP Kinase

MSRSNPPNNASASRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKITPFDHSMFCLRT
LREMKLLRYFNHENIISILDIQKPRSYDSFNEVYLIQELMETDMHRVIRTQDLSDDHCQYYQTLRALKA
MHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNSGFMTEYVAARWYRAPEIMLTFKE
YTKAIDVWSVGCILAEMLSGKPLFPGKDLTFPDHHQLTLILDVLGTPTMEDYGKSRRAREYIRSLPFKK
KVPFRTLFPKTSDLALDLLEKLLAFNPVKRITVEDALKHPYLEPYHDPDDEPTAPPIPEEFFDFDKHKDT
LSKEQLKQLIYQEIMR

>gi|23534536|sp| AAN34610| MAP Kinase

MSRSNPPNNASASRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKITPFDHSMFCLRT
LREMKLLRYFNHENIISILDIQKPRSYDSFNEVYLIQELMETDMHRVIRTQDLSDDHCQYYQTLRALKA
MHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNSGFMTEYVATRWYRAPEIMLTFKE
YTKAIDVWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYYGIKRAREYIRSLPFKKKVPF
RTLFPKTSDLALDLLEKLLAFNPVKRITVEDALKHPYLEPYHDPDDEPTAPPIPEEFFDFDKHKDTLSKE
QLKQLIYQEIMR

>gi|4321114|sp| AAC49521| MAP Kinase

MSRANPPSNSSGSRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKITPFDHSMFCLRTL
REMKLLRYFNHENIISILDIQKPRSYETFNEVYLIQELMETDMHRVIRTQDLSDDHCQYYQTLRALKA
MHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQENNSGFMTEYVATRWYRAPEIMLTFKE
YTKAIDVWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYYGIKSRRAREYIRSLPFKKKV
PFRTLFPKTSDLALDLLEKLLAFNPVKRITVEEALKHPYLEPYHDPDDEPTAPPIPEEFFDFDKHKDNLS
KEQLKQFIYQEIMR

>gi|5739482|sp| AAD50496| MAP Kinase

MSRANAPNPSGSRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKITPFDHSMFCLRTL
REMKLLRYFNHENIISILDIQKPRSYETFNEVYLIQELMETDMHRVIRTQDLSDDHCQYFQTLRALKA
MHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNSGFMTEYVATRWYRAPEIMLTFKE
YTKAIDVWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYYGIKSRREYIRSLPFKKKVPF
RTLFPKTSDLALDLLEKLLAFNPVKRITVEDALKHPYLEPYHDPDDEPTAPPIPEEFFDFDKHKDNLSKE
QLKQLIYQEIMR

>gi|340518833|sp| EGR49073| MAP Kinase

MSRSNPPNNASASRKISFNVSEQYDIQDVVGEGAYGVVCSAIHKPSGQKVAIKKITPFDHSMFCLRT
LREMKLLRYFNHENIISILDIQKPRSYESFNEVYLIQELMETDMHRVIRTQDLSDDHCQYYQTLRALKA
MHSANVLHRDLKPSNLLLNANCDLKVCDFGLARSAASQEDNSGFMTEYVATRWYRAPEIMLTFKE
YTKAIDVWSVGCILAEMLSGKPLFPGKDYHHQLTLILDVLGTPTMEDYYGIKRAREYIRSLPFKKKVPF
RTLFPKTSDLALDLLEKLLAFNPVKRITVEDALKHPYLEPYHDPDDEPTAPPIPEEFFDFDKHKDTLSKE
QLKQLIYQEIMR

>FB|FBgn0003256 symbol:rl species:7227 "Drosophila melanogaster" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008271

InterPro:IPR008349 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PRINTS:PR01770 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 GO:GO:0005634 GO:GO:0005737 GO:GO:0008134 GO:GO:0006916 GO:GO:0007507 GO:GO:0007067 GO:GO:0006355 GO:GO:0008284 GO:GO:0030054 GO:GO:0007474 GO:GO:0008595 GO:GO:0045467 GO:GO:0008293 SUPFAM:SSF56112 GO:GO:0050803 GO:GO:0019901 GO:GO:0006974 GO:GO:0071276 GO:GO:0048149 GO:GO:0034614 GO:GO:0007369 BRENDA:2.7.11.24 GO:GO:0071243 GO:GO:0034334 KO:K04371 EMBL:M95124 EMBL:CM000457 EMBL:AY070996 PIR:A46036 PIR:B46036 RefSeq:NP_001015121.2 RefSeq:NP_001015122.1 RefSeq:NP_001015123.1 RefSeq:NP_001104348.1 RefSeq:NP_001104349.1 UniGene:Dm.20303 ProteinModelPortal:P40417 SMR:P40417 DIP:DIP-17266N IntAct:P40417 MINT:MINT-312120 STRING:P40417 EnsemblMetazoa:FBtr0113699 GeneID:3354888 KEGG:dme:Dmel_CG12559 CTD:3354888 FlyBase:FBgn0003256 eggNOG:inNOG07258 GeneTree:EMGT00050000001140 InParanoid:P40417 OMA:RINMEND OrthoDB:EOG4PG4GD PhylomeDB:P40417 NextBio:849506 Bgee:P40417 GermOnline:CG12559 GO:GO:0004705 GO:GO:0046534 GO:GO:0050804 Uniprot:P40417

MFYAVDFDKSYLRICLKSKKKLSLYIHILSYRLLVKFIINISSFPEETLVMEEFNSSGSVVNGTGSTEVPQS
NAEVIRGQIFEVGPRYIKLAYIGEGAYGMVVSADDTLTNQRVAIKKISPFEHQTYRTLREITILTRFKHE
NIIDIRDILRVDSIDQMRDVYIVQCLMETDLYKLLKTQRLSNDHICYFLYQILRGLKYIHSANVLHRDLK
PSNLLLNKTCDLKICDFGLARIADPEHDHTGFLTEYVATRWRPEIMLNSKGYTKSIDIWSVGCILAEML
SNRPIFPGKHYLDQLNHILGVLGSPSRDDLECIINEKARNYLESLPFKPNVPWAKLFPNADALALDLLG
KMLTFNPHKRIPVEEALAHPYLEQYYDPGEPAEVPFRINMENDDISRDALKSLIFEETLKFKERQPDN
AP

>FB|FBgn0010269 symbol:Dsor1 species:7227 "Drosophila melanogaster" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 EMBL:AE014298 GO:GO:0008595 SUPFAM:SSF56112 GO:GO:0007298 GO:GO:0004702 GO:GO:0004713 GO:GO:0000165 GO:GO:0004708 EMBL:D13782 EMBL:AY135075 EMBL:AY135076 EMBL:AY135077 EMBL:AY135078 EMBL:AY135079 EMBL:AY135080 EMBL:AY135081 EMBL:AY135082 EMBL:AY135083 EMBL:AY135084 EMBL:AY135085 EMBL:AY135086 EMBL:AY135087 EMBL:AY135088 EMBL:AY135089 EMBL:AY135090 EMBL:AY135091 EMBL:AY135092 EMBL:AY135093 EMBL:AY058692 PIR:A45176 RefSeq:NP_511098.1 UniGene:Dm.2620 ProteinModelPortal:Q24324 SMR:Q24324 DIP:DIP-29770N IntAct:Q24324 STRING:Q24324 EnsemblMetazoa:FBtr0071313 GeneID:31872 KEGG:dme:Dmel_CG15793 NMPDR:fig|7227.3.peg.17128 CTD:31872 FlyBase:FBgn0010269 eggNOG:inNOG04970 GeneTree:EMGT00050000000989 InParanoid:Q24324 OMA:DIAGWVC OrthoDB:EOG4ZKH2R PhylomeDB:Q24324 BRENDA:2.4.1.222 NextBio:775740 Bgee:Q24324 GermOnline:CG15793 GO:GO:0042386 KO:K04368 Uniprot:Q24324

MSKNKLNLVLPPVNTEATVAAATVAPTPPFKTPSGTDTHSLLGKPKTSIDALTETLEGLDMGDTERK
RIKMFLSQKEKIGELSDEDLEKLGELGSGNGGVVMKVRHTHTHLIMARKLIHLEVKPAIKILRELKVLH
ECNFPHIVGFYGAFYSDGEISICMEYMDGGSLDLILKRAGRIPESILGRITLAVLKGLSYLRDNHAIIHRD

VKPSNILVNSSGEIKICDFGVSGQLIDSMANSFVGTRSYMSPERLQTYSVQSDIWSLGLSLVEMAIG
MYPIPPPNTATLESIFADNAEESGQPTDEPRAMAIFELLDYIVNEPPPKLEHKIFSTEFKDFVDICLKKQ
PDERADLKTLLSHPWIRKAELEEVDISGWVCKTMDPPTPKRNTSPN

>FB|FBgn0013987 symbol:MAPk-Ak2 species:7227 "Drosophila melanogaster" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 GO:GO:0008360 EMBL:AE014298 SUPFAM:SSF56112 GO:GO:0004674 GO:GO:0007155 BRENDA:2.7.11.1 GO:GO:0045793 EMBL:U20757 PIR:JC4297 RefSeq:NP_001188547.1 RefSeq:NP_524769.1 RefSeq:NP_727032.1 RefSeq:NP_788861.1 UniGene:Dm.1442 ProteinModelPortal:P49071 SMR:P49071 DIP:DIP-21714N IntAct:P49071 MINT:MINT-760885 STRING:P49071 PRIDE:P49071 EnsemblMetazoa:FBtr0070837 EnsemblMetazoa:FBtr0070838 EnsemblMetazoa:FBtr0070839 EnsemblMetazoa:FBtr0302940 EnsemblMetazoa:FBtr0308577 GeneID:44573 KEGG:dme:Dmel_CG3086 CTD:44573 FlyBase:FBgn0013987 eggNOG:inNOG04151 InParanoid:P49071 OMA:NGKVVQC OrthoDB:EOG4X69QW PhylomeDB:P49071 NextBio:837468 Bgee:P49071 GermOnline:CG3086 KO:K04443 Uniprot:P49071

MLSLQNQRQPKTTPLTDDYVTSNTVLGYGINGKVVQCTHRRTQQNYALKVLLDSERARREVDLHW
RVSGCRYIVNIIDVYENTFKDRKCLLVVMECMEGGELFQRIQDKADGAFTEREAAQIMHEICVDYLH
SRDIAHRDLKPENLLYTTTQPNATLKLTDFGFAKETFTSYTLQTPCYTPYYVAPEVLGPEKYDKSCDIW
SLGVVMYIIMCGFPPFYSNHGLAISPGMKNRIRTGQYDFPDPEWTNVSQAAKLKGMLNVDPSKRL
RIQDVISNKWIAQYNAVPQTPLCTGRMLKEAEETWPEVQEEMTRSLATMRVDYDQMQIKALDKS
NNPLLTKRRKKIEEMELYMANATRN

>FB|FBgn0015765 symbol:Mpk2 species:7227 "Drosophila melanogaster" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008352 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PRINTS:PR01773 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 EMBL:AE014297 GO:GO:0005524 GO:GO:0005634 GO:GO:0042742 GO:GO:0050832 SUPFAM:SSF56112 GO:GO:0042594 GO:GO:0009408 GO:GO:0071276 GO:GO:0006970 GO:GO:0045793 GO:GO:0042542 GO:GO:0034614 GO:GO:0000165 BRENDA:2.7.11.24 GO:GO:0071243 GO:GO:0002385 GeneTree:EMGT00050000001140 GO:GO:0008348 KO:K04441 EMBL:U86867 EMBL:AF035546 EMBL:AF035547 EMBL:AY071670 RefSeq:NP_001163711.1 RefSeq:NP_477163.1 RefSeq:NP_732959.1 UniGene:Dm.2996 ProteinModelPortal:O62618 SMR:O62618 IntAct:O62618 MINT:MINT-4080391 STRING:O62618 PRIDE:O62618 EnsemblMetazoa:FBtr0084580 EnsemblMetazoa:FBtr0084581 EnsemblMetazoa:FBtr0300572 GeneID:42866 KEGG:dme:Dmel_CG5475 CTD:42866 FlyBase:FBgn0015765 eggNOG:inNOG08395 InParanoid:O62618 OMA:YAEPSDE OrthoDB:EOG4Z6145 PhylomeDB:O62618 NextBio:830992 ArrayExpress:O62618 Bgee:O62618 GermOnline:CG5475 GO:GO:0016909 Uniprot:O62618

MSVSITKKFYKLDINRTEWEIPDIYQDLQPVGSGAYGQVSKAVVRGTNMHVAIKKLARPFQSAVHA
KRTYRELRLLKHMDHENVIGLLDIFHPHPANGSLENFQQVYLVTHLMDADLNNIIRMQHLSHVQFL
VYQILRGLKYIHSAGVIHRDLKPSNIAVNEDCELRILDFGLARPTENEMTGYVATRWYRAPEIMLNW

MHYDQTVDIWSVGCIMAELITRRTLFPGTDHIHQLNLIMEMLGTPPAEFLKKISEARSYIQSLPPMK
GRSFKNVFKNANPLAIDLLEKMLELDAEKRITAEEALSHPYLEKYAEPSVEQTSPPYDHSFEDMDLPV
DKWKELIYKEVTNFKPPPSYAQVLKDVK

>FB|FBgn0024326 symbol:Mkk4 species:7227 "Drosophila melanogaster" InterPro:IPR000719 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 InterPro:IPR017442 EMBL:AE014297 GO:GO:0005524 GO:GO:0030424 SUPFAM:SSF56112 GO:GO:0048666 GO:GO:0004702 GO:GO:0007257 GO:GO:0008545 KO:K04430 EMBL:AF035551 EMBL:AY070600 RefSeq:NP_001163551.1 RefSeq:NP_477353.1 UniGene:Dm.2942 ProteinModelPortal:O61444 SMR:O61444 IntAct:O61444 MINT:MINT-1710570 STRING:O61444 PRIDE:O61444 EnsemblMetazoa:FBtr0081892 EnsemblMetazoa:FBtr0300443 GeneID:41020 KEGG:dme:Dmel_CG9738 NMPDR:fig|7227.3.peg.11715 UCSC:CG9738-RA CTD:41020 FlyBase:FBgn0024326 eggNOG:inNOG04230 InParanoid:O61444 OMA:SILAKIT OrthoDB:EOG463XTC PhylomeDB:O61444 NextBio:821753 ArrayExpress:O61444 Bgee:O61444 Uniprot:O61444

MAERPKNLFATGSSRSRNPPDQLSLNNLSIRHPPSSTSSTSSGSTSSGSSSSSQHNHVTRCFGAQQP
QQTPPVASSQVPPVPAASSSSAADRHRERIRQQACGKLQFGEGGANTHTFTSDDLEDEGERGAFG
AVNKMTFKKLDKVMAVKRIRSTVDEKEQKQLLMDLEVVMKSNECIYIVQFYGALFKEGDCWICMEL
MDTSLDKFYKYIYEKQQRHIPESILAKITVATVNALNYLKEELKIIHRDVKPSNILRRGDIKLCDFGISGQ
LVDSIAKTKDAGCRPYMAPERIDPERAKGYDVRSDVWSLGITLMEVATGNFPYRKWDSVFEQLCQV
VQGEPPRLLTSYNGMEFSKEFVDFVNTCLIKKESDRPKYSRLLEPFRRGETSHTDVAVYVADILESME
KDGITQFTANQQAES

>FB|FBgn0024846 symbol:p38b species:7227 "Drosophila melanogaster" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008352 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PRINTS:PR01773 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 GO:GO:0005634 GO:GO:0042742 GO:GO:0006955 EMBL:AE014134 GO:GO:0050832 SUPFAM:SSF56112 GO:GO:0040018 GO:GO:0042594 GO:GO:0009651 GO:GO:0009408 GO:GO:0071276 GO:GO:0045793 GO:GO:0030510 GO:GO:0001934 GO:GO:0042542 GO:GO:0034614 GO:GO:0007476 GO:GO:0045088 GO:GO:0000165 BRENDA:2.7.11.24 GO:GO:0071243 GeneTree:EMGT00050000001140 KO:K04441 eggNOG:inNOG08395 OrthoDB:EOG4Z6145 GO:GO:0016909 EMBL:AF035548 EMBL:AB006364 EMBL:AY058548 RefSeq:NP_477361.1 UniGene:Dm.2953 ProteinModelPortal:O61443 SMR:O61443 DIP:DIP-22779N IntAct:O61443 MINT:MINT-760858 STRING:O61443 PRIDE:O61443 EnsemblMetazoa:FBtr0080534 GeneID:34780 KEGG:dme:Dmel_CG7393 NMPDR:fig|7227.3.peg.2312 CTD:34780 FlyBase:FBgn0024846 InParanoid:O61443 OMA:DIFRGAN PhylomeDB:O61443 NextBio:790183 ArrayExpress:O61443 Bgee:O61443 GermOnline:CG7393 Uniprot:O61443

MSRKMAKFYKLDINRTEWEIPETYQNLQPVGQGAYGQVCKAVVRGTSTKVAIKKLARPFQSAVHA
KRTYRELRLLKHMDHENVIGLLDVFHPGQPADSLDQFQQVYMVTHLMDADLNNIIRTQKLSDVQF
LVYQILRGLKYIHSAGVIHRDLKPSNIAVNEDCELRILDFGLARPAESEMTGYVATRWYRAPEIMLNW
MHYNQTADIWSVGCIMAELLTGRTLFPGTDHIHQLNLIMEVLGTPADEFMSRISSSRNYIRSLPVMP

RRNFRDIFRGANPLAIDLLEKMLELDADKRITAEQALAHPYMEKYHDPTDEQTAALYDQSFEENELP
VEKWREMVFSEVTAFKPTAAFAELLPKEQ

>FB|FBgn0261524 symbol:lic species:7227 "Drosophila melanogaster" InterPro:IPR000719 InterPro:IPR008271 InterPro:IPR011009 Pfam:PF00069 PROSITE:PS00108 PROSITE:PS50011 InterPro:IPR017442 GO:GO:0005524 SUPFAM:SSF56112 GO:GO:0040018 GO:GO:0000187 GO:GO:0045793 GO:GO:0004702 GO:GO:0001934 GO:GO:0007314 GO:GO:0004708 GO:GO:0031435 GeneTree:EMGT00050000000989 GO:GO:0002385 FlyBase:FBgn0261524 EMBL:AJ238572 ProteinModelPortal:Q9U983 STRING:Q9U983 PRIDE:Q9U983 InParanoid:Q9U983 PhylomeDB:Q9U983 ArrayExpress:Q9U983 Bgee:Q9U983 Uniprot:Q9U983

MSKRHRLTPFTIAKEPEAAIVPPRNLDSRATIQIGDRTFDIDADSLEKICDLGRGAYGIVDKMRHKQT
DTVLAVKRIPMTVNIREQHRLVMDLDISMRSSDCPYTVHFYGAMYREGDVWICMEVMSTDKFYPK
VFLHDLRMEESVLGKIAMSVVRALHYLHAQLKVIHRDVKPSNILINRAGQVKICDFGISGYLVDSIAKT
IDAGCKPYMAPERIDPQGNPAQYDIRSDVWSLGIGMIEMATGRYPYDNWRTPFEQLRQVVEDSPP
RLPEGTFSPEFEDFIALQKEYMARPNYEQLLKHSFIVEHLQRNTDISEFVARILDLPDAAGAVG

>GENEDB_PFALCIPARUM|PF14_0294 symbol:PfMAP1 species:5833 "Plasmodium falciparum" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 SUPFAM:SSF56112 EMBL:AE014187 GeneTree:EPrGT00050000000232 HSSP:P24941 GO:GO:0004707 KO:K04371 GenomeReviews:AE014187_GR OMA:GNKKYVD RefSeq:XP_001348468.1 ProteinModelPortal:Q8ILF0 IntAct:Q8ILF0 MINT:MINT-1564665 EnsemblProtists:PF14_0294:mRNA GeneID:811876 KEGG:pfa:PF14_0294 NMPDR:fig|36329.1.peg.2170 EuPathDB:EupathDB:PF14_0294 Uniprot:Q8ILF0

MPKEDCKTEKSIDSIDENVLKKYDILKKVGKGAYGVVFKGRCKKNKNIVAVKKIFGAFQNCTDAQRTF
REIIFLYELNGHDNIIKLMDVIKAKNDNDIYLIFDFMETDLHEVIKADLLEEIHKKYIILLRALKYIHSGGLL
HRDIKPSNILVNSECHIKVADFGLARSISTHVNENKVPILTDYVATRWYRAPEILLGSTHYTEDVDMW
SLGCIMGELLCGKPLFTGNSTMNQLEKIIQVIGKPNKKDIEDIRPAEKIISSFVDLKKKNLKDICYKASNE
SLDLLEKLLQFNPSKRISAENALKHKYVEEFHSIIDEPTCRHIITIPINDNTKYRVNFYRNVVYFVIMRRN
KFHSNVLNQGESKKEEKKDRYYRRDKDKKCCENNKVHMEDKEYKNKIIFSQGDKPEDIKEDHKKCKI
CDEIHVDTSKQIDSINLEHVVLNNNDVSYVDKKKKTKYEPVYKERGKMKKDKMGNVYCKDRERRVF
YEARKKESITNFTTATTISKSDTEEMSQMEINEIESNEMKGKIKEQIKEQIKEQIKEQIKEQIKKTQNNIS
KISIGSNTMSSTISKTEPNSRNYFINKKSVESFYTKERKNNDILFHANNKKVIFFKDKNKIKNHSSEKKKI
KYKVFGFKKYENEQNVPHYLETKCSNTPLGKNYYYKKYVDGSNKKYVDGGNKKYVDGGNKKYVDG
SNKKYVDGSNRKYVDGGNKKYVDGSSKKYVDGGNKKYVDGSSKKYVDEGNKKYVDGGNKKYVDG
GNKYVDGDKKYNHNYNHFNNNYYYYSRRGSLKSVNKEEENCSQRTWKNTAKLHLPLVVNKSTKPL
NTLSHDYYNKDEENKYMNNSMLKKEVKKKIWRHLIDNENKKNQDMTDYYYNPIINKTEKNNKRNF
KCGEKKTEEKCVSNE

>MGI|MGI:109298 symbol:Mapkapk2 species:10090 "Mus musculus" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 MGI:MGI:109298 GO:GO:0005524 GO:GO:0005634 GO:GO:0005737 SUPFAM:SSF56112 GO:GO:0004674 HOGENOM:HBG755340 GO:GO:0048255 GO:GO:0048839 HOVERGEN:HBG106948 OMA:NGKVVQC KO:K04443 CTD:9261 EMBL:X76850 EMBL:BC063064 IPI:IPI00113079 PIR:S78100 RefSeq:NP_032577.1 UniGene:Mm.221235 ProteinModelPortal:P49138 SMR:P49138 IntAct:P49138 STRING:P49138 PhosphoSite:P49138 PRIDE:P49138 Ensembl:ENSMUST00000016672 GeneID:17164 KEGG:mmu:17164 eggNOG:roNOG12079 InParanoid:P49138 OrthoDB:EOG4HQDJP PhylomeDB:P49138 NextBio:291442 ArrayExpress:P49138 Bgee:P49138 CleanEx:MM_MAPKAPK2 CleanEx:MM_RPS6KC1 Genevestigator:P49138 GermOnline:ENSMUSG00000016528 Uniprot:P49138

MLSGSPGQTPPAPFPSPPPPAPAQPPPPFPQFHVKSGLQIRKNAITDDYKVTSQVLGLGINGKVLRIF
DKRTQQKFALKMLQDCPKARREVELHWRASQCPHIVHIVDVYENLYAGRKCLLIVMECLGELFSRIQ
DRGDQAFTEREASEIMKSIGEAIQYLHSINIAHRDVKPENLLYTSKRPNAILKLTDFGFAKETTSHNSLT
TPCYTPYYVAPEVLGPEKYDKSCDMWSLGVIMYILLCGYPPFYSNHGLIPGMKTRIRMGQYEFPNPE
WSEVSEEVKMLIRNLLKTEPTQRMTITEFMNHPWIMQSTKVPQTPLHTSRVLKEDKERWEDVKEE
MTSALATMRVDYEQIKIKKIEDASNPLLLKRRKKARAVEDAAAH

>MGI|MGI:1336881 symbol:Stk30 species:10090 "Mus musculus" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 MGI:MGI:1336881 GO:GO:0005524 SUPFAM:SSF56112 HOGENOM:HBG755340 GO:GO:0004693 GeneTree:ENSGT00600000084046 HOVERGEN:HBG106271 KO:K08830 EMBL:AB022695 EMBL:BC037614 IPI:IPI00267984 IPI:IPI00271851 RefSeq:NP_036103.1 UniGene:Mm.140948 ProteinModelPortal:Q9WVS4 SMR:Q9WVS4 IntAct:Q9WVS4 STRING:Q9WVS4 PhosphoSite:Q9WVS4 PRIDE:Q9WVS4 Ensembl:ENSMUST00000070565 GeneID:26448 KEGG:mmu:26448 NMPDR:fig|10090.3.peg.27114 UCSC:uc007pbv.1 UCSC:uc007pbx.1 CTD:26448 InParanoid:Q9WVS4 PhylomeDB:Q9WVS4 NextBio:304549 ArrayExpress:Q9WVS4 Bgee:Q9WVS4 CleanEx:MM_RAGE Genevestigator:Q9WVS4 GermOnline:ENSMUSG00000056458 Uniprot:Q9WVS4

MKNYKAIGKIGEGTFSEVMKMQSLRDGNYYACKQMKQHFESIEQVNSLREIQALRRLNPHPNILAL
HEVVFDRKSGSLALICELMDMNIYELIRGRRHPLSEKKIMLYMYQLCKSLDHMHRNGIFHRKPENILV
KQDVLKLGDFGSCRSVYSKQPYTEYISTRWYRAPECLLTDGFYTYKMDLWSAGCVFYEIASLQPLFPG
VNELDQISKIHDVIGTPCQKTLTKFKQSRAMSFDFPFKKGSGIPLLTANLSQLSLLHAMVAYDPDERIA
AHQALQHPYFQVQRAAETQTLAKHRRAFCPKFSMVPESSSHNWSFSQEGRKQKQSLRHEEGHAR
RQGPTSLMELPKLRLSGMTKLSSCSSPALRSVLGTGANGKVPVLPLCAAVNKKTDTQKDIKPHLKHY
HLPTINRKGGEY

>MGI|MGI:894279 symbol:Mknk2 species:10090 "Mus musculus" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 MGI:MGI:894279 GO:GO:0005524 GO:GO:0006915 GO:GO:0005515

GO:GO:0006417 GO:GO:0046872 SUPFAM:SSF56112 GO:GO:0004674 GO:GO:0007243 HOGENOM:HBG755340 GeneTree:ENSGT00550000074510 HOVERGEN:HBG106949 KO:K04372 eggNOG:roNOG13477 CTD:2872 OMA:VQKKTAE EMBL:AB164081 EMBL:AK008277 EMBL:AK030830 EMBL:AK154235 EMBL:Y11092 EMBL:BC010256 IPI:IPI00267802 IPI:IPI00623703 RefSeq:NP_067437.1 UniGene:Mm.42126 UniGene:Mm.472174 ProteinModelPortal:Q8CDB0 SMR:Q8CDB0 IntAct:Q8CDB0 STRING:Q8CDB0 PhosphoSite:Q8CDB0 PRIDE:Q8CDB0 Ensembl:ENSMUST00000003433 Ensembl:ENSMUST00000072616 Ensembl:ENSMUST00000105337 GeneID:17347 KEGG:mmu:17347 UCSC:uc007gee.1 InParanoid:Q8CDB0 PhylomeDB:Q8CDB0 ArrayExpress:Q8CDB0 Bgee:Q8CDB0 CleanEx:MM_MKNK2 Genevestigator:Q8CDB0 GermOnline:ENSMUSG00000020190 Uniprot:Q8CDB0

MVQKRTAELQGFHRSFKGQNPFELAFSLDLAQHRDSDFSPQCEARPDMPSSQPIDIPDAKKRGRKK
KRCRATDSFSGRFEDVYQLQEDVLGEGAHARVQTCVNLITNQEYAVKIIEKQLGHIRSRVFVEMLYQ
CQGHRNVLELIEFFEEEDRFYLVFEKMRGGSILSHIHRRRHFNELEASVVVQDVASALDFLHNKGIAH
RDLKPENILCEHPNQVSPVKICDFDLGSGIKLNGDCSPISTPELLTPCGSAEMPEVVEAFSEEASIYDKR
CDLWSLGVILYILLSGYPPFVGHCGSDCGWDRGEACPACQNMLFESIQEGKYEFPDKDWSHISFAA
KDLISKLLVRDAKQRLSAAQVLQHPWVQGCAPENTLPTPLVLRNCAKDLTSFAAEAIAMNRQLAQC
EEDAGQDQPVVIRATSRCLQLSPPSQSKLAQRRQRASLSATPVVLVGDRA

>POMBASE|SPAC1006.09 symbol:win1 species:4896 "Schizosaccharomyces pombe" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017240 InterPro:IPR017441 Pfam:PF00069 PIRSF:PIRSF037579 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 GO:GO:0007346 GO:GO:0000186 GO:GO:0005515 EMBL:CU329670 GenomeReviews:CU329670_GR SUPFAM:SSF56112 GO:GO:0031098 GO:GO:0004709 GO:GO:0051519 GeneTree:EFGT00050000000597 BRENDA:2.7.11.25 eggNOG:fuNOG05884 OMA:HILENGS OrthoDB:EOG4GF6P7 EMBL:AJ223190 PIR:T37556 PIR:T50298 PIR:T50457 RefSeq:NP_594856.2 ProteinModelPortal:O74304 IntAct:O74304 STRING:O74304 EnsemblFungi:SPAC1006.09.1 GeneID:2542988 KEGG:spo:SPAC1006.09 GeneDB_Spombe:SPAC1006.09 BioCyc:SPOM-XXX-01:SPOM-XXX-01-003086-MONOMER ArrayExpress:O74304 Uniprot:O74304

MENILDPSVVNSHILENGSRRSSINPILDSELRDKTFEKAHRRSLTLLSSFTSSMLELPNNGKEENHRRP
SVARSSSDRSKASAKEDLFSEAFRMAEQPPAEALTISTPVDPINIDELDRAYAVSPSSNLLHPPTSSSSI
PIPIKNAGHSNLDHPIRPSLQSSISSNRIIKSPGIKEDDYMHRGRSISSPMIDVEHINSTAVPSKTKNLPE
KPKRSHKLRNSITFAKIEDHPERKSQLRRLSSSLKCFDPEYDNPSLSIRRDSSTYYFSNVNETYDEEDSDL
DSETSTVNWVQSVLNLPSLLSDDLMANPKNKERFEWQYMLTSVLTGDIVRSEKLRLRKIASSREGRN
SDYSDNLWMEIWCWLTHRSVDSYRENLKHLTGVDVLLAIMNFHWDESNELTPIVAVDNMLQKLD
KYERLYPSRRSILQEHSLYASESFQHKLDVLTAYSNVTHALEIQVNIIRSWVGNEEMDITKNTTNSINN
VSQISNGPFVERFYRETGLIRAFQRITNMNSVLSKVCNTIVTYADDLKSYGLPLIADDYMRLLSFPFRLI
KEFLNLRLSCAENITSISLFTIDSLLDDLRNTMKVAVHIIQQHTVLIKPFRDDSKFVDENQSLNNILVASL
KFYFNLLHKVRNCALLHFKETEILEGEWDFLLAVCPHIEHGFQIMSKSLSSLVGEILTNINRYLKDQLQ
GPDTDDSALITSFYIKVLDCVRIRFRKLMSFTRILKAHLENSCEYVIKENSLSLLIQRLEESNHVTYTASEH
EGAYVIVPGHLVDSPNILREVLSMTFNKGDNNFESVPPYAVVLAPDSSICWNGHVTDLDIPEVSISIA
PNCVRLVTLATANQLSVIEDYFISIVGDTVSLVDSAKANSSKINKQMTKIKNSLKLASLLDVIQTIRTRY
HGMNCQNLIHYSFSYAIEFAQRLMRLSILDASSIGLIRRKMIQLAISWVGFIYEDCSPTDRNTFRWTV

TALEFAMIMTYGSNILMIDKKSFEELKEKVGKCVALLLLFDVMGTKAGRSMDQQAGDIPARLVRNN
SDRSRLSDNELASFVKEEVMHRIIELESNRRDRLYKSQLIGRVLDDTTKENRLLKELASSKSNITIRWQ
QGGLIGSGSFGTVYRAVNLDTGDLMAVKEVLHKPRISRMIKRIKGEMLVLELFDHPNVVSYYGIEVH
REKVNIFMELCQGSSLFEFLRYGRIEDELVIQVYVLQLLEGLAYIHSCGVSHQDVKPENILFDHNGIMK
FTDFGSAKMSGSASTKIFEQTQQEEEEFEDSEFLQHLDQNRGYSLTGTPTYMAPELILGNPSERVGA
MDIWSLGCVIVEMATGSPPWPRLDNHFSLMYHIAAHNPPIIPADDQLSPLGQNFLKRCFVSDPNQ
RATAAELLMDPWVYLRAGTEFDLMSSVVESAPSTNGAPLEL

>POMBASE|SPAC1D4.13 symbol:byr1 species:4896 "Schizosaccharomyces pombe" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005829 GO:GO:0005524 GO:GO:0005634 GO:GO:0005515 EMBL:CU329670 GenomeReviews:CU329670_GR SUPFAM:SSF56112 GO:GO:0004674 HOGENOM:HBG755340 GO:GO:0030435 KO:K00924 GO:GO:0006995 GeneTree:EFGT00050000000597 EMBL:X07445 PIR:S00473 RefSeq:NP_593026.1 ProteinModelPortal:P10506 IntAct:P10506 STRING:P10506 EnsemblFungi:SPAC1D4.13.1 GeneID:2542137 KEGG:spo:SPAC1D4.13 NMPDR:fig|4896.1.peg.2996 GeneDB_Spombe:SPAC1D4.13 eggNOG:fuNOG07450 OMA:KVIQLNI OrthoDB:EOG43V342 BioCyc:SPOM-XXX-01:SPOM-XXX-01-000747-MONOMER BRENDA:2.7.12.2 ArrayExpress:P10506 GO:GO:0004708 GO:GO:0000751 GO:GO:0032005 Uniprot:P10506

MFKRRRNPKGLVLNPNASVKSSDNDHKEELINNQKSFESNVEAFMEQCAHMNRRPAWISDLDNS
SLEVVRHLGEGNGGAVSLVKHRNIFMARKTVYVGSDSKLQKQILRELGVLHHCRSPYIVGFYGQYKN
NISLCMEYMDCGSLDAILREGGPIPLDILGKIINSMVKGLIYLYNVLHIIHRDLKPSNVVVNSRGEIKLC
DFGVSGELVNSVAQTFVGTSTYMSPERIRGGKYTVKSDIWSLGISIIELATQLWSFSNIDDSIGILDLLH
CIVQEEPPRLPSSFPEDLRLFVDACLHKDPTLRASPQQLCAMPYFQQALMINVDLASWASNFRSS

>POMBASE|SPAC23A1.06c symbol:cmk2 species:4896 "Schizosaccharomyces pombe" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 InterPro:IPR020650 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 GO:GO:0005737 GO:GO:0005509 EMBL:CU329670 GenomeReviews:CU329670_GR GO:GO:0034599 SUPFAM:SSF56112 GO:GO:0005516 GO:GO:0031098 GO:GO:0030428 GO:GO:0051519 GeneTree:EFGT00070000008711 InterPro:IPR020636 PANTHER:PTHR24347 GO:GO:0004683 GO:GO:0033314 PIR:T38226 RefSeq:NP_594436.1 ProteinModelPortal:O42844 STRING:O42844 EnsemblFungi:SPAC23A1.06c.1 GeneID:2541982 KEGG:spo:SPAC23A1.06c NMPDR:fig|4896.1.peg.4406 GeneDB_Spombe:SPAC23A1.06c eggNOG:fuNOG05982 HOGENOM:HBG738506 OrthoDB:EOG49W5Q5 BioCyc:SPOM-XXX-01:SPOM-XXX-01-002544-MONOMER ArrayExpress:O42844 PANTHER:PTHR24347:SF28 Uniprot:O42844

MSILAGFKNLLKHSKSSKGRSNASKSVDVSVNRDVAAYTELAAKNVNAGGDEEIRVANYPGLEKYQL
IENLGDGAFSQVYKAYSIDRKEHVAVKVIRKYEMNKKQRQGVFKEVNIMRRVKHKNVVNLFVETED
FYHLVMELAEGGELFHQIVNFTYFSENLARHIIIQVAEAVKHLHDVCGIVHRDIKPENLLFQPIEYLPSQ
NYTPPSLEPNKLDEGMFLEGIGAGGIGRILIADFGFSKVVWNSKTATPCGVYAAPEIVNDELYSKNVD

MWAMGCVLHTMLCGFPPFFDENIKDLASKVVNGEFEFLSPWWDDISDSAKDLITHLLTVDPRERY
DIHQFFQHPWIKGESKMPENFTYKPKLHGTPGGPKLSLPRSLVKGIDIPTTPIKSATHPLLSSYSEPKTP
GVSSVHEAMGVAYDIRRLNHLGFSPEQLSKKSMNTGSIKELILDEETTTDDDDYIISSFPLNDTLGSEG
KDPFSLNLKESSLYSRRSAKRVN

>POMBASE|SPAC24B11.06c symbol:sty1 species:4896 "Schizosaccharomyces pombe" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008271 InterPro:IPR008352 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PRINTS:PR01773 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GeneDB_Spombe:SPAC24B11.06c GO:GO:0005829 GO:GO:0005524 GO:GO:0005634 GO:GO:0005515 EMBL:CU329670 GO:GO:0006355 GenomeReviews:CU329670_GR GO:GO:0070301 GO:GO:0045931 SUPFAM:SSF56112 GO:GO:0006351 HOGENOM:HBG755340 GO:GO:0043556 GO:GO:0010520 GO:GO:0006883 GO:GO:0051403 GO:GO:0051595 GO:GO:0034644 GO:GO:0051519 GO:GO:0031990 GO:GO:0043949 GO:GO:0010847 GO:GO:0010848 GO:GO:0035065 GO:GO:0051101 GO:GO:0034504 GeneTree:EFGT00050000000591 BRENDA:2.7.11.24 GO:GO:0070314 GO:GO:0071243 GO:GO:0070321 GO:GO:0004707 GO:GO:0071473 OMA:XVDLLEK KO:K04441 EMBL:X89262 EMBL:U26739 PIR:S68675 RefSeq:NP_592843.1 ProteinModelPortal:Q09892 SMR:Q09892 IntAct:Q09892 STRING:Q09892 EnsemblFungi:SPAC24B11.06c.1 GeneID:2541652 KEGG:spo:SPAC24B11.06c NMPDR:fig|4896.1.peg.2813 eggNOG:fuNOG05772 OrthoDB:EOG496319 BioCyc:SPOM-XXX-01:SPOM-XXX-01-000583-MONOMER ArrayExpress:Q09892 GO:GO:0043557 Uniprot:Q09892

MAEFIRTQIFGTCFEITTRYSDLQPIGMGAFGLVCSAKDQLTGMNVAVKKIMKPFSTPVLAKRTYREL
KLLKHLRHENIISLSDIFISPFEDIYFVTELLGTDLHRLLTSRPLETQFIQYFLYQILRKFVHSAGVIHRDLK
PSNILINENCDLKICDFGLARIQDPQMTGYVSTRYYRAPEIMLTWQKYNVEVDIWSAGCIFAEMIEG
KPLFPGRDHVNQFSIITELLGTPPMEVIETICSKNTLRFVQSLPQEVPFAEKFKNADPDAIDLLEKMLV
FDPRKRISAADALAHNYLAPYHDPTDEPVADEVFDWSFQDNDLPVETWKVMMYSEVLSFHNMD
NELQS

>POMBASE|SPAC31G5.09c symbol:spk1 species:4896 "Schizosaccharomyces pombe" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008271 InterPro:IPR008352 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PRINTS:PR01773 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005829 GO:GO:0005524 GO:GO:0005634 EMBL:CU329670 GO:GO:0005816 GenomeReviews:CU329670_GR SUPFAM:SSF56112 HOGENOM:HBG755340 GO:GO:0000165 GeneTree:EFGT00050000000591 GO:GO:0000751 GO:GO:0032005 BRENDA:2.7.11.24 GO:GO:0004707 KO:K04371 eggNOG:fuNOG04760 OrthoDB:EOG4P8JSR EMBL:AB004551 EMBL:D31735 EMBL:X57334 EMBL:AB084886 EMBL:AB084887 PIR:S15663 RefSeq:NP_594009.1 ProteinModelPortal:P27638 SMR:P27638 IntAct:P27638 STRING:P27638 EnsemblFungi:SPAC31G5.09c.1 GeneID:2542474 KEGG:spo:SPAC31G5.09c NMPDR:fig|4896.1.peg.3979 GeneDB_Spombe:SPAC31G5.09c OMA:LWLIMEV BioCyc:SPOM-XXX-01:SPOM-XXX-01-001640-MONOMER ArrayExpress:P27638 Uniprot:P27638

MASATSTPTIADGNSNKESVATSRSPHTHDLNFELPEEYEMINLIGQGAYGVVCAALHKPSGLKVAV
KKIHPFNHPVFCLRTLREIKLLRHFRHENIISILDILPPPSYQELEDVYIVQELMETDLYIRSQPLSDDHCQ
YFTYQILRALKAMHSAGVVHRDLKPSNLLLNANCDLKVADFGLARSTTAQGGNPGFMTEYVATRW
YRAPEIMLSFREYSKAIDLWSTGCILAEMLSARPLFPGKDYHSQITLILIGTPTMDDFSRIKSARARKYIK
SLPFTPKVSFKALFPQASPDAIDLLEKLLTFNPDKRITAEEALKHPYVAAYHDASDEPTASPMPPNLVD
LYCNKEDLEIPVLKALIFREVNFR

>POMBASE|SPAC9G1.02 symbol:wis4 species:4896 "Schizosaccharomyces pombe" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017240 Pfam:PF00069 PIRSF:PIRSF037579 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005829 GO:GO:0005524 GO:GO:0007346 EMBL:CU329670 GenomeReviews:CU329670_GR SUPFAM:SSF56112 GO:GO:0051403 GO:GO:0004709 GO:GO:0051519 GeneTree:EFGT00050000000597 BRENDA:2.7.11.25 eggNOG:fuNOG05884 OrthoDB:EOG4GF6P7 KO:K11230 OMA:ISHFDIM EMBL:Y07750 EMBL:Y11989 EMBL:U81521 PIR:T39225 RefSeq:NP_593557.1 ProteinModelPortal:O14299 STRING:O14299 EnsemblFungi:SPAC9G1.02.1 GeneID:2542873 KEGG:spo:SPAC9G1.02 NMPDR:fig|4896.1.peg.3527 GeneDB_Spombe:SPAC9G1.02 BioCyc:SPOM-XXX-01:SPOM-XXX-01-001233-MONOMER ArrayExpress:O14299 Uniprot:O14299

MGLEHTFYPAEDRFEPLLEHSEPVNFVPKENAKSYVRQGFASPHQSLMDNLVDSTESTKRSENFVSH
IPLTPSHSGQSEKLMSTRTSHSPYISPTMSYTNHSPANLTRNSSFNHQHYSTTLRSPPSMRGIDVNSS
HYPHISRPRTSSDSQKMYTRAPVDYYYIQENPYFNNIDQDSISDKSLPSTNQSLHHSEEDTESDNDFS
ESIHPEFDIDVFYKVSNILYDESDLQDPEKRERLEWHSMLSSVLKGDVMQTEKRRLRLTEPDGHSGTY
ISEVWLGLQAWLHLNADQAEVIRKSREGVEPVLREVIDFQIQDEETTKPPLEQVTEILEKVEQCKQFYI
SSREMEENVPLSASKEFNYKLNALISWSNVMESIQVETLVLQKWVGNDEFDLTMRTPQFNYDGVE
NTSSFEIFRQSGLQRTFEQRTLTTLNRIIHQAKQTISENAQAFEEMKLPTYEDKLLPLVRFPIKLLEEALR
LRLAYAKKIKGPNFLIVDSMLDDFKIALSVAVRIKREYIKIASPSPGWSLPTNVDEDYDNLLSLKFYFKLL
TLKLSSGNKNLYFKEIDFLENEWAFLNEHIYWINGGDIHMAGQFSYLSNSLLLNVHRYVESHLNGPTE
RTAASLTNWYSTLLKNTQIRFRKILRFSETLNSRFENASDFVISEGHPDLNRLSTTGHFLAYTANLERD
GVFVIADHTLSENPEALKALLFSKDISNLETIQQNCSYVLILCPVHPIVWKGRIEKVDVPDFSVDLKTNR
VRIIASNKREHLQAAKSVFQSISGDLVTLAVECRSITRYKEFIRLSKLCMRISSTVVDCVSAVREACSGV
NCHDLIYHVFSFAAEFGQRILRFLSFDSYWQTKLKRKITSLAVEWISFICDECDLMDRKTFRWGVGAL
EFLMLMIRGNNILLIDDAMFLKREKVGSMAFLLTHFDVLGAKSKVAAKLQRESTEVSSSPRLTSFGDV
EEEALSIQLLQKETMLRIDELEIERNNTLLERLAIGHVLDDSVFRNRDFIKLASSFSNITIRWQQGHFVR
SGMFGDVYTGNMETGDLAVKEIKLQDSRTFRSTVDQIHNEMTVLERLNHPNVVTYYGVEVHREKV
YIFMEFCQGGSLADLLAHGRIEDENVLKVYVVQLLEGLAYIHSQHILHRDIKPANILLDHRGMIKYSDF
GSLYVSPPTPEVRYEDIQPELQHLAGTPMYMAPEIILGTKKGDFGAMDIWSLGCVILEMMTGSTPW
SEMDNEWAIMYHVAAMHTPSIPQNEKISSLARDFIEQCFERDPEQRPRAVDLLTHPWITDFRKTIIT
MPPTITKKTSLSHTITEEKTAQLLAGRHDDSKAETDSLAASYKEESALPVASNVGLRQPNELRIDSINLP
PAIVTPDTINYSVD

>POMBASE|SPAPYUG7.02c symbol:sin1 species:4896 "Schizosaccharomyces pombe" GO:GO:0005829 GO:GO:0005515 EMBL:CU329670 GenomeReviews:CU329670_GR GO:GO:0045931 GO:GO:0031929 GO:GO:0031098 GeneTree:EFGT00050000003019 OrthoDB:EOG4DFSWT GO:GO:0031932 InterPro:IPR008828 PANTHER:PTHR13335 Pfam:PF05422 EMBL:AF155208 PIR:T50302 RefSeq:NP_594703.1 IntAct:Q9P7Y9

STRING:Q9P7Y9 EnsemblFungi:SPAPYUG7.02c.1 GeneID:2542972 KEGG:spo:SPAPYUG7.02c NMPDR:fig|4896.1.peg.4673 GeneDB_Spombe:SPAPYUG7.02c BioCyc:SPOM-XXX-01:SPOM-XXX-01-002784-MONOMER ArrayExpress:Q9P7Y9 Uniprot:Q9P7Y9

MELTREKVLLLTFLRMQYSHILPDSIENRVISTEAPEWELDKSLQDLLIHDYDYSKTSFSSSPPIVANDT
VSNVRKPSDTKQVNGAGGQVNHSRAEDSDYATSDLSESSDVGDDDNSCIFSFSKVPMDVASIKEEE
RLDPKISTLNNIDAIANLKLTNMVESSQAVNLTSSKQSSINQQSSVSTDYDDLRSISEESFHLSQGEIPL
TFPMNSSLTDTEADAVVAVDALFPGKQRGTHNTVNKARSVSNAKAPTARALLEHKENSSQNGPLA
ENFATFSGHAESNALRLNIYFPSSESPSKPLFVELRKNVLVSEAIGYILLQYVNQQLVPPIEDEAQNPNY
WNLRIVEDDGELDEDFPALDRVGPLSKFGFDAFALVKAPAIKENQAAYPFKSKHPTSIPEANNKTHIR
HTSSTSSQSQKQAQDVKDTLNTSHVVQVRLPPYGDNARFCNIEISKTTRLAMVLNQVCWMKQLER
FKYTLRVAGSDTVLPLDKTFSSLDGNPTLELKKKRDKKGSTQQLPTSSPQNSVYGSIKKDAQSSTYNA
TDIMSSNTYQEFLVWKRQPVSFMGRHERLLAIDGEYVHIMPSESKNIFETPKTSSIHAGSIILCKQSKK
SPCNFKMIVSKNRETKRYDFVLSAEAAIIVSRIRALMNTVKKIN

>POMBASE|SPBC119.08 symbol:pmk1 species:4896 "Schizosaccharomyces pombe" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008271 InterPro:IPR008351 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PRINTS:PR01772 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005829 GO:GO:0005524 GO:GO:0005634 GO:GO:0005515 GO:GO:0005816 GO:GO:0008360 GO:GO:0033554 GO:GO:0032153 EMBL:CU329671 SUPFAM:SSF56112 GenomeReviews:CU329671_GR HOGENOM:HBG755340 GO:GO:0031505 GO:GO:0006883 GO:GO:0033205 GO:GO:0051519 GO:GO:0050850 GO:GO:0000165 GeneTree:EFGT00050000000591 BRENDA:2.7.11.24 GO:GO:0004707 KO:K08293 eggNOG:fuNOG04682 OrthoDB:EOG4S7NZG EMBL:X98243 EMBL:U65405 PIR:T39306 RefSeq:NP_595289.1 ProteinModelPortal:Q92398 STRING:Q92398 EnsemblFungi:SPBC119.08.1 GeneID:2539920 KEGG:spo:SPBC119.08 NMPDR:fig|4896.1.peg.1155 GeneDB_Spombe:SPBC119.08 OMA:HRNITCI BioCyc:SPOM-XXX-01:SPOM-XXX-01-003371-MONOMER ArrayExpress:Q92398 Uniprot:Q92398

MDRRHRVYRVFNQEMYVEPNFKVVKELGQGAYGIVCAARNVASKDQEAVAIKKITNVFSKSILTKR
ALREIKLLIHFRNHRNITCIYDLDIINPYNFNEVYIYEELMEADLNAIIKSGQPLTDAHFQIYQILCGLKYI
HSANVIHRDLKPGNLLVNADCELKICDFGLARGCSENPEENPGFMTEYVATRWYRAPEIMLSFSSYH
KGIDVWSVGCILAELLGGTPLFKGKDFVHQLNLILHQLGTPDEETLSHSSRAQEYVRSLPKQRPIPFET
NFPKANPLALDLLAKLLAFDPNRRISVDDALEHPYLAVWHDPSDEPVCDSVFDFSFEYIEDANELRRV
ILDEVLNFRQKVRRRSHPTNPTVNIPQPAQTVPSNDNSFVSSSSSSQTSNKKRHDHSYNETAAIDHK
SDDNRHN

>POMBASE|SPBC1D7.05 symbol:byr2 species:4896 "Schizosaccharomyces pombe" InterPro:IPR000719 InterPro:IPR001660 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR011510 InterPro:IPR017441 Pfam:PF00069 Pfam:PF07647 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 PROSITE:PS50105 SMART:SM00220 SMART:SM00454 InterPro:IPR017442 GO:GO:0005886 GO:GO:0005524 GO:GO:0005737 GO:GO:0005515 EMBL:CU329671 SUPFAM:SSF56112 GenomeReviews:CU329671_GR GO:GO:0030435 InterPro:IPR013761

Gene3D:G3DSA:1.10.150.50 SUPFAM:SSF47769 GO:GO:0004709 GeneTree:EFGT00050000000597 GO:GO:0000751 GO:GO:0032005 EMBL:M74293 EMBL:X68851 PIR:A39723 RefSeq:NP_595714.2 PDB:1I35 PDB:1K8R PDBsum:1I35 PDBsum:1K8R ProteinModelPortal:P28829 SMR:P28829 DIP:DIP-136N IntAct:P28829 MINT:MINT-221819 STRING:P28829 EnsemblFungi:SPBC1D7.05.1 GeneID:2540612 KEGG:spo:SPBC1D7.05 GeneDB_Spombe:SPBC1D7.05 OMA:RIGENIL OrthoDB:EOG4QG0P3 BioCyc:SPOM-XXX-01:SPOM-XXX-01-004863-MONOMER BRENDA:2.7.11.25 ArrayExpress:P28829 GO:GO:0031142 Uniprot:P28829

MEYYTSKEVAEWLKSIGLEKYIEQFSQNNIEGRHLNHLTLPLLKDLGIENTAKGKQFLKQRDYLREFPR
PCILRFIACNGQTRAVQSRGDYQKTLAIALKKFSLEDASKFIVCVSQSSRIKLITEEEQICFNSSSPERDR
LIIVPKEKPCPSFEDLRRSWEIELAQPAALSSQSSLSPKLSSVLPTSTQKRSVRSNNAKPFESYQRPPSEL
INSRISDFFPDHQPKLLEKTISNSLRRNLSIRTSQGHNLGNFGQEILPRSSRRARPSELVCPLSSLRISVA
EDVNRLPRIDFDPPLTVSSTQRISRPPSLQKSITMVGVEPLYQSNGNEKSSKYNVFSESAHGNHQVLS
FSPGSSPSFIEQPSPISPTSTTSEDTNTLEEDTDDQSIKWIRGALIGSGSFGQVYLGMNASSGELMAV
QILDSVSESKDRHAKLLDALAGEIALLQELSHEHIVQYLGSNLNSDHLNIFLEYVPGGSVAGLLTMYGS
FEETLVKNFIKQTLKGLEYLHSRGIVHRDIKGANILVDNKGKIKISDFGISKKLELNTSKTGGARPSFQGS
SFWMAPEVVKQTMHTEKTDIWSLGCLVIEMLTSKHPYPNCDQMQAIFRIGENILPEFPSNISSSAID
FLEKTFAIDCNLRPTASELLSHPFVS

>POMBASE|SPBC409.07c symbol:wis1 species:4896 "Schizosaccharomyces pombe" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005829 GO:GO:0005524 GO:GO:0005634 GO:GO:0007346 GO:GO:0005515 GO:GO:0007067 GO:GO:0051301 GO:GO:0070301 GO:GO:0046685 EMBL:CU329671 SUPFAM:SSF56112 GO:GO:0004674 GenomeReviews:CU329671_GR GO:GO:0071470 GO:GO:0051403 GO:GO:0051519 GeneTree:EFGT00050000000597 BRENDA:2.7.12.2 GO:GO:0004708 GO:GO:0070314 GO:GO:0043555 eggNOG:fuNOG05342 OrthoDB:EOG4RV60P KO:K11227 EMBL:X62631 PIR:S18648 RefSeq:NP_595457.1 ProteinModelPortal:P33886 STRING:P33886 EnsemblFungi:SPBC409.07c.1 GeneID:2541055 KEGG:spo:SPBC409.07c NMPDR:fig|4896.1.peg.1323 GeneDB_Spombe:SPBC409.07c HOGENOM:HBG329512 OMA:DYHELAN BioCyc:SPOM-XXX-01:SPOM-XXX-01-003522-MONOMER ArrayExpress:P33886 Uniprot:P33886

MSSPNNQPLSCSLRQLSISPTAPPGDVGTPGSLLSLSSSSSSNTDSSGSSLGSLSLNSNSSGSDNDSKV
SSPSREIPSDPPLPRAVPTVRLGRSTSSRSRNSLNLDMKDPSEKPRRSLPTAAGQNNIPPTPPGPFPG
GLSTDIQEKLKAFHASRSKSMPEVVNKISSPTTPIVGMGQRGSYPLPNSQLAGRLSNSPVKSPNMPE
SGLAKSLAAARNPLLNRPTSFNRQTRIRRAPPGKLDLSNSNPTSPVSPSMSRRGLNIPPTLKQAVSET
PFSTFSDILDAKSGTLNFKNKAVLNSEGVNFSSGSSFRINMSEIIKLEELGKGNYGVVYKALHQPTGVT
MALKEIRLSLEEATFNQIIMELDILHKAVSPYIVDFYGFFEGSVFICMEYMDAGSMDKLYAGGIKDEG
VLARTAYAVVQGLKTLKEEHNIIHRDVKPTNVLVNSNGQVKLCDFGVSGNLVASISKTNIGCQSYMA
PERIRVGGPTNGVLTYTVQADVWSLGLTIEMAGAYPYPPESYTSIFAQLSAICDGDPPSLPDSFSPEA
RDFVNKCLNKNPSLRPDYHELANHPWLLKYQNADVDMASWAKGALKEKGEKRS

>POMBASE|SPBC543.07 symbol:pek1 species:4896 "Schizosaccharomyces pombe" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108

PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005829 GO:GO:0005524 GO:GO:0005634 GO:GO:0008360 EMBL:CU329671 SUPFAM:SSF56112 GO:GO:0004674 GenomeReviews:CU329671_GR HOGENOM:HBG755340 GO:GO:0031505 GO:GO:0006883 GO:GO:0004713 GO:GO:0033205 GO:GO:0030428 GO:GO:0051519 GO:GO:0050850 GeneTree:EFGT00050000000597 GO:GO:0000165 BRENDA:2.7.12.2 GO:GO:0004708 eggNOG:fuNOG04753 OrthoDB:EOG4D29ZP KO:K08294 EMBL:AF157632 EMBL:D82023 PIR:T51294 PIR:T51992 RefSeq:NP_596795.1 ProteinModelPortal:Q9Y884 STRING:Q9Y884 EnsemblFungi:SPBC543.07.1 GeneID:2540919 KEGG:spo:SPBC543.07 NMPDR:fig|4896.1.peg.2661 GeneDB_Spombe:SPBC543.07 OMA:INADPNP BioCyc:SPOM-XXX-01:SPOM-XXX-01-004776-MONOMER ArrayExpress:Q9Y884 Uniprot:Q9Y884

MSKKPVLNLDTSNGFSEEYISHPERNDNQGIVEITDLVFSSESKLTQRKESRDSKTFVPSFLEELDDDH
LHELVTNGGILYMNSLGEGVSGSVRKCRIRGTQMIFAMKTVLAAPNTALQKQLLRELKRSCTSPYIVK
YYGACYNNAECQLNIAMEYCGAGSLDAIYKRVRSQGGRTGERPLGKIAFGVLSGLSYLHDRKIIHRDI
KPSNILLTSKGQVKLCDFGVSGELVNSLAGTFTGTSYYMAPERISGGSTSSDIWSLGLTLMEVALNRF
PFPPEGSPPPMPIELLSYIINMPPPLLPQEPGIKWSKSFQHFLCVCLDKDKTRRPGPQKMLTHPWVK
AFERIHVDMEEFLRQVWSD

>POMBASE|SPCC1322.08 symbol:srk1 species:4896 "Schizosaccharomyces pombe" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR020650 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 GO:GO:0005634 GO:GO:0007126 GO:GO:0005737 GO:GO:0007088 GO:GO:0005515 EMBL:CU329672 GenomeReviews:CU329672_GR SUPFAM:SSF56112 KO:K00924 GO:GO:0031098 GO:GO:0040020 GeneTree:EFGT00070000008711 InterPro:IPR020636 PANTHER:PTHR24347 GO:GO:0004683 GO:GO:0010972 eggNOG:fuNOG05982 HOGENOM:HBG738506 OrthoDB:EOG49W5Q5 PANTHER:PTHR24347:SF28 PIR:T40939 RefSeq:NP_588136.1 ProteinModelPortal:O94547 IntAct:O94547 STRING:O94547 EnsemblFungi:SPCC1322.08.1 GeneID:2539027 KEGG:spo:SPCC1322.08 NMPDR:fig|4896.1.peg.474 GeneDB_Spombe:SPCC1322.08 OMA:CVLYTIL BioCyc:SPOM-XXX-01:SPOM-XXX-01-000078-MONOMER ArrayExpress:O94547 Uniprot:O94547

MRFKSIQQNIEDEGKVNVREVNPDSYAERDHGYTAGIFSDAEENFGITQQVADSTQNPTSKPKSRH
AHFHETVHENPSEYSRSKCKQPTNEKEYDKAIEALVAKAIVEEHSGQQFPVYKGLEQYTLLMGDGAF
SNVYKAIHNRTGEKVAIKVVQRAQPNTDPRDPRKRQGVESHNILKEVQIMRRVKHPNIIQLLEFIQTP
EYYYLVLELADGGELFHQIVRLTYFSEDLSRHVITQVAHAIRYLHEDCGVVHDKPENLLFDSIDFVPSR
VRKYRAGDDPDKVDEGEFIPGVGAGTIGRIRLADFGLSKVVWDSHTQTPCGTMGYTAPEIVRDERY
SKGVDMWALGCVLYTILCGFPPFYDESISLLTKKVSRGEYSFLPWDDISKSAKDLISHLLTVDPESRYDI
HQFLAHPWISGSREPTFPATDAPNTAQRENPFTYDFLEPEDVAAAGSAARTPGVNSLREVFNISYAA
HRMEQEKIRKRGQRGNQGIMNFMGDMDDLMEEDDYDGTKSVEHSMKRVNLSGENDPSLASRQ
PAQSQQQSSQRSRNKFKGFQLNLSKATLYNRRHRQKV

>RGD|1305728 symbol:Mknk2 species:10116 "Rattus norvegicus" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220

InterPro:IPR017442 RGD:1305728 GO:GO:0005524 GO:GO:0006417 GO:GO:0046872 SUPFAM:SSF56112 GO:GO:0004674 GeneTree:ENSGT00550000074510 HOVERGEN:HBG106949 KO:K04372 OrthoDB:EOG4GTKD2 eggNOG:roNOG13477 CTD:2872 OMA:VQKKTAE EMBL:BC085941 IPI:IPI00366191 RefSeq:NP_001011985.1 UniGene:Rn.6769 ProteinModelPortal:Q5U2N4 SMR:Q5U2N4 STRING:Q5U2N4 Ensembl:ENSRNOT00000041106 GeneID:299618 KEGG:rno:299618 UCSC:NM_001011985 InParanoid:Q5U2N4 PhylomeDB:Q5U2N4 NextBio:645528 ArrayExpress:Q5U2N4 Genevestigator:Q5U2N4 GermOnline:ENSRNOG00000029028 Uniprot:Q5U2N4

MVQKRTAELQGFHRSFKGQNPFELAFTLDPAQHGDSDFSPQCEARPDMPSSQPIDIPDAKKRGRK
KKRCRATDSFSGRFEDVYQLQEDVLGEGAHARVQTCVNLITNQEYAVKIIEKQLGHIRSRVFVEMLY
QCQGHRNVLELIEFFEEEDRFYLVFEKMRGGSILSHIHRRRHFNELEASVVVQDVASALDFLHNKGIA
HRDLKPENILCEHPNQVSPVKICDFDLGSGIKLNGDCSPISTPELLTPCGSAEMPEVVEAFSEEASIYDK
RCDLWSLGVILYILLSGYPPFVGHCGSDCGWDRGEACPACQNMLFESIQEGKYEFPDKDWSHISFA
AKDLISKLLVRDAKQRLSAAQVLQHPWVQGCAPENTLPTPLVLQRNSCAKDLTSFAAEAIAMNRQL
AQCEEDAGQDQPVLIRATSRCLQLSPPSQSKLAQRRQRASATPVVLVGDRV

>IPI:IPI00566958 RefSeq:NP_001037732.1 UniGene:Rn.7910 ProteinModelPortal:Q4G050 SMR:Q4G050 STRING:Q4G050 PRIDE:Q4G050 GeneID:500526 KEGG:rno:500526 eggNOG:roNOG13477 InParanoid:Q4G050 NextBio:706427 ArrayExpress:Q4G050 Genevestigator:Q4G050 GermOnline:ENSRNOG00000010381 Uniprot:Q4G050

MGSSEPLPIVDSDKRRKKKRKTRATDSLPGKFEDVYQLTSELLGEGAYAKVQGAVSLQSGKEYAVKII
EKQAGHSRSRVFREVETLYQCQGNRNILELIEFFEDDTRFYLVFEKLQGGSILAHIQKRFNELEASRVV
RDVATALDFLHTKGIAHRDLKPENILCESPEKVSPVKICDFDLGSGVKLNNSCTPITTPELTTPCGSAEY
MAPEVVEVFRDEATFYDKRCDLWSLGVVLYIMLSGYPPFVGHCGADGDRGEVCRMCQNKLFESIQ
EGKYEFPDKDWAHISTEAKDLISKLLVRDAKQRLSAAQVLQHPWVQGQAPERGLPTPQVLQRNSST
MDLTLFAAEAIALNRQLSQHEENELAEEHEALAEGLCSMKLPPKSRLARRRALAHAGREANSCSTPA
GL

>RGD|619882 symbol:Mark1 species:10116 "Rattus norvegicus" InterPro:IPR000449 InterPro:IPR000719 InterPro:IPR001772 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 Pfam:PF00627 Pfam:PF02149 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 PROSITE:PS50032 SMART:SM00220 InterPro:IPR017442 RGD:619882 GO:GO:0005886 GO:GO:0005524 GO:GO:0005737 GO:GO:0015630 GO:GO:0016055 GO:GO:0000287 SUPFAM:SSF56112 GO:GO:0004674 GO:GO:0007243 GO:GO:0050321 GO:GO:0000226 GO:GO:0070300 InterPro:IPR015940 SMART:SM00165 PROSITE:PS50030 GO:GO:0001786 GO:GO:0005546 GO:GO:0001764 Gene3D:G3DSA:3.30.310.80 SUPFAM:SSF103243 CTD:4139 GeneTree:ENSGT00600000084258 HOVERGEN:HBG052453 KO:K08798 EMBL:Z83868 IPI:IPI00194772 RefSeq:NP_446399.1 UniGene:Rn.21430 ProteinModelPortal:O08678 SMR:O08678 STRING:O08678 PhosphoSite:O08678 PRIDE:O08678 GeneID:117016 KEGG:rno:117016 eggNOG:maNOG04703 InParanoid:O08678 OrthoDB:EOG4C2H8X PhylomeDB:O08678 NextBio:619755 ArrayExpress:O08678 Genevestigator:O08678 GermOnline:ENSRNOG00000002339 Uniprot:O08678

MSARTPLPTVNERDTENHTSVDGYTETHIPPTKSSSRQNIPRCRNSITSATDEQPHIGNYRLQKTIGK
GNFAKVKLARHVLTGREVAVKIIDKTQLNPTSLQKLFREVRIMKILNHPNIVKLFEVIEKTLYLVMEYAS
GGEVFDYLVAHGRMKEKEARAKFRQIVSAVQYCHQKCIVHRDLKAENLLLDADMNIKIADFGFSNE
FTVGNKLDTFCGSPPYAAPELFQGKKYDGPEVDVWSLGVILYTLVSGSLFGQNLKELRERVLRGKYRV
PFYMSTDCENLLKKLLVLNPIKRGSLEQIMKDRWMNVGHEEEELKPYSEPELDLNDAKRIDIMVTM
GFARDEINDALVSQKYDEVMATYILLGRKPPEFEGGESLSSNLQRSRPSSDLNNSTLQSPAHLKVQRS
ISANQKQRRFSDHAGPSIPPAVSYTKRPQANSVESEQKEEWDKDTARRLGSTTVGSKSEVTASPLVG
PDRKKSSAGPSNNVYSGGSMTRRNTYVCERSTRYALQNGRDSSLTEMSASSMSSTGSTVASAGPSA
RPRHQKSMSTSGHPIKVTLPTIKDGSEAYRPGTAQRVPAASPSAHSISASTPDRTRFPRGSSSRSTFH
GEQLRERRSAAYSGPPASPSHDTALAHARGTSTGIISKITSKFVRRDPSEGEASGRTDTARGSSGEPK
DKEEGKEAKPRSLRFTWSMKTTSSMDPNDMVREIRKVLDANTCDYEQRERFLLFCVHGDARQDSL
VQWEMEVCKLPRLSLNGRFKRIGTSIAFKNIASKIANELKL

>RGD|708483 symbol:Mark2 species:10116 "Rattus norvegicus" InterPro:IPR000719 InterPro:IPR001772 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 Pfam:PF02149 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 PROSITE:PS50032 SMART:SM00220 InterPro:IPR017442 RGD:708483 GO:GO:0005886 GO:GO:0005524 GO:GO:0005737 GO:GO:0005515 GO:GO:0016055 GO:GO:0000287 SUPFAM:SSF56112 GO:GO:0004674 GO:GO:0046777 GO:GO:0007243 GO:GO:0050321 GO:GO:0010976 GO:GO:0050770 InterPro:IPR015940 SMART:SM00165 PROSITE:PS50030 GO:GO:0051493 GO:GO:0008289 GO:GO:0030010 GO:GO:0001764 Gene3D:G3DSA:3.30.310.80 GO:GO:0045197 SUPFAM:SSF103243 GeneTree:ENSGT00600000084258 HOVERGEN:HBG052453 KO:K08798 CTD:2011 EMBL:Z83869 IPI:IPI00194773 RefSeq:NP_067731.1 UniGene:Rn.42926 PDB:1Y8G PDB:1ZMU PDB:1ZMV PDB:1ZMW PDB:2R0I PDB:2WZJ PDBsum:1Y8G PDBsum:1ZMU PDBsum:1ZMV PDBsum:1ZMW PDBsum:2R0I PDBsum:2WZJ ProteinModelPortal:O08679 SMR:O08679 DIP:DIP-29029N STRING:O08679 PhosphoSite:O08679 PRIDE:O08679 GeneID:60328 KEGG:rno:60328 NMPDR:fig|10116.3.peg.3612 UCSC:NM_021699 eggNOG:maNOG12980 PhylomeDB:O08679 NextBio:611957 ArrayExpress:O08679 Genevestigator:O08679 GermOnline:ENSRNOG00000021184 Uniprot:O08679

MSSARTPLPTLNERDTEQPTLGHLDSKPSSKSNMLRGRNSATSADEQPHIGNYRLLKTIGKGNFAKV
KLARHILTGKEVAVKIIDKTQLNSSSLQKLFREVRIMKVLNHPNIVKLFEVIETEKTLYLEYASGGEVFDY
LVAHGRMKEKEARAKFRQIVSAVQYCHQKFIVHRDLKAENLLLDADMNIKIADFGFSNEFTFGNKLD
TFCGSPPYAAPELFQGKKYDGPEVDVWSLGVILYTLVSGSLPFDGQNLERERVLRGKYRIPFYMSTDC
ENLLKKFLILNPSKRGTLEQIMKDRWMNVGHEDDELKPYVEPLPDYKDPRRTELMVSMGYTREEIQ
DSLVGQRYNEVMATYLLLGYKSSELEGDTITLKPRPSADLNSAPSPSHKVQRSVSANPKQRRSSDQA
VPAIPTSNSYSKKTQSNNAENKRPEEETGRKASSTAKVPASPLPGLDRKKTTPTPSTNSVLSTSTNRSR
NSPLLDRASLGQASIQNGKDSTAPQRVPVAPSANISSSSGAPDRTNFPRGVSSRSTFHAGQLRQVR
DQQNLPFGVTPASPSGHSQGRRGASGSIFSKFTSKFVRRNLNEPESKDRVETLRPHVVGGGGTDKE
KEEFREAKPRSLRFTWSMKTTSSMPNEMREIRKVLDANSCQSELHERYMLLCVHGTPGHENFVQW
EMEVCKLPRLSLNGVRFKRISGTSMAFKNIASKIANELKL

>SGD|S000000669 symbol:SSK22 species:4932 "Saccharomyces cerevisiae" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017240 InterPro:IPR017441 Pfam:PF00069 PIRSF:PIRSF037579 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220

InterPro:IPR017442 SGD:S000000669 GO:GO:0005524 GO:GO:0005515 SUPFAM:SSF56112 GO:GO:0004674 EMBL:X59720 EMBL:BK006937 GeneTree:EFGT00050000000597 GO:GO:0000161 PIR:S19488 RefSeq:NP_009998.2 ProteinModelPortal:P25390 SMR:P25390 DIP:DIP-5989N IntAct:P25390 MINT:MINT-592715 STRING:P25390 EnsemblFungi:YCR073C GeneID:850436 KEGG:sce:YCR073C NMPDR:fig|4932.3.peg.725 CYGD:YCR073c eggNOG:fuNOG05884 HOGENOM:HBG398769 OMA:HILENGS OrthoDB:EOG4GF6P7 NextBio:966030 ArrayExpress:P25390 Genevestigator:P25390 GermOnline:YCR073C KO:K11230 Uniprot:P25390

MMMDILNTQQQKAAEGGRVLAPHTISSKLVKRLSSHSSHKLSRSDLKALGGSETISDGPSQLTFKDR
YVFNESLYLKKLKKTALDDYYTRGIKLTNRYEEDDGDDEIIRLSNGDRIDEDLHSGVKFFTPYCRKMRS
DSDELAWNEIATERFKWQSMLARVLKGDIVKGEKTRIANQVKKPGLNKELSDEIWLELKAWLNGRT
MQEMEQSLTYLRDSSDSVFEEIMKFQIPQGKILSLDALEAILQDLMNRYHSVYWPNLKKMYKDKPIT
NTAEFTARIDVMNSWLNFKTNLTLRRQELDDWINRFSPISSSDNCQEDFDGVPQWNCKMKILAEQ
LMKEKNIESIFQKKIFYPLSPWMFKLKLHFIVYRETLTKMNIKYPERRSLLAFPVYLIKEVILTRLSYARKL
KNPTMMMIDQMIDDFNAFIRLSVQLKYTLTKYCSNLPFDVDFDPTFENTVIEAIRYLFFLLNLKLIDSS
KQNFKAPDLLLKYWDHLKNTGHYINGAETVPNELKLTLRLVHKLQFYLLKQQNFPPTFANASEAEK
WLSSIFENLGAMKRKLNRFSNILVKAFQNSAVYQINHNAQLVKKLKDAHYFLVYSGNTFESSGVYMF
AAPELLGCDNDTILRILRNKSIGDLVPLDIGNNLNVYDITTKETDLNILVSKGEDSKGIPYYRVVANSSS
DLDRHAHQSKKKNFSTDPFDQHLDEKNNEVFELEVALSSLGALVVLYPGEPVVWDGPVYKLPGNNL
FASNEMDLGKIGNNTLILNQGSNYALTYQIDKFNQTVGDSVSFIEKRCSLNSIESSLQKINKAYYKLTYT
VLNNYKGILGSFMKQCPGNELLNSIFMFGRDFGRSFLKYNAFSSKRKYVIIFLMVKLGMNWLKFLVE
ECPTDQRTRWCVLAMDFAMQMTSGYNILALNVKQFQELKERVSVCMSLLISHFDVMGARATEAE
NGMQQARLNIDTEENIDEEATLEINSRLRLEAIKTLEKTMKRNPRQMGKVLDATDQGNKYLLSLSSL
SNVSRWQKRSFIGGGTFGQVYSAINLENGEILAVKEIKIHDTTTMKKIFPLIKEEMTVLEMLNHPNIV
QYYGVEVHRDKVNIFMEYCEGGSLASLLDHGRIEDEMVTQVYTFELLEGLAYLHQGVVHRDIKENIL
LDFNGIIKYVDFGTARTVVGSRTRTVRNAAVQDFGVETKSLNEMMGTPMYMAPETISGSAVKGKL
GADDVWALGCVVLEMATGRRPWSNLDNEWAIMYHVAAGRIPQLPNRDEMAAGRAFLERLVQD
PTMRATAVELLIDPWMIQIREIAFGNSEKDQVPILSS

>SGD|S000001072 symbol:SLT2 species:4932 "Saccharomyces cerevisiae" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 SGD:S000001072 GO:GO:0005524 GO:GO:0005634 GO:GO:0005737 GO:GO:0005515 GO:GO:0005934 EMBL:BK006934 SUPFAM:SSF56112 EMBL:U00062 HOGENOM:HBG755340 GO:GO:0008361 GO:GO:0001101 GO:GO:0031505 GO:GO:0042990 GO:GO:0000917 GO:GO:0030242 GeneTree:EFGT00050000000591 BRENDA:2.7.11.24 GO:GO:0004707 eggNOG:fuNOG04682 OrthoDB:EOG4S7NZG GO:GO:0030969 KO:K04464 OMA:IKEIGHG EMBL:X59262 PIR:S43737 RefSeq:NP_011895.1 ProteinModelPortal:Q00772 SMR:Q00772 DIP:DIP-1448N IntAct:Q00772 MINT:MINT-395773 STRING:Q00772 PeptideAtlas:Q00772 EnsemblFungi:YHR030C GeneID:856425 KEGG:sce:YHR030C NMPDR:fig|4932.3.peg.3042 CYGD:YHR030c NextBio:982003 ArrayExpress:Q00772 Genevestigator:Q00772 GermOnline:YHR030C Uniprot:Q00772

MADKIERHTFKVFNQDFSVDKRFQLIKEIGHGAYGIVCSARFAEAAEDTTVAIKKVTNVFSKTLLCKRS
LRELKLLRHFRGHKNITCLYDMDIVFYPDGSINGLYLYEELMECDMHQIIKSGQPLTDYQSFTYQILCG
LKYIHSADVLHRDLKPGNLLVNADCQLKICDFGLARGYSENPVENSQFLTEYVATRWYRAPEIMLSY
QGYTKAIDVWSAGCILAEFLGGKPIFKGKDYVNQLNQILQVLGTPPDELRIGSKNVQDYIHQLGFIPK
VPFVNLYPNANSQALDLLEQMLAFDPQKRITVDEALEHPYLSIWHDPADEPVCSEKFEFSFESVND
MEDLKQMVIQEVQDFRLFVRQPLLEEQRQLQLQQQQQQQQQQQQQQPSDVDNGNAAASEEN
YPKQMATSNSVAPQQESFGIHSQNLPRHDADFPPRPQESMMEMRPATGNTADIPPQNDNGTLL
DLEKELEFGLDRKYF

>SGD|S000001599 symbol:PRR1 species:4932 "Saccharomyces cerevisiae" InterPro:IPR000719 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 InterPro:IPR017442 SGD:S000001599 GO:GO:0005524 GO:GO:0005737 SUPFAM:SSF56112 EMBL:BK006944 EMBL:S93804 GO:GO:0004702 KO:K08286 GO:GO:0046020 GO:GO:0031138 GeneTree:EFGT00050000000602 eggNOG:fuNOG05175 OrthoDB:EOG4DRDN7 EMBL:Z28115 PIR:S27381 RefSeq:NP_012806.1 ProteinModelPortal:P28708 SMR:P28708 DIP:DIP-1919N IntAct:P28708 MINT:MINT-395513 STRING:P28708 EnsemblFungi:YKL116C GeneID:853744 KEGG:sce:YKL116C NMPDR:fig|4932.3.peg.3787 CYGD:YKL116c HOGENOM:HBG202419 OMA:ARCGSED NextBio:974801 ArrayExpress:P28708 Genevestigator:P28708 GermOnline:YKL116C InterPro:IPR016240 PIRSF:PIRSF000609 Uniprot:P28708

MDEYSSIYSQPKTPRLKQEGFPDSIGDQHEKALIDENGEEDKKMASTEGTTGDSRSTPLTVSIPTFEN
VQALPTPMTYTPLSPGNLSMSPIDQSSLNIPKRRSHARLLDDMLSVTQPNQRVVSELIANLSPQRVV
SLPTVTEEALVNDSVDSDNYTKEPYFPESSSSTEKCDDDIFQGFLLDHWDRPLLWKKVRPIGSGNFST
VLLYELMDQSNPKLKQVAVKRLKYPEELSNVEQINTSLRYKETLSRLENSTELQVLKSLNHPCIVKLLGI
NNPIFVTSKKPLCDLIIKTPRALPPCDMIMSYCPAGDLLAAVMARNGRLEAWLIQRIFTEVVLAVKYL
HENSIIHRDLKLENILLKYSFDDINSFRDSPIYCKQNFELDFGLCKKIENNEMCTARCGSEDYVSPEILM
GVPYDGHLSDTWALGVILYSLFEDRLPFDPPPNASARQRSRATSHRIARFDWRWYRLSDYKTNVGK
QIVENTLTRKNQRWSINEIYESPFVKTIDTLFS

>SGD|S000001644 symbol:KDX1 species:4932 "Saccharomyces cerevisiae" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 SGD:S000001644 GO:GO:0005524 SUPFAM:SSF56112 GO:GO:0004674 HOGENOM:HBG755340 EMBL:BK006944 EMBL:Z26877 GeneTree:EFGT00050000000591 KO:K08293 EMBL:Z28161 PIR:S37790 RefSeq:NP_012761.1 ProteinModelPortal:P36005 SMR:P36005 DIP:DIP-6316N IntAct:P36005 MINT:MINT-698763 STRING:P36005 PeptideAtlas:P36005 EnsemblFungi:YKL161C GeneID:853696 KEGG:sce:YKL161C NMPDR:fig|4932.3.peg.3740 CYGD:YKL161c eggNOG:fuNOG04682 OMA:TERCIFR OrthoDB:EOG4S7NZG NextBio:974678 ArrayExpress:P36005 Genevestigator:P36005 GermOnline:YKL161C Uniprot:P36005

MATDTERCIFRAFGQDFILNKHFHLTGKIGRGSHSLICSSTYTESNEETHVAIRKIPNAFGNKLSCKRTL
RELKLLRHLRGHPNIVWLFDTDIVFYPNGALNGVYLYEELMECDLSQIIRSEQRLEDFQSFIYQILCALK
YIHSANVLHCDLKPKNLLVNSDCQLKICNFGLSCSYSENHKVNDGFIKGYITSIWYKAPEILLNYQECTK

AVDIWSTGCILAELLGRKPMFEGKDYVDHLNHILQILGTPPEELEIASQKVYNYIFQFGNIPGRSFESIL
PGANPEALELLKKMLEFDPKKRITVEDALEHPYLSMWHDIDEEFSCQKTFRFEFEHIESMAELGNEVI
KEVFDFRKVVRKHPISGDSPSSSLSLEDAIPEVQVHPSRKVLPSYSPEFSYVSQLPSLTTTQPYQNLMGI
SSNSFQGVN

>SGD|S000002318 symbol:STE7 species:4932 "Saccharomyces cerevisiae" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 SGD:S000002318 GO:GO:0005524 GO:GO:0005737 GO:GO:0005515 GO:GO:0043332 GO:GO:0007124 SUPFAM:SSF56112 GO:GO:0004674 EMBL:BK006938 EMBL:Z67750 GO:GO:0001403 GeneTree:EFGT00050000000597 EMBL:X97751 GO:GO:0001402 eggNOG:fuNOG07450 OrthoDB:EOG43V342 BRENDA:2.7.12.2 GO:GO:0004708 GO:GO:0010525 GO:GO:0000196 KO:K11226 EMBL:M14097 EMBL:Z74207 PIR:A25048 RefSeq:NP_010122.1 ProteinModelPortal:P06784 SMR:P06784 DIP:DIP-9N IntAct:P06784 MINT:MINT-411435 STRING:P06784 PeptideAtlas:P06784 EnsemblFungi:YDL159W GeneID:851396 KEGG:sce:YDL159W NMPDR:fig|4932.3.peg.858 CYGD:YDL159w OMA:GLMIIEL NextBio:968558 ArrayExpress:P06784 Genevestigator:P06784 GermOnline:YDL159W GO:GO:0071508 Uniprot:P06784

MFQRKTLQRRNLKGLNLNLHPDVGNNGQLQEKTETHQGQSRIEGHVMSNINAIQNNSNLFLRRGI
KKKLTLDAFGDDQAISKPNTVVIQQPQNEPVLVLSSLSQSPCVSSSSSLSTPCIIDAYSNNFSPSSTNST
PSTIQGLSNIATPVENEHSISLPPLEESLSPAAADLKDTLSGTSNGNYIQLQDLVQLGKIGAGNSGTVV
KALHVPDSKIVAKKTIPVEQNNSTIINQLVRELSIVKNVKPHENIITFYAYNQHINNEIIILMEYSDCGSL
DKILSVYKRFVQRGTVSSKKTWFNELTISKIAYGVLNGLDHLYRQYKIIHRDIKPSNVLINSKGQIKLCD
FGVSKKLINSIADTFVGTSTYMSPERIQGNVYSIGDWSLGLMIIELVTGEFPLGGHNDTPDGILDLLQR
IVNEPSPRLPKDRIYSKEMTDFVNRCCIKNERERSSIHELLHHDLIMKYVSPSKDDKFRHWCRKIKSKIK
EDKRIKREALDRAKLEKKQSESTH

>SGD|S000002373 symbol:PRR2 species:4932 "Saccharomyces cerevisiae" InterPro:IPR000719 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 InterPro:IPR017442 SGD:S000002373 GO:GO:0005524 SUPFAM:SSF56112 EMBL:BK006938 EMBL:X99000 GO:GO:0004702 GO:GO:0046020 GeneTree:EFGT00070000008718 GO:GO:0031138 eggNOG:fuNOG04936 OrthoDB:EOG4C2MJV HOGENOM:HBG203152 EMBL:Z74262 PIR:S67773 RefSeq:NP_010067.1 ProteinModelPortal:Q12310 SMR:Q12310 DIP:DIP-1640N IntAct:Q12310 MINT:MINT-387579 STRING:Q12310 EnsemblFungi:YDL214C GeneID:851312 KEGG:sce:YDL214C NMPDR:fig|4932.3.peg.800 CYGD:YDL214c NextBio:968337 ArrayExpress:Q12310 Genevestigator:Q12310 GermOnline:YDL214C Uniprot:Q12310

MSLSRILRYNQRNNKTTASLTAEHAYSDNWAYSVSLGDPTSVGVNMAAKTGEALNKSYDSVFSSLP
VADSVPRTDFTASSRDDENTDVQKLTTSWMEKIDTKMPENISKIDSNIISSPMVSKVEARFPKGRLR
KNSTDFTSSFSNSLSLPKSYGKLIFFTSKKNSSSTKKNLANDISDNKHNNNSSNTIGHNIPVTTATATCD
EIACTSTEHEYNVYEEERMFTTRVYSLEDSVSSLSTNPLDDTYSEAVQVNRIEDTESTAHIRKHSYTTSL
SSIKRLFKITSFSNNNSNSCDHQESTVADDCAISSSLKETTSSPVSTGSFSLMIENEDSDRDQIIQALYS

NIEASTDLVSRKYRDLDVVLGEGSGGKVKLVQRVLDKVALKEYRSKKKRESERKYIKNIISEYCIASTLK
NPNICETLEILYEKGKIFQILEYCEYDLFSLVMSEKMHYEEICCLFKQLINGVKYLHDIGLSHRDLKLDNC
VVTRRGILKLIDFGASSVFHYLSSMIEANGIVGSDPYLSPEVFYFNEYDPRALDVWSVGIIFFCMITRRF
PWKYPKVKDVQFKAFCSGRGVSSFKDLVTRPATDDSNNYDNDGYEEGVIDMGPNFILHRLPEETHK
IMRRILEVSPFRITIGILQDGWIKEIETCQVVGAASPNEASLRIINKGNHIHTNIDQRYAHIGGLHQRT

>SGD|S000003272 symbol:KSS1 species:4932 "Saccharomyces cerevisiae" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 SGD:S000003272 GO:GO:0005524 GO:GO:0005634 GO:GO:0005737 GO:GO:0008134 EMBL:BK006941 GO:GO:0007049 SUPFAM:SSF56112 HOGENOM:HBG755340 GO:GO:0000750 GO:GO:0042597 GO:GO:0001403 GO:GO:0043433 GO:GO:0001402 GeneTree:EFGT00050000000591 BRENDA:2.7.11.24 EMBL:DQ115391 GO:GO:0004707 KO:K04371 eggNOG:fuNOG04760 OrthoDB:EOG4P8JSR EMBL:M26398 EMBL:Z72825 EMBL:AY557773 PIR:A33297 RefSeq:NP_011554.1 ProteinModelPortal:P14681 SMR:P14681 DIP:DIP-60N IntAct:P14681 MINT:MINT-411417 STRING:P14681 PeptideAtlas:P14681 EnsemblFungi:YGR040W GeneID:852931 KEGG:sce:YGR040W NMPDR:fig|4932.3.peg.2670 CYGD:YGR040w OMA:HEINEEP NextBio:972657 ArrayExpress:P14681 Genevestigator:P14681 GermOnline:YGR040W Uniprot:P14681

MARTITFDIPSQYKLVDLIGEGAYGTVCSAIHKPSGIKVAIKKIQPFSKKLFVTRTIREIKLLRYFHEHENII
SILDKVRPVSIDKLNAVYLVEELMETDLQKVINNQNSGFSTLSDDHVQYFTYQIALKSIHSAQVIHRDI
KPSNLLLNSNCDLKVCDFGLARCLASSSDSRETLVGFMTEYVATRWYRAPEIMLTFQEYTTAMDIWS
CGCILAEMVSGKPLFPGRDYHHQLWLILEVLGTPSFEDFNQIKSRKEYIANLPMRPPLPWETVWSKT
DLNPDMIDLLDKMLQFNPDKRISAAEALRHPYLAMYHDPSDEPEYPPLNLDDEFWKLDNKIMRPEE
EEEVPIEMLKDMLYDELMKTME

>SGD|S000003631 symbol:BCK1 species:4932 "Saccharomyces cerevisiae" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 SGD:S000003631 GO:GO:0005524 GO:GO:0005737 GO:GO:0005515 GO:GO:0043332 EMBL:BK006943 SUPFAM:SSF56112 GO:GO:0007584 GO:GO:0007243 GO:GO:0001101 GO:GO:0004713 GO:GO:0030968 GO:GO:0004709 GO:GO:0030010 GO:GO:0030242 GeneTree:EFGT00050000000597 EMBL:M84389 EMBL:D10389 EMBL:X60227 EMBL:X77923 EMBL:Z49370 EMBL:Z49369 EMBL:M88604 PIR:S20117 RefSeq:NP_012440.1 ProteinModelPortal:Q01389 SMR:Q01389 DIP:DIP-2223N IntAct:Q01389 MINT:MINT-604289 STRING:Q01389 EnsemblFungi:YJL095W GeneID:853350 KEGG:sce:YJL095W NMPDR:fig|4932.3.peg.3409 CYGD:YJL095w eggNOG:fuNOG05291 HOGENOM:HBG202176 OMA:HRDMKAD OrthoDB:EOG4WM83H NextBio:973753 ArrayExpress:Q01389 Genevestigator:Q01389 GermOnline:YJL095W KO:K11229 Uniprot:Q01389

MPFLRKIAGTAHTHSRSDSNSSVKFGHQPTSSVASTKSSSKSPRATSRKSIYDDIRSQFPNLTPNSTSS
QFYESTPVIEQSFNWTTDDHISAGTLENPTSFTNSSYKNDNGPSSLSDSRKSSGGNSVLSFDKLILSW
DPTDPDEWTMHRVTSWFKFHDFPESWILFFKKHQLFGHRFIKLLAYDNFAVYEKYLPQTKTASYTRF

QQLLKKTMTKNVTNSHIRQKSASKLKSSRSSSESIKSKLKNSKSQEDISSSTSESALSPTKSGPSKTDEK
NFLHSTSTHQKTKSASSLYRRSFISLRGSSSSNASSAKSPSNIKLSIPARPHSIIESNSTLTKSASPPASPSY
PSIFRRHHKSSSSESSLLNSLFGSGIGEEAPTPNQGHSLSSENLAKGKSKHYETNVSSPLKQSSLPTSDD
KGNLWNKFKRKSQIGVPSPNTVAYVTSQETPSLKSNSSTATLTVQTADVNIPSPSSSPPPIPKTANRSL
EVISTEDTPKISSTTASFKTYPCINPDKTVPVPVNNQKYSVKNFLLDQKFYPLKKTGLNDSENKYILVTK
DNVSFVPLNLKSVAKLSSFKESALTKLGINHKNVTFHMTDFDCDIGAAIPDDTLEFLKKSLFLNTSGKIY
IKDQMLQQKKPAPLTSENNVPLKSVKSKSSMRSGTSSLIASTDDVSIVTSSSDITSFDEHASGSGRRYP
QTPSYYYDRVSNTNPTEELNYWNIKEVLSHEENAPKMVFKTSPKLELNLPDKGSKLNIPTPIENESKSF
QVLRKDEGTEIDFNHRRESPYTKPELAPKREAPKPPANTSPQRTLSTSKQNKPIRLVRASTKISRSKRS
KPLPPQLLSSPIEASSSSPDSLTSSYTPASTHVLIPQPYKGANDVMRRLKDQDSTSSPSLKMKQKVNRS
NSTVSTSNSIFYSPSPLLKRGNSKRVVSSTSAADIFEENDITFADAPPMFDSDDSDDDSSSSDDIIWSK
KKTAPETNNENKKDEKSDNSSTHSDEIFYDSQTQDKMEKMTFRPSEVVYQNLEKFFPRANLDKPITE
GIASPTSPKSLDSLLSPKNVASSRTEPSTPSRPVPPDSSYEFIQDGLNGKNKPLNQAKTPKRTKTIRTIA
HEASLARKNSVKLKRQNTKMWGTRMVETENHMVSIKAKNSKGEYKEFAWMKGEMIGKGSFGAV
YLCLNVTTGEMMAVKQVEVPKYSSQNEAILSTVEALRSEVSTLKDLDHLNIVQYLGFENKNNIYSLFL
EYVAGGSVGSLIRMYGRFDEPLKHLTTQVLKLAYLHSKGILHRDMKADNLLLDQDGICKISDFGISRK
SKDIYSNSDMTMRGTVFWMAPEMVDTKQGYSAKVDIWSLGCIVLEMFAGKRPWSNLEVVAAMF
KIGKSKSAPPIPEDTLPISQIGRNFLDCFEINPEKRPTANELLSHPFSEVNETFNFKSTRLAKFIKSNDKL
NSSKLRITSQENKTE

>SGD|S000003664 symbol:PBS2 species:4932 "Saccharomyces cerevisiae" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 SGD:S000003664 GO:GO:0005524 GO:GO:0005935 GO:GO:0005934 GO:GO:0007015 EMBL:BK006943 SUPFAM:SSF56112 GO:GO:0004674 GO:GO:0046677 GO:GO:0006972 GO:GO:0004713 GO:GO:0004596 GO:GO:0017196 GeneTree:EFGT00050000000597 GO:GO:0034605 BRENDA:2.7.12.2 GO:GO:0004708 GO:GO:0005078 GO:GO:0000169 GO:GO:0031416 EMBL:J02946 EMBL:U12237 EMBL:Z49403 PIR:S56909 RefSeq:NP_012407.2 PDB:2VKN PDBsum:2VKN ProteinModelPortal:P08018 SMR:P08018 DIP:DIP-2368N IntAct:P08018 MINT:MINT-546167 STRING:P08018 PeptideAtlas:P08018 GeneID:853313 KEGG:sce:YJL128C NMPDR:fig|4932.3.peg.3374 CYGD:YJL128c eggNOG:fuNOG05342 HOGENOM:HBG447816 OMA:LQKIPER OrthoDB:EOG4RV60P NextBio:973654 ArrayExpress:P08018 Genevestigator:P08018 GermOnline:YJL128C GO:GO:0000208 KO:K11227 Uniprot:P08018

MEDKFANLSLHEKTGKSSIQLNEQTGSDNGSAVKRTSSTSSHYNNINADLHARVKAFQEQRALKRS
ASVGSNQSEQDKGSSQSPKHIQQIVNKPLPPLPVAGSSKVSQRMSSQVVQASSKSTLKNVLQETQN
ITDVNINIDTTKITATTIGVNTGLPATDITPSVSNTASATHKAQLLNPNRRAPRRPLSTQHPTRPNVAP
HKAPAIINTPKQSLSARRGLKLPPGGMSLKMPTKTAQQPQQFAPSPSNKKHITSNSKVVEGKRSNP
GSLINGVQSTSTSSSTEGPHDTVGTTPRTGNSNNSSNSGSSGGGGLFANFSKYVDIKSGSLNFAGKLS
LSSKGIDFSNGSSSRITLDELEFLDELGHGNYGNVSKVLHKPTNIMTKEVRLELDEAKFRQILMELEVL
HKCNSPYIVDFYGAFFIEGAVYMCMEYMDGGSLDKIYDESSEIGGIDEPQLAFIANAVIHGLKELKEQ
HNIIHRDVKPTNILCSANQGTVKLCDFGVSGNLASLKTNIGCQSYMAPERIKSLNPDRATYTVQSDI
WSLGLSILEMALGRYPYPPETYDNIFSQLSAIVDGPPPRLPSDKFSSDAQDFVSLCLQKIPERRPTYAA
LTEHPWLVKYRNQDVHMSEYITELERRKILRERGENGLSKNVPALHMGGL

>SGD|S000005314 symbol:SSK2 species:4932 "Saccharomyces cerevisiae" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017240 InterPro:IPR017441 Pfam:PF00069 PIRSF:PIRSF037579 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 SGD:S000005314 GO:GO:0005829 GO:GO:0005524 GO:GO:0005515 GO:GO:0005935 GO:GO:0005934 SUPFAM:SSF56112 EMBL:BK006947 GO:GO:0046777 GO:GO:0030036 GO:GO:0004709 GeneTree:EFGT00050000000597 BRENDA:2.7.11.25 GO:GO:0000161 GO:GO:0007234 eggNOG:fuNOG05884 HOGENOM:HBG398769 OrthoDB:EOG4GF6P7 KO:K11230 EMBL:L41927 EMBL:Z71646 PIR:S59801 RefSeq:NP_014428.1 ProteinModelPortal:P53599 SMR:P53599 DIP:DIP-2436N IntAct:P53599 MINT:MINT-691754 STRING:P53599 PeptideAtlas:P53599 EnsemblFungi:YNR031C GeneID:855765 KEGG:sce:YNR031C NMPDR:fig|4932.3.peg.5508 CYGD:YNR031c OMA:ISHFDIM NextBio:980205 ArrayExpress:P53599 Genevestigator:P53599 GermOnline:YNR031C Uniprot:P53599

MSHSDYFNYKPYGDSTEKPSSSKMRQSSSSSSSRLRSESLGRNSNTTQARVASSPISPGLHSTQYFRS
PNAVYSPGESPLNTVQLFNRLPGIPQGQFFHQNAISGSSSSSARSSRRPSNIGLPLPKNQSLPKLSTQP
VPVHKKVEASKTESEIIKKPAPVNSNQDPLLTTPTLVISPELASLNTTNTSIMSTPQNITNQTSNKHIPT
RSQPNGSTSSSTLQDIVTTNSSQRSVGHHGGSTTSLRTYKKQYVLNQYLRKMRNRANDDYYTRGIV
ASSNFEDDEENFSNKGEDDLELEMDDLLKVEGEDKDNDFNFGYNFITSSTKNNENVVSMSLNYLKG
KLDWLRDVNNDQPCEIEDEEWHSILGSEDLLSKLLQNPMVNREWQTMLSKVLKGDIVRNEKTKIA
NQGKGPGFNTQFSDDIWIELKAWMNGRTVEDQNKSLRIFRDSTDSVFQEIMAFKLEDNMSADEA
AETIKSLVDKYYRVLNLWPNIKRMHAEKPITKTEAFRRIDLNSWLNFKFNFDTNIAYLKKWIVGNKEL
ESTTEVDNTTVNLDDPAVFATNCKRFAEQIMKEKDIELIFQKKIFFPLAPWILKAKFFFLKYQKTWNEL
NLSYLDQDLEFLLMFPMRLVKDIILILSYAKIQNPTLMMIDQMMDDFSTYIKLAVQMKFTVASYCND
WFFKVKIDPEFDHTVVEGLEYFFSILELRILYSGKNSFKTSKEPDLLLKYWEMFRNVGYYIDDAGELIAA
EFTKLTLRLVHRLHALLRQQTPPKLENEAAAEKWLVQIFEILGSMKRKLNRFTNILTKAFQNFVRYKIE
DHNYLLKQLKETGHFLIYTGGYLEQNGTYLIGSPELLGCKDDDILRIIKNSDIGCDLVPKLEINNSLTIYN
ADDNWNSSSLGSDISNDGTPFYYIKNDLTTQPRSYNGNRVNREPDFENSRSTEEEFYELETRLNSLGY
VLVLTPQEPLLWEGEMYNLSDNKTIKPEGLNLKVIPNSIDLMCQGSSYALEYQCDRFQQSGSSVSFE
KKSSSETVKNNLQRINKAYFRCTYSVLKNYTKIVTTFKKVSPVNDLLNNIFLFGRDFGLNFLRINVANN
EKRSIIILLMMRLSIGWLKFLAEDCDPTDQRVFRWCVTSMEFAMHMVSGNILALDECFSSLKQKISE
CMSLLISHFDIIGARSIEVEKINQQARSNLDLEDVFDDDMMLQVNSEFRVQSIMELEERIKRNPHQT
GKVIDDSDKGNKYLVSLASSISNVSMRWQKRNFIGGGTFGRYSAVDLDNGILAVKEINIQDSKSMQK
IFPLIKEEMSVLEILNHPNIVSYYGVEVHRDKVNIFMEYCEGGSLAALLEHGRIEDEMVTQVYTLQLLE
GLAYLHESGIVHRDVKPENILLDFNGVIKYVFGAAKKIANNTRLASMNKIENADGEHEDVTHVSDSK
AVKNNENALLDMMGTPMYMAPESITGSTTKGKLGADDVWSLGCVVLEMITGRRPWANLDNEW
AIMYHVAAGHTPQFPTKDEVSSAGMKFLRCLIQNPSKRAAVELLMDPWIVQIREIAFGDDSSSTDTE
ERE

>SGD|S000005757 symbol:MKK1 species:4932 "Saccharomyces cerevisiae" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 SGD:S000005757 GO:GO:0005524 GO:GO:0007165 GO:GO:0005515 EMBL:BK006948 GO:GO:0005934 SUPFAM:SSF56112 GO:GO:0004674 HOGENOM:HBG755340 GO:GO:0030242 GeneTree:EFGT00050000000597 BRENDA:2.7.12.2 EMBL:D13001 EMBL:Z75139 EMBL:AY899252 PIR:A48069 RefSeq:NP_014874.1 ProteinModelPortal:P32490

SMR:P32490 DIP:DIP-2224N IntAct:P32490 MINT:MINT-548860 STRING:P32490 EnsemblFungi:YOR231W GeneID:854406 KEGG:sce:YOR231W NMPDR:fig|4932.3.peg.5986 CYGD:YOR231w eggNOG:fuNOG04753 OMA:SEYIVRY OrthoDB:EOG4D29ZP NextBio:976589 ArrayExpress:P32490 Genevestigator:P32490 GermOnline:YOR231W KO:K08294 Uniprot:P32490

MASLFRPPESAKCNPNSPRLKLPLLRNNQVDENNIYLTSNGSSTTAYSSHTPEPLTSSTSTLFSQTRLH PSDSSMTLNTMKKRPAPPSLPSLSINSQSKCKTLPELVPIADVSDGKHDLGLKQRVIAELSGNSDLTPS SMASPFSHTNTSSPYLRNDLSNSVGSDFSNLISAYEQSSSPIKSSSQPKSSSESYIDLNSVRDVDQLDE NGWKYANLKDRIETLGILGEGAGGSVSKCKLKNGSKIFALKVINTLTPEYQKQIFRELQFNRSFQSEYI VRYYGMFTDDENSSIYIAMEYMGGRSLDAIYKNLLERGGRISEKVLGKIAEAVLRGLSYLHEKKVIHRD IKPQNILLNENGQVKLCDFGVSGEAVNSLATTFTTSYMAPERIQGQPYSVTSDVWSLGLTILEVANG KFPCSSEKMAANIAPFELLMWILTFTPELKDEPESNIIWSPSFKSFIDYCLKKDSRERPSPRQMINHPW IKGQMKKNVNMEKFVRKCWKD

>SGD|S000006061 symbol:MKK2 species:4932 "Saccharomyces cerevisiae" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 SGD:S000006061 GO:GO:0005622 GO:GO:0005524 GO:GO:0007165 GO:GO:0005515 SUPFAM:SSF56112 GO:GO:0004674 HOGENOM:HBG755340 EMBL:BK006949 GO:GO:0004713 GO:GO:0030242 GeneTree:EFGT00050000000597 BRENDA:2.7.12.2 EMBL:U43703 eggNOG:fuNOG04753 OrthoDB:EOG4D29ZP KO:K08294 EMBL:D13785 EMBL:U10280 PIR:S69045 RefSeq:NP_015185.1 ProteinModelPortal:P32491 SMR:P32491 DIP:DIP-1447N IntAct:P32491 MINT:MINT-395755 STRING:P32491 PeptideAtlas:P32491 EnsemblFungi:YPL140C GeneID:855963 KEGG:sce:YPL140C NMPDR:fig|4932.3.peg.6315 CYGD:YPL140c OMA:MFRPPES NextBio:980765 ArrayExpress:P32491 Genevestigator:P32491 GermOnline:YPL140C Uniprot:P32491

MASMFRPPESNRSHQKTPKLTLPVNLVQNAKSTNDGQHLNRSPYSSVNESPYSNNSTSATSTTSSM ASNSTLLYNRSSTTTIKNRPVPPPLPPLVLTQKKDGIEYRVAGDSQLSERFSNLHVDITYKLSSAPISTKL SNIDTTFIKKDLDTPEGEDSYPSTLLSAYDFSSSGSNSAPLSANNIISCSNLIQGKDVDQLEEEAWRFG HLKDEITTLGILGEGAGGSVAKCRLKNGKKVFALKTINTMNTDPEYQQFRELQFNKSFKSDYIVQYYG MFTDEQSSSIYIAMEYMGGKSLEATYKNLLKRGGRISERVIGKIAESVLRGLSYLHERKVIHRDIKPQNI LLNEKGEIKLCDFGVSGEAVNSLAMTFTGTSFYMAPERIQGQPYSVTCDVWSLGLTLLEVAGGRFPF ESDKITQNVAPIELLTMILTFSPQLKDEPELDISWSKTSFIDYCLKKDARERPSPRQMLKHPWIVGQM KKKVNMERFVKKCWEKEKDGI

>SGD|S000006258 symbol:SMK1 species:4932 "Saccharomyces cerevisiae" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 SGD:S000006258 GO:GO:0005739 GO:GO:0005524 GO:GO:0008360 SUPFAM:SSF56112 HOGENOM:HBG755340 EMBL:Z71255 EMBL:BK006949 GO:GO:0030476 GO:GO:0042174 EMBL:Z49219 GeneTree:EFGT00050000000591 BRENDA:2.7.11.24 GO:GO:0004707 KO:K08293 EMBL:L35047 PIR:S48879 RefSeq:NP_015379.1 ProteinModelPortal:P41808 SMR:P41808 DIP:DIP-1636N IntAct:P41808 MINT:MINT-400914 STRING:P41808 EnsemblFungi:YPR054W GeneID:856167

KEGG:sce:YPR054W NMPDR:fig|4932.3.peg.6515 CYGD:YPR054w eggNOG:fuNOG07907 OMA:LYCYQEL OrthoDB:EOG447K2W NextBio:981316 ArrayExpress:P41808 Genevestigator:P41808 GermOnline:YPR054W Uniprot:P41808

MNCTLTDNTRAINVASNLGAPQQRTIFAKERISIPGYYEIIQFLGKGAYGTVCSVKFKGRSPAARIAVK
KISNIFNKEILLKRAIRELKFMNFFKGHKNIVNLIDLEIVTSSPYDGLYCYQELIDYDKVIHSSVQLSEFHIK
YFLYQILCGLKYIHSADVIHRDLKPGNILCTLNGCLKICDFGLARGIHAGFFKCHSTVQPHITNYVATR
WYRAPELLLSNQPYSKSVDIWAVGCILAEFYARKPVFMGRDSHIFEIIKVLGTPDKDILIKFGTIKAWN
LGKNSNNPVYKKIPWSNIFPFASHEAINLIESLLHWDSTHRLNVEQAISHPFLNEVRKPDDEPVCLQG
PFDFTYESELNSMSKLRDYLVEEVKNFKTDLSSL

>TAIR|locus:2014099 symbol:MKK7 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR001245 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PRINTS:PR00109 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 EMBL:CP002684 GO:GO:0005524 GO:GO:0042742 GO:GO:0009926 GO:GO:0002229 SUPFAM:SSF56112 GO:GO:0004674 EMBL:AC013354 HSSP:P49137 GO:GO:0004708 GO:GO:0009862 GeneTree:EPGT00070000028134 UniGene:At.28338 ProtClustDB:CLSN2914344 EMBL:DQ185389 EMBL:DQ446261 IPI:IPI00524935 RefSeq:NP_173271.1 UniGene:At.51662 ProteinModelPortal:Q9LPQ3 SMR:Q9LPQ3 IntAct:Q9LPQ3 STRING:Q9LPQ3 EnsemblPlants:AT1G18350.1 GeneID:838416 KEGG:ath:AT1G18350 NMPDR:fig|3702.1.peg.2169 TAIR:At1g18350 InParanoid:Q9LPQ3 OMA:MGERPIA PhylomeDB:Q9LPQ3 Genevestigator:Q9LPQ3 Uniprot:Q9LPQ3

MALVRKRRQINLRLPVPPLSVHLPWFSFASSTAPVINNGISASDVEKLHVLGRGSSGIVYKVHHKTTG
EIYALKSVNGDMSPAFTRQLAREMEILRRTDSPYVVRCQGIFEKPIVGEVSILMEYMDGLESLRGAVT
EKQLAGFSRQILKGLSYLHSLKIVHRDIKPANLLLNSRNEVKIADFGVSKIITRSLDYCNSYVGTCAYMS
PERFDSAAGENSDVYAGDIWSFGVMILELFVGHFPLLPQGQRPDWATMVVCFGEPPRAPEGCSDE
FRSFVDCCLRKESSERWTASQLLGHPFLRESL

>TAIR|locus:2017662 symbol:MKK4 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 EMBL:CP002684 GenomeReviews:CT485782_GR GO:GO:0005524 GO:GO:0005634 GO:GO:0005737 EMBL:AC025294 SUPFAM:SSF56112 GO:GO:0004674 HOGENOM:HBG755340 GO:GO:0010227 GO:GO:0009626 GO:GO:0009814 GO:GO:2000038 GO:GO:2000037 eggNOG:KOG0581 EMBL:AB015315 EMBL:AF324667 EMBL:AF326878 EMBL:AF349517 EMBL:AF375398 EMBL:AY129469 IPI:IPI00525732 PIR:T51339 RefSeq:NP_175577.1 UniGene:At.351 ProteinModelPortal:O80397 SMR:O80397 IntAct:O80397 STRING:O80397 PRIDE:O80397 EnsemblPlants:AT1G51660.1 GeneID:841591 KEGG:ath:AT1G51660 NMPDR:fig|3702.1.peg.4640 GeneFarm:829 TAIR:At1g51660 GeneTree:EPGT00070000028134 InParanoid:O80397 OMA:INTDLNQ PhylomeDB:O80397 ProtClustDB:PLN00034 ArrayExpress:O80397 Genevestigator:O80397 GermOnline:AT1G51660 KO:K13413 Uniprot:O80397

MRPIQSPPGVSVPVKSRPRRRPDLTLPLPQRDVSLAVPLPLPPTSGGSGGSSGSAPSSGGSASSTNTN
SSIEAKNYSDLVRGNRIGSGAGGTVYKVIHRPSSRLYALKVIYGNHEETVRRQICREIERDVNHPNVVK
CHEMFDQNGEIQVLLEFMDKGSLEGAHVWKEQQLADLSRQILSGLAYLHSRHIVHRDIKPSNLLINS

AKNVKIADFGVSRILAQTMDPCNSSVGTIAYMSPERINTDLNQGKYDGYGIWSLGVSILEFYLGRFPF
PVSRQGDWASLMCAICMSQPPEAPATASPEFRHFISCCLQREPGKRRSAMQLLQHPFILRASPSQN
RSPQNLHQLLPPPRPLSSSSSPTT

>TAIR|locus:2024887 symbol:MPK18 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 EMBL:CP002684 GenomeReviews:CT485782_GR GO:GO:0005524 GO:GO:0005737 GO:GO:0005515 SUPFAM:SSF56112 HOGENOM:HBG755340 GO:GO:0043622 EMBL:AC018748 EMBL:AC024260 GO:GO:0004707 eggNOG:KOG0660 GeneTree:EPGT00050000000060 EMBL:AF360353 EMBL:BT000870 IPI:IPI00517081 PIR:C96575 RefSeq:NP_175756.2 UniGene:At.25395 ProteinModelPortal:Q9C5C0 SMR:Q9C5C0 IntAct:Q9C5C0 STRING:Q9C5C0 PRIDE:Q9C5C0 EnsemblPlants:AT1G53510.1 GeneID:841786 KEGG:ath:AT1G53510 NMPDR:fig|3702.1.peg.4851 GeneFarm:857 TAIR:At1g53510 InParanoid:Q9C5C0 Genevestigator:Q9C5C0 GermOnline:AT1G53510 Uniprot:Q9C5C0

MQQNQVKKGTKEMEFFTEYGDANRYRILEVIGKGSYGVVCAAIDTHTGEKVAIKKINDVFEHISDAL
RILREVKLLRLLRHPDIVEIKSIMLPPSKREFKDIYVVFELMESDLHQVIKANDDLTREHFFLYQMLRAL
KFMHTANVYHRDLKPKNILANANCKLKVCDFGLARVAFNDTPTTVFWTDYVATRWYRAPELCGSF
FSKYTPAIDVWSIGCIFAEVLTGKPLFPGKSVVHQLELITDLLGTPKSETIGRNDKARKYLTEMRKKNP
VTFSQKFSKADPLALRLLQRLLAFDPKDRPTPAEALADPYFKGLSKIEREPSSQQISKMEFEFERRRLTK
DDIRELIYREILEYHPQLLKDYMSGSEGSNFVYPSAIGLRQFTYLEENSSRNGPVIPLERKHASLPRSTV
HSTVVHSTSQPNLGATDSRRVSFEPSKNGASSAGHPSTSAYPTKSIGPPPRVPPSGRPGRVVESSVSY
ENGRNLKEAYFRSAVSSPHCYFRPNTTNPNRNIEASSFPPKPQNPVHQFSPTEPPAATTNQADVET
MNHPNPYFQPQLPKTDQLNNNTHMAIDAKLLQAQSQFGPAGAAAVAVAAHRNIGTISYSAAS

>TAIR|locus:2025341 symbol:MPK11 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008271 InterPro:IPR008351 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PRINTS:PR01772 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 EMBL:CP002684 GenomeReviews:CT485782_GR GO:GO:0005829 GO:GO:0005524 GO:GO:0009737 GO:GO:0005515 EMBL:AC061957 SUPFAM:SSF56112 HOGENOM:HBG755340 GO:GO:0004707 KO:K04371 GeneTree:EPGT00050000000049 EMBL:BX815051 IPI:IPI00545591 IPI:IPI00891335 PIR:C86146 RefSeq:NP_001117210.1 RefSeq:NP_563631.2 UniGene:At.49840 ProteinModelPortal:Q9LMM5 SMR:Q9LMM5 IntAct:Q9LMM5 STRING:Q9LMM5 PRIDE:Q9LMM5 EnsemblPlants:AT1G01560.2 GeneID:839523 KEGG:ath:AT1G01560 GeneFarm:845 TAIR:At1g01560 InParanoid:Q9LMM5 OMA:DINNEPV PhylomeDB:Q9LMM5 ProtClustDB:CLSN2925421 Genevestigator:Q9LMM5 GermOnline:AT1G01560 Uniprot:Q9LMM5

MSIEKPFFGDDSNRGVSINGGRYVQYNVYGNLFEVSKKYVPPLRPIGRGASGIVCAAWNSETGEEV
AIKKIGNAFGNIIDAKRTLREIKLLKHMDHDNVIAIIDIIRPPQPDNFNDVHIVYELMDTDHIIRSNQPL
TDDHSRFFLYQLLRGLKYVHSANVLHRDLKPSNLLLNANCDLKIGDFGLARTKSETDFMTEYVVTRW
YRAPELLLNCSEYTAAIDIWSVGCILGEIMTREPLFPGRDYVQQLRLITEISPDDSSLGFLRSDNARRYV

RQLPQYPRQNFAARFPNMSVNAVDLLQKMLVFDPNRRITVDEALCHPYLAPLHEYNEEPVCVRPF
HFDFEQPSLTEENIKELIYRESVKFNP

>TAIR|locus:2025515 symbol:EDR1 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR001245 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF07714 PRINTS:PR00109 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 GO:GO:0005783 EMBL:CP002684 GO:GO:0005829 GO:GO:0005524 GO:GO:0009617 GO:GO:0008219 SUPFAM:SSF56112 GO:GO:0046777 GO:GO:0009414 GO:GO:0009723 GO:GO:0009620 GO:GO:0005802 GO:GO:0005769 GO:GO:0004709 HSSP:Q62838 GeneTree:EPGT00070000027922 EMBL:AF305913 EMBL:EF470626 EMBL:EF470630 EMBL:EF470631 EMBL:EF470634 EMBL:EF470643 EMBL:EF470645 IPI:IPI00542452 PIR:T00726 RefSeq:NP_563824.1 UniGene:At.20614 ProteinModelPortal:Q9FPR3 SMR:Q9FPR3 STRING:Q9FPR3 PRIDE:Q9FPR3 EnsemblPlants:AT1G08720.1 GeneID:837393 KEGG:ath:AT1G08720 NMPDR:fig|3702.1.peg.1083 TAIR:At1g08720 InParanoid:Q9FPR3 PhylomeDB:Q9FPR3 ProtClustDB:CLSN2687733 Genevestigator:Q9FPR3 Uniprot:Q9FPR3

MKHIFKKLHRGGNQEQQNRTNDAAPPSDQNRIHVSANPPQATPSSVTETLPVAGATSSMASPAPT
AASNRADYMSSEEEYQVQLALAISASNSQSSEDPEKHQIRAATLLSLGSHQRMDSRRDSSEVQRLSR
QYWEYGVLDYEEKVVDSFYDVYSLSTDSAKQGEMPSLEDLESNHGTPGFEAVVVNRPIDSSLHELLEI
AECIALGCSTTSVSVLVQRLAELVTEHMGGSAEDSSIVLARWTEKSSEFKAALTVFPIGFVKIGISRHR
ALLFKVLADSVRLPCRLVKGSHYTGNEDDAVNTIRLEDEREYLVDLMTDPGTLIPADFASASNNTVEP
CNSNGNKFPTAQFSNDVPKLSEGEGSSHSSMANYSSSLDRRTAETDSSYPKVGPLRNIDYSSPSSVTS
STQLENNSSTAIGKGSRGAIIECSRTNMNIVPYNQNSEEDPKNLFADLNPFQNKGADKLYMPTKSGL
NNVDDFHQQKNNPLVGRSPAPMMWKNYSCNEAPRKESYIENLLPKLHRDPRYGNTQSSYATSSSN
GAISSNVHGRDNVTFVSPVAVPSSFTSTENQFRPSIVEDMNRNTNNELDLQPHTAAVVHGQQNDE
SHIHDHRKYTSDDISTGCDPRLKDHESTSSLDSSYRNDPQVLDDADVGECEIPWNDLVIAERIGLGSY
GEVYHADWHGTEVAVKKFLDQDFSGAALAEFRSEVRIMRRLRHPNVVFFLGAVTRPPNLSIVTEFLP
RGSLYRILHRPKSHIDERRRKMALDAMGMNCLHTSTPTIVHRDLKTPNLLVDNNWNVKVGDFGLS
RLKHNTFLSSKSTAGTPEWMAPEVLRNEPSNEKCDVYSFGVILWELATLRLPWRGMNPMQVVGA
VGFQNRRLEIPKELDPVGRIILEWQTDPNLRPSFAQLTEVLKPLNRLVLPTPQ

>TAIR|locus:2026674 symbol:YDA species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 EMBL:CP002684 GO:GO:0005524 SUPFAM:SSF56112 GO:GO:0004674 GO:GO:0010103 EMBL:AC011622 HSSP:P00523 EMBL:AY357947 EMBL:AY357948 IPI:IPI00535780 PIR:A96662 RefSeq:NP_176557.1 UniGene:At.21875 ProteinModelPortal:Q9CAD5 SMR:Q9CAD5 STRING:Q9CAD5 PRIDE:Q9CAD5 EnsemblPlants:AT1G63700.1 GeneID:842674 KEGG:ath:AT1G63700 NMPDR:fig|3702.1.peg.5777 TAIR:At1g63700 GeneTree:EPGT00070000028114 InParanoid:Q9CAD5 OMA:PDHLSEE PhylomeDB:Q9CAD5 ProtClustDB:CLSN2682591 Genevestigator:Q9CAD5 Uniprot:Q9CAD5

MPWWSKSKDEKKKTNKESIIDAFNRKLGFASEDRSSGRSRKSRRRRDEIVSERGAISRLPSRSPSPSTR
VSRCQSFAERSPAVPLPRPIVRPHVTSTDSGMNGSQRPGLDANLKPSWLPLPKPHGATPDNTGAEP
DFATASVSSGSSVGDIPSDSLLSPLASDCENGNRTPVNISSRDQSMHSNKNSAEMFKPVPNKNRILS
ASPRRRPLGTHVKNLQIPQRDLVLCSAPDSLLSSPSRSPMRSFIPDQVSNHLISKPYSDVSLLGSGQCS

SPGSGYNSGNNSIGGDMATQLFWPQSRCSPECSPVPSPRMTSPGPSSRIQSGAVTPLHPRAGGSTT
GSPTRRLDDNRQQSHRLPLPPLLISNTCPFSPTYSAATSPSVRSARAEATVSPGSRWKKGRLLGMGS
FGHVYLGFNSESGEMCAMKEVTLCSDDPKSRESAQQLGQEISVLSRLRHQNIVQYYGSETVDDKLYI
YLEYVSGGSIYKLLQEYGQFGENAIRNYTQQILSLAYHAKNTVHRDIKGANILVDPHGRVKVADFGM
AKHITAQSGPLSFKGSPYWMAPEVIKNSNGSNLAVDIWSLGCTVLEMATTKPPWSQYEGVPAMFK
IGNSKELPDIPDHLSEEGKDFVRKCLQRPANRTAAQLLDHAFVRNVMPMERPIVSGEPAEAMNVAS
STMRSLDIGHARSLPCLDSEDATNYQQKGLKHGSGFSISQSPRNMSCPISPVGSPIFHSHSPHISGRR
SPSPISSPHALSGSSTPLTGGGAIPHHQRQTTVNFLHEGIGSSRSPGSGGNFYTNSFFQEPSRQQDRS
RSSPRTPPHVFWDNNGSIQPGYNWNKDNQPVLSDHVSQQLLSEHLKLKSLDLRPGFSTPGSTNRG
P

>TAIR|locus:2027814 symbol:MPK15 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 EMBL:CP002684 GenomeReviews:CT485782_GR GO:GO:0005524 SUPFAM:SSF56112 HOGENOM:HBG755340 EMBL:AC012679 GO:GO:0004707 eggNOG:KOG0660 EMBL:AF387019 EMBL:BT001159 IPI:IPI00521183 IPI:IPI00786155 PIR:G96763 RefSeq:NP_565070.2 UniGene:At.19296 ProteinModelPortal:Q9C9U4 SMR:Q9C9U4 IntAct:Q9C9U4 STRING:Q9C9U4 PRIDE:Q9C9U4 EnsemblPlants:AT1G73670.1 GeneID:843702 KEGG:ath:AT1G73670 GeneFarm:846 TAIR:At1g73670 GeneTree:EPGT00050000000060 InParanoid:Q9C9U4 OMA:YESIARI PhylomeDB:Q9C9U4 ProtClustDB:CLSN2682149 Genevestigator:Q9C9U4 GermOnline:AT1G73670 Uniprot:Q9C9U4

MGGGGNLVDGVRRWLFFQRRPSSSSSSNNHDQIQNPPTVSNPNDDEDLKKLTDPSKLRQIKVQQR
NHLPMEKKGIPNAEFFTEYGEANRYQIQEVVGKGSYGVVGSAIDTHTGERVAIKKINDVFDHDATRI
LREIKLLRLLLHPDVVEIKHIMLPPSRREFRDVYVVFELMESDLHQVIKANDDLTPEHHQFFLYQLLRG
LKYVHAANVFHRDLKPKNILANADCKLKICDFGLARVSFNDAPTAIFWTDYVTWYRAPELCGSFFSK
YTPAIDIWSVGCIFAEMLLGKPLFPGKNVVHQLDIMTDFLGTPPPEAISKIRNDKARRYLGNMRKKQ
PVPFSKKFPKADPSALRLLERLIAFDPKDRPSAEEALADPYFNGSSVREPSTQPISKLEFEFERKKLTKD
DIRELIYREILEYHPQMLEEYLRGGNQLSFMYPSGVDRFRRQFAHLEENQGPGGRSNALQRQHASLP
RERVPASKNETVEERSNDIERRTTAAVASTLDSKASQAEGTENGGGGGYSARNLMKSSSISGSKCIG
VQSKTNIEDSIVEEQDETVAVKVASLHNS

>TAIR|locus:2028301 symbol:MKK10 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 EMBL:CP002684 GO:GO:0005524 SUPFAM:SSF56112 GO:GO:0004674 EMBL:AC007767 EMBL:AC084110 GO:GO:0004708 GeneTree:EPGT00070000028134 EMBL:DQ446313 IPI:IPI00517865 PIR:G86447

RefSeq:NP_174510.1 UniGene:At.51876 ProteinModelPortal:Q9LQM8 SMR:Q9LQM8 IntAct:Q9LQM8 EnsemblPlants:AT1G32320.1 GeneID:840124 KEGG:ath:AT1G32320 NMPDR:fig|3702.1.peg.3582 TAIR:At1g32320 InParanoid:Q9LQM8 OMA:FAGDVWS PhylomeDB:Q9LQM8 ProtClustDB:CLSN2682787 Genevestigator:Q9LQM8 Uniprot:Q9LQM8

MTLVRERRHQEPLTLSIPPLIYHGTAFSVASSSSSSPETSPIQTLNDLEKLSVLGQGSGGTVYKTRHRRT
KTLYALKVLRPNLNTTVTVEADILKRIESSFIIKCYAVFVSLYDLCFVMELMEKGSLALLAQQVFSEPMV
SSLANRILQGLRYLQKMGIVHGDIKPSNLLINKKGEVKIADFGASRIVAGGDYGSNGTCAYMSPERV
DLEKWGFGGEVGFAGDVWSLGVVVLECYIGRYPLTKVGDKPDWATLCICCNEKVDIPVSCSLEFRD
FVGRCLEKDWRKRDTVEELLRHSFVKNR

>TAIR|locus:2035989 symbol:NP1 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 EMBL:CP002684 GenomeReviews:CT485782_GR GO:GO:0005524 SUPFAM:SSF56112 GO:GO:0006979 GO:GO:0046777 GO:GO:0009908 EMBL:AC000106 EMBL:AB000796 EMBL:AB000797 EMBL:AK117282 EMBL:BT005949 IPI:IPI00531470 IPI:IPI00538145 PIR:H86221 RefSeq:NP_563832.2 UniGene:At.48170 UniGene:At.70237 ProteinModelPortal:O22040 SMR:O22040 PRIDE:O22040 EnsemblPlants:AT1G09000.1 GeneID:837421 KEGG:ath:AT1G09000 NMPDR:fig|3702.1.peg.1117 GeneFarm:898 TAIR:At1g09000 eggNOG:KOG0198 GeneTree:EPGT00070000028518 HOGENOM:HBG318239 InParanoid:O22040 OMA:HKESAST PhylomeDB:O22040 ProtClustDB:CLSN2690809 ArrayExpress:O22040 Genevestigator:O22040 GermOnline:AT1G09000 GO:GO:0004709 Uniprot:O22040

MQDFFGSVRRSLVFRPSSDDDNQENQPPFPGVLADKITSCIRKSKIFIKPSFSPPPPANTVDMAPPIS
WRKGQLIGRGAFGTVYMGMNLDSGELLAVKQVLIAANFASKEKTQAHIQELEEEVKLLKSHPNIVRY
LGTVREDDTLNILLEFVPGGSISSLLEKFGPFPESVVRTYTRQLLLGLEYLHNHAIMHRDIKGANILVDN
KGCIKLADFGASKQVAELATMTGAKSMKGTPYWMAPEVILQTGHSFSAISVGCTVIEMVTGKAPW
SQQYKEVAAIFFIGTTKSHPPIPDTLSSDAKDFLLKCLQEVPNLRPTASELLKHPFVMGKHKESASTDL
GSVLNNLSTPLPLQINNTKSTPDSTCDDVGDMCNFGSLNYLVPVKSIQNKNLWQQNDNGGDEDD
MCLIDDENFLTFDGEMSSTLEKDCHLKKSCDDISDMSIALKSKFDESPGNGEKESTMSMECDQPSYS
EDDDELTESKIKAFLDEKAADLKKLQTPLYEEFYNLITSPSCMESNLSNSKREDTARGFLKLPPKSRSPS
RGPLGGSPSRATDATSCSKSPGSGGSRELNINNGGDEASQDGVSARVTDWRGLVVDTKQELSQCV
ALSEIEKKWKEELDQELERKRQEIMRAGLGSPRDRGMSRQREKSRFASPGK

>TAIR|locus:2043904 symbol:MPK6 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008271 InterPro:IPR008351 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PRINTS:PR01772 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 GO:GO:0009737 GO:GO:0005634 EMBL:CP002685 GenomeReviews:CT485783_GR GO:GO:0005515 GO:GO:0051301 SUPFAM:SSF56112 HOGENOM:HBG755340 GO:GO:0009409 GO:GO:0009651 GO:GO:0048364 GO:GO:0009723 GO:GO:0005802 GO:GO:0042542 GO:GO:0009626 GO:GO:0048481 GO:GO:0009574 GO:GO:0009524 GO:GO:0010120 GO:GO:0010224 BRENDA:2.7.11.24 EMBL:AC002333 GO:GO:0009864

GO:GO:0004707 eggNOG:KOG0660 GO:GO:2000038 GO:GO:2000037 GeneTree:EPGT00050000000049 GO:GO:0080136 EMBL:D21842 EMBL:AY120737 EMBL:BT008855 IPI:IPI00530555 PIR:S40472 RefSeq:NP_181907.1 UniGene:At.22266 UniGene:At.53112 ProteinModelPortal:Q39026 SMR:Q39026 DIP:DIP-31825N IntAct:Q39026 STRING:Q39026 PRIDE:Q39026 EnsemblPlants:AT2G43790.1 GeneID:818982 KEGG:ath:AT2G43790 NMPDR:fig|3702.1.peg.11540 GeneFarm:821 TAIR:At2g43790 InParanoid:Q39026 OMA:IEKMLTF PhylomeDB:Q39026 ProtClustDB:CLSN2683092 ArrayExpress:Q39026 Genevestigator:Q39026 GermOnline:AT2G43790 KO:K14512 Uniprot:Q39026

MDGGSGQPAADTEMTEAPGGFPAAAPSPQMPGIENIPATLSHGGRFIQYNIFGNIFEVTAKYKPPI
MPIGKGAYGIVCSAMNSETNESVAIKKIANAFDNKIDAKRTLREIKLLRHMDHENIVAIRDPPPLRNA
FNDVYIAYELMDTDLHQIIRSNQALSEEHCQYFLYQILRGLKYIHSANVLHRDLKPSNLLLNANCDLKI
CDFGLARVTSESDFMTEYVVTRWYRAPELLLNSSDYTAAIDVWSVGCIFMLDRKPLFPGRDHVHQL
RLLMELIGTPSEEELEFLNENAKRYIRQLPPYPRQSITDKFPTVHPLAIDLIEKMLTFDPRRRITVLDALA
HPYLNSLHDISDEPECTIPFNFDFENHALSEEQMKELIYEAAFNPEYQQ

>TAIR|locus:2049552 symbol:MPK17 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 EMBL:CP002685 GenomeReviews:CT485783_GR SUPFAM:SSF56112 GO:GO:0046777 HOGENOM:HBG755340 KO:K00924 EMBL:AC005560 GO:GO:0004707 GeneTree:EPGT00050000000060 EMBL:BT006469 IPI:IPI00521822 PIR:H84424 RefSeq:NP_001030939.1 RefSeq:NP_001030940.1 RefSeq:NP_001030941.1 RefSeq:NP_178254.2 UniGene:At.20212 ProteinModelPortal:Q84M93 SMR:Q84M93 IntAct:Q84M93 STRING:Q84M93 PRIDE:Q84M93 EnsemblPlants:AT2G01450.1 EnsemblPlants:AT2G01450.2 EnsemblPlants:AT2G01450.3 EnsemblPlants:AT2G01450.4 GeneID:814673 KEGG:ath:AT2G01450 NMPDR:fig|3702.1.peg.7748 GeneFarm:870 TAIR:At2g01450 InParanoid:Q84M93 OMA:ADANKTH PhylomeDB:Q84M93 ProtClustDB:CLSN2690627 Genevestigator:Q84M93 GermOnline:AT2G01450 Uniprot:Q84M93

MLEKEFFTEYGEASQYQIQEVVGKGSYGVVASAECPHTGGKVAIKKMTNVFEHVSDAIRILREIKLLR
LLRHPDIVEIKHIMLPPCRKEFKDIYVVFELMESDLHHVLKVNDDLTPQHHQFFLYQLLLKFMHSAHV
FHRDLKPKNILANADCKIKICDLGLARVSFTDSPSAVFWTDYVATRWYRAPELCGSFYSNYTPAIDM
WSVGCIFAEMLTGKPLFPGKNVVHQLELVTDLLGTPSPITLSRIRNEKARYGNMRRKDPVPFTHKFP
NIDPVALKLLQRLIAFDPKDRPSAEEALADPYFQGLANVDYEPSRQPISKLEFEFERRKLTRDDVRELM
YREILEYHPQMLQEYLQGEENINSHFLYPSGVDQFKQEFALEHNDDEEEHNSPPHQRKYTSLPRERV
CSSEDEGSDSVHAQSSSASVVFTPPQTPNTATGLSSQKASQVDKAATPVKRSACLMRSDSICASRCV
GVSSAVS

>TAIR|locus:2052357 symbol:MPK20 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 EMBL:CP002685 GenomeReviews:CT485783_GR GO:GO:0005515 SUPFAM:SSF56112 HOGENOM:HBG755340 EMBL:AC006931 GO:GO:0004707

eggNOG:KOG0660 GeneTree:EPGT00050000000060 EMBL:AF412082 EMBL:BT001021 IPI:IPI00536584 PIR:D84859 RefSeq:NP_565989.1 UniGene:At.14161 ProteinModelPortal:Q9SJG9 SMR:Q9SJG9 IntAct:Q9SJG9 STRING:Q9SJG9 PRIDE:Q9SJG9 EnsemblPlants:AT2G42880.1 GeneID:818888 KEGG:ath:AT2G42880 NMPDR:fig|3702.1.peg.11437 GeneFarm:849 TAIR:At2g42880 InParanoid:Q9SJG9 OMA:DYINGTE PhylomeDB:Q9SJG9 ProtClustDB:CLSN2917317 ArrayExpress:Q9SJG9 Genevestigator:Q9SJG9 GermOnline:AT2G42880 Uniprot:Q9SJG9

MQQDNRKKNNLEMEFFSDYGDANRFKVQEVIGKGSYGVVCSAIDTLTGEKVAIKKIHDIFEHISDAA
RILREIKLLRLLRHPDIVEIKHIMLPPSRREFKDIYVVFELMESDLHQVIKANDDLTREHFFLYQLLRALK
YIHTANVYHRDLKPKNILANANCKLKICDFGLARVAFNDTPTTIFWTDYVATRWYRAPELCGSFYSKY
TPAIDIWSIGCIFAEVLMGKPLFPGKNVVHQLDLMTDLLGTPSLDTIRRNEKARRYLTSMRKKPPIPF
AQKFPNADPLSLKLLERLLAFDPKDRPTAEEALADPYFKGLAKVEREPSCQPITKMEFEFERRKVTKED
IRELISREILEYHPQLLKDHMNGADKASFLYPSAVDFRQFAHLEENSGKTGPVAPLERKHASLPRSTVI
HSTAVARGGQPKLMNNTNTLNPETTQNIPFNHATIQAQQRNLSAAKPSTFMGPVAPFDNGRISRD
AYDPRSFIRSTNLPFSQQSAATVAMGKQERRTMEPEKQARQISQYNRYAPDVAINIDNNPFIMART
GMNKAENISDRIIIDTNLLQATAGIGVAAAAAAAAPGGSAHRKVGAVRYGMSKMY

>TAIR|locus:2053119 symbol:MPK7 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 EMBL:CP002685 GenomeReviews:CT485783_GR GO:GO:0005515 SUPFAM:SSF56112 HOGENOM:HBG755340 GO:GO:0042542 BRENDA:2.7.11.24 EMBL:AC007212 GO:GO:0004707 KO:K08293 ProtClustDB:CLSN2679557 GeneTree:EPGT00070000028880 EMBL:D21843 EMBL:AK222214 IPI:IPI00517640 PIR:B84561 PIR:S40473 RefSeq:NP_179409.1 UniGene:At.265 UniGene:At.68138 ProteinModelPortal:Q39027 SMR:Q39027 IntAct:Q39027 STRING:Q39027 PRIDE:Q39027 EnsemblPlants:AT2G18170.1 GeneID:816330 KEGG:ath:AT2G18170 NMPDR:fig|3702.1.peg.8810 GeneFarm:812 TAIR:At2g18170 InParanoid:Q39027 OMA:QANPLAI PhylomeDB:Q39027 ArrayExpress:Q39027 Genevestigator:Q39027 GermOnline:AT2G18170 Uniprot:Q39027

MAMLVEPPNGIKQQGKHYYSMWQTLFEIDTKYVPIKPIGRGAYGVVCSSINRETNERVAIKKIHNVF
ENRVDALRTLRELKLLRHVRHENVIALKDVMLPANRSSFKDVYLVYELMDTDLHQIIKSSLSDDHCKY
FLFQLLRGLKYLHSANILHRDLKPGNLLVNANCDLKICDFGLARTSQGNEQFMTEYVVTRWYRAPEL
LLCCDNYGTSIDVWSVGCIFAEILGRKPIFPGTECLNQLKLIINVVGSQQEDRFIDNPKARRFIKSLPYS
RGTHLSNLYPQANPLAIDLLQRMLVFDPTKRISVTDALLHPYMAGLFDPGSNPPAHVPISLDIDENM
EEPVIREMMWNEMLYYHPEAEISNA

>TAIR|locus:2074835 symbol:MAPKKK20 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 InterPro:IPR017442 GO:GO:0005524 EMBL:CP002686 GenomeReviews:BA000014_GR GO:GO:0005515 SUPFAM:SSF56112 GO:GO:0004674 HOGENOM:HBG755340 GO:GO:0048235 EMBL:AL132976 GeneTree:EPGT00050000000062 ProtClustDB:CLSN2684401 IPI:IPI00533781 PIR:T45577 RefSeq:NP_190600.1 UniGene:At.35507 ProteinModelPortal:Q9SND6 SMR:Q9SND6 IntAct:Q9SND6

PRIDE:Q9SND6 EnsemblPlants:AT3G50310.1 GeneID:824193 KEGG:ath:AT3G50310 NMPDR:fig|3702.1.peg.16279 TAIR:At3g50310 InParanoid:Q9SND6 OMA:EMLSEEG PhylomeDB:Q9SND6 Genevestigator:Q9SND6 Uniprot:Q9SND6

MEWVRGETIGFGTFSTVSTATKSRNSGDFPALIAVKSTDAYGAASLSNEKSVLDSLGDCPEIIRCYGE
DSTVENGEEMHNLLLEYASRGSLASYMKKLGGEGLPESTVRRHTGSVLRGLRHIHAKGFCDIKLANIL
LFNDGSVKIADFGLAMRVDGDLTALRKSVEIRGTPLYMAPECVNDNEYGSAADVWALGCAVVEMF
SGKTAWSVKEGSHFMSLLIRIGVGDELPKIPEMLSEEGKDFLSKCFVKDPAKRWTAEMLLNHSFVTI
DLEDDHRENFVVKVKDEVLMSPKCPFEFDDWDSFTLDSNPSFDSPVERLGSLVSGSIPDWSVGGS
WLTVR

>TAIR|locus:2077417 symbol:MAPKKK6 species:3702 "Arabidopsis thaliana" InterPro:IPR000225 InterPro:IPR000719 InterPro:IPR001245 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR011989 InterPro:IPR016024 InterPro:IPR017441 Pfam:PF00069 PRINTS:PR00109 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00185 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 GO:GO:0005773 EMBL:CP002686 GenomeReviews:BA000014_GR SUPFAM:SSF48371 Gene3D:G3DSA:1.25.10.10 SUPFAM:SSF56112 GO:GO:0004674 GO:GO:0007009 GO:GO:0009555 EMBL:AC013483 eggNOG:KOG0198 HSSP:P24941 GeneTree:EPGT00070000030343 ProtClustDB:CLSN2684781 IPI:IPI00534802 RefSeq:NP_187455.1 UniGene:At.43491 ProteinModelPortal:Q9SFB6 SMR:Q9SFB6 PRIDE:Q9SFB6 EnsemblPlants:AT3G07980.1 GeneID:819989 KEGG:ath:AT3G07980 NMPDR:fig|3702.1.peg.12838 TAIR:At3g07980 HOGENOM:HBG317456 InParanoid:Q9SFB6 OMA:DFLENAC PhylomeDB:Q9SFB6 Genevestigator:Q9SFB6 Uniprot:Q9SFB6

MARQMTSSQFHKSKTLDNKYMLGDEIGKGAYGRVYIGLDLENGDFVAIKQVSLENIGQEDLNTIM
QEIDLLKNLNHKNIVKYLGSLKTKTHLHIILEYVENGSLANIIKPNKFGPFPESLVTVYIAQEGLVYLHEQ
GVIHRDIKGANILTTKEGLVKLADFGVATKLNEADFNTHSVVGTPYWMAPEVIELSGVCAASDIWSV
GCTIIELLTCVPPYYDLQPMPALYRIVQDDTPPIPDSLSPDITDFLRLCFKSRQRPDAKTLLSHPWIRNS
RRALRSSLRHSGTIRYMKETDSSSEKDAEGSQEVVESVSAEKVEVTKTNSKSKLPVIGGASFRSEKDQS
SPSDLGEEGTDSEDDINSDQGPTLSMHDKSSRQSGTCISDAKGTSQDVLENHEKYDRDEIPGNLETE
ASEGRRNTLATKLVGKEYSIQSSHSFSQKGEDGLRKAVKTPSSFGGNELTRFSDPPGDASLHDLFHPL
DKVPEGKTNEASTSTPTANVNQGDSPVAGGKDLATKLRARIAQKQMEGETGHSQDGGDLFRLMM
GVLKDDVLNIDDLVFDEKVPPENLFPLQAVEFSRLVSSLRPDESEDAIVTSSLKLVAMFRQRPGQKAV
FVTQNGFLPLMDLLDIPKSRVIAVLQINEIVKDNTDFLENACLVGLIPLVMSFAGFERDRSREIRKEAA
YFLQQLCQSSPLTLQMFISCRGIPVLVGFLEADYAKHREMVHLAIDGMWQVFKLKKSTSRNDFCRIA
AKNGILLRLVNTYSLSETRLASISGDALILDGQTPRARSGQLDPNNPIFSQRETSPSVIDHPDGLKTRN
GGGEEPSHALTSNSQSSDVHQPDALHPDGDRPRLSSVVADATEDVIQQHRISLSANRTSTDKLQKL
AEGSNGFPVQPDQVRPLLSLLEKEPPSRKISGQLDYVKHIAGIERHESRLPLLYASDEKKTNGDLEFIM
AEFAEVSGRGKENGNLDTAPRYSSKTMTKKVMAIERVASTCGIASQTASGVLSGSGVLNAPGSTTSS
LLAHALSADVSMDYLEKVADLLLEFARAETTVKSYMCSQSLLSRLFQMFNRVEPPILLKILECTNHLST
DPNCLENLQRADAIKQLIPNLELKEGPLVYQIHHEVLSALFNLCKINKRREQAAENGIPHLMLFVMSD
SPLKQYALPLLCDMAHASRNSREQLRAHGGLDVYLSLLDDEYWSVIALDSIAVCLAQDVDQKVEQA
FLKKDAIQKLVNFFQNCPERHFVHILEPFLKIITKSSSINKTALNGLTPLLARLDHQDAIARLNLLKLIKAV
YEKHPKPKQLIVENDLPQKLQNLIEERRDGQRSGGQVLVKQMATSLLKALHINTIL

>TAIR|locus:2080457 symbol:MPK10 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008271 InterPro:IPR008351 InterPro:IPR011009 Pfam:PF00069 PRINTS:PR01772 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 EMBL:CP002686 GenomeReviews:BA000014_GR GO:GO:0005515 SUPFAM:SSF56112 HOGENOM:HBG755340 EMBL:AL138647 GO:GO:0004707 KO:K04371 eggNOG:KOG0660 IPI:IPI00516851 PIR:T47803 RefSeq:NP_191538.1 UniGene:At.54009 ProteinModelPortal:Q9M1Z5 SMR:Q9M1Z5 IntAct:Q9M1Z5 STRING:Q9M1Z5 PRIDE:Q9M1Z5 EnsemblPlants:AT3G59790.1 GeneID:825148 KEGG:ath:AT3G59790 NMPDR:fig|3702.1.peg.17335 GeneFarm:844 TAIR:At3g59790 GeneTree:EPGT00050000000049 InParanoid:Q9M1Z5 OMA:CEALAFN PhylomeDB:Q9M1Z5 ProtClustDB:CLSN2915557 Genevestigator:Q9M1Z5 GermOnline:AT3G59790 Uniprot:Q9M1Z5

MEPTNDAETLETQGEVTTAIWPSSQILKTTIDIPGTLSHDGRYIQYNLFGHIFELPAKYKPPIRPIGRGA
CGIVCSAVDSETNEKVAIKKITQVFDNTIEAKRTLREIKLLRHFDHENIVAIRDVILQRDSFEDVYIVNEL
MEFDLYRTLKSDQELTKDHGMYFMYQILRGLKYIHSANVLHRDLKPSNLLLSTQCDLKICDFGLARAT
PESNLMTEYVVTRWYRAPELLLGSSDYTAAIDVWSVGCIFMEIMRPLFPGKDQVNQLRLLLELIGTP
SEEELGSLSEYAKRYIRQLPTLPRQSFTEKFPNVPPLAIDLVEKMLTFDPKQRISVKEALAHPYLSSFHDI
TDEPECSEPFNFDLDEHPFSEEQFRELIYCEAAFPETSND

>TAIR|locus:2082390 symbol:MKK8 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS50011 InterPro:IPR017442 GO:GO:0005524 EMBL:CP002686 GenomeReviews:BA000014_GR SUPFAM:SSF56112 HOGENOM:HBG755340 EMBL:AC018907 GO:GO:0004708 eggNOG:KOG0581 GeneTree:EPGT00070000028134 IPI:IPI00540653 RefSeq:NP_187274.1 UniGene:At.53202 ProteinModelPortal:Q9M8J5 SMR:Q9M8J5 PRIDE:Q9M8J5 EnsemblPlants:AT3G06230.1 GeneID:819797 KEGG:ath:AT3G06230 NMPDR:fig|3702.1.peg.12625 TAIR:At3g06230 InParanoid:Q9M8J5 OMA:QAPTTIP PhylomeDB:Q9M8J5 ProtClustDB:CLSN2915411 Genevestigator:Q9M8J5 Uniprot:Q9M8J5

MVMVRDNQFLNLKLSPIQAPTTIPPCRFPIIPATKVSATVSSCASNTFSVANLDRISVLGSGNGGTVF
KVKDKTTSEIYALKKVKENWDSTSLREIEILRMVNSPYVAKCHDIFQNPSGEVSILMDYLGSLESLRGV
TEKQLALMSRQVLEGKNYLHEHKIVHRDIKPANLLRSSKEEVKIADFGVSKIVVRSLNKCNSFVGTFAY
MSPERLDSEADGVTEEDKSNVYAGDIWSFGLTMLEILVGYYPMLPDQAVCAVCFGEPPKAPEECSD
DLKSFMDCCLRKKASER

>TAIR|locus:2089576 symbol:MPK19 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 EMBL:CP002686 GenomeReviews:BA000014_GR SUPFAM:SSF56112 HOGENOM:HBG755340 EMBL:AB023038 GO:GO:0004707 eggNOG:KOG0660 GeneTree:EPGT00050000000060 EMBL:BX824157 IPI:IPI00520000 RefSeq:NP_188090.2 UniGene:At.8069 ProteinModelPortal:Q9LUC3 SMR:Q9LUC3 STRING:Q9LUC3

PRIDE:Q9LUC3 EnsemblPlants:AT3G14720.1 GeneID:820700 KEGG:ath:AT3G14720 NMPDR:fig|3702.1.peg.13612 GeneFarm:834 TAIR:At3g14720 InParanoid:Q9LUC3 PhylomeDB:Q9LUC3 ProtClustDB:CLSN2681530 Genevestigator:Q9LUC3 GermOnline:AT3G14720 Uniprot:Q9LUC3

MQKTQEKKNMKEMEFFTEYGDANRYRILEVIGKGSYGVVCAAIDTQTGEKVAIKKINDVFEHVSDA
LRILREVKLLRLLRHPDIVEIKSIMLPPSKREFKDIYVVFELMESDLHQVIKANDDLTREHFFLYQMLRA
LKYMHTANVYHRDLKPKNILANANCKLKVCDFGLARVSFNDTPTTVFWTDYVATRWYRAPELCGSF
CSKYTPAIDIWSIGCIFAEVLTGKPLFPGKSVVHQLDLITDLLGTPKSETIGRNEKARKYLNEMRKKNLV
PFSQKFPNADPLALRLLQRLLAFDPKDRPTAAEALADPYFKCLAKVEREPSCQPISKMEFEFERRRLTK
DDIRELIYREILEYHPQLLKDYMNSEGSSFLYPSAIGHRKFAYLEENSGKSGPVIPPDRKHASLPRSAVH
SSAVNSNAQPSLNASDSRRVSIEPSRNGVVPSTSAYSTKPLGPPPRVPSGKPGRVVESSVTYENDRNL
KESSYDARTSYYRSTVLPPQTVSPNCFLPTMNQEKRSGTEAASQPKPQFVPTQCNSAKPAELNPNPY
VQSQHKVGIDAKLLHAQSQYGPAGAAAVAVAAHRNIGAVGYGMS

>TAIR|locus:2092717 symbol:MPK9 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005829 GO:GO:0005739 GO:GO:0005524 GO:GO:0005634 EMBL:CP002686 GenomeReviews:BA000014_GR GO:GO:0009738 SUPFAM:SSF56112 HOGENOM:HBG755340 EMBL:AB020749 GO:GO:0004707 GeneTree:EPGT00050000000060 EMBL:AB038694 IPI:IPI00522453 RefSeq:NP_566595.1 UniGene:At.471 ProteinModelPortal:Q9LV37 SMR:Q9LV37 STRING:Q9LV37 PRIDE:Q9LV37 EnsemblPlants:AT3G18040.1 GeneID:821329 KEGG:ath:AT3G18040 NMPDR:fig|3702.1.peg.13998 GeneFarm:865 TAIR:At3g18040 InParanoid:Q9LV37 OMA:VDREPST PhylomeDB:Q9LV37 ProtClustDB:CLSN2917175 Genevestigator:Q9LV37 Uniprot:Q9LV37

MDPHKKVALETEFFTEYGEASRYQIQEVIGKGSYGVVASAIDTHSGEKVAIKKINDVFEHVSDATRILR
EIKLLRLLRHPDIVEIKHVMLPPSRREFRDIYVVFELMESDLHQVIKANDDLTPEHYQLYQLLRGLKFIH
TANVFHRDLKPKNILANSDCKLKICDFGLARVSFNDAPSAIFWTDYVATRWYRAPELCGSFFSKYTPA
IDIWSIGCIFAEMLTGKPLFPGKNVVHQLDIMTDLLGTPPPEAIARREKARRYLGNMRRKPPVPFTHK
FPHVDPLALRLLHRLLAFDPKDRPSAEEALADPYFYGLANVDREPSTQPIPKLEFEFERRKITKEDVREL
IYREILEYHPQMLQEYLRGGEQTSFMYPSGVDRFRQAHLEENYGKGEKGSPLQRQHASLPRERVPA
PKKENGSHNHDIENRSIASLVTTLESPPTSQHEGSDYRNGTSQTGYSARSLLKSASISASKCIGMKPRN
KSEYGESNNDTVDALSQKVAALHT

>TAIR|locus:2092890 symbol:MAPKKK7 species:3702 "Arabidopsis thaliana" InterPro:IPR000225 InterPro:IPR000719 InterPro:IPR001245 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR011989 InterPro:IPR016024 InterPro:IPR017441 Pfam:PF00069 PRINTS:PR00109 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00185 SMART:SM00220 InterPro:IPR017442 GO:GO:0005829 GO:GO:0005886 GO:GO:0005524 EMBL:CP002686 SUPFAM:SSF48371 Gene3D:G3DSA:1.25.10.10 SUPFAM:SSF56112 GO:GO:0004674 GO:GO:0007009 GO:GO:0009555 EMBL:AP000603 HSSP:P24941 OMA:FALPILC IPI:IPI00538435 RefSeq:NP_187962.1 UniGene:At.28120 ProteinModelPortal:Q9LJD8 SMR:Q9LJD8 PRIDE:Q9LJD8 EnsemblPlants:AT3G13530.1 GeneID:820555 KEGG:ath:AT3G13530

NMPDR:fig|3702.1.peg.13460 TAIR:At3g13530 GeneTree:EPGT00070000030343 InParanoid:Q9LJD8 PhylomeDB:Q9LJD8 ProtClustDB:CLSN2684781 Genevestigator:Q9LJD8 Uniprot:Q9LJD8

MARQMTSSQFHKSKTLDNKYMLGDEIGKGAYGRVYKGLDLENGDFVAIKQVSLENIVQEDLNTIM
QEIDLLKNLNHKNIVKYLGSSKTKTHLHIILEYVENGSLANIIKPNKFGPFPESLVAVYIAQEGLVYLHEQ
GVIHRDIKGANILTTKEGLVKLADFGVATKLNEADVNTHSVVGTPYWMAPEVIEMSGVCAASDIWS
VGCTVIELLTCVPPYYDLQPMPALFRIVQDDNPPIPDSLSPDITDFLRQCFKSRQRPDAKTLLSHPWIR
NSRRALQSSLRHSGTIKYMKEATASSEKDDEGSQDAAESLSGENVGISKTDSKSKLPLVGVSSFRSEK
DQSTPSDLGEEGTDNSEDDIMSDQVPTLSIHEKSSDAKGTQDSDFHGKSERGETPENLVTETSEARK
NTSAIKHVGKELSIPVDQTSHSFGRKGEERGIRKAVKTPSSVSGNELARFSDPPGDASLHDLFHPLDK
VSEGKPNEASTSMPTSNVNQGDSPVADGGKNLATLRATIAQKQMEGETGHSNDGGDLFRLMMG
VLKDDVIDIDGLVFDEKVPAENLFPLQAVEFSRLVSSLRPDESEDAIVSSCQKLVAMFRQRPEQKVVF
VTQHGFLPLMDLLDIPKSRVICAVLQINEIKDNTDFQENACLVGLIPVVMSFAGPERDRSREIRKEAA
YFLQQLCQSSPLTLQMFIACRGIPVLVGFLEADYAKYREMVHLAIDGMWQVFKLKRSTPRNDFCRIA
AKNGILLRLINTLYSLNATRLAISGGLDGQAPRVRSGQLDPNNPIFGQNETSSLSMIDQPDVLKTRHG
GGEEPSHASTSNSQRSDVHQPDALHPDGDKPRVSSVAPDASTSGTEDVRQQHRISLSANRTSTDKL
QKLAEGASNFPVTQTQVRPLLSLLDKEPPSRHYSGQLDYVKHITGIERHESRLPLLHGSNEKKNNGDL
DFLMAEFAEVSGRGKENGSLDTTTRYPSKTMTKKVLAIEGVASTSGIASQTASGVLSGSGVLNARPG
SATSSGLLAHMVSTLSADVAREYLEKVADLLLEFARADTTVKSYMCSQSLLSRLFQMFNRVPILLKILE
CTNHLSTDPNCLENLQRADAIKHLIPNLELKDGHLVYQIHHEVLSALFNLCKINKRRQEQAAENGIIPH
LMLFIMSDSPLKQYALPLLCDMAHASRNSREQLRAHGGLDVYLSLLDDEWVIALDSIAVCLAQDND
NRKVEQALLKQDAIQKLVDFFQSCPERHFVHILEPFLKIITKSYRINKTLAVNGLTPLLISRLDHQDAIAR
LNLLKLIKAVYEHHPRPKQLIVENDLPQKLQNLIEERRGQSGGQVLVKQMATSLLKALHINTIL

>TAIR|locus:2094761 symbol:MKK5 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 EMBL:CP002686 GenomeReviews:BA000014_GR EMBL:AB023045 SUPFAM:SSF56112 GO:GO:0004674 HOGENOM:HBG755340 GO:GO:0010227 GO:GO:0009626 GO:GO:0009814 GO:GO:2000037 eggNOG:KOG0581 GeneTree:EPGT00070000028134 ProtClustDB:PLN00034 KO:K13413 EMBL:AB015316 EMBL:Y07694 EMBL:AY081272 EMBL:AY114558 IPI:IPI00543365 PIR:T51340 PIR:T52635 RefSeq:NP_188759.1 UniGene:At.24898 UniGene:At.71795 ProteinModelPortal:Q8RXG3 SMR:Q8RXG3 IntAct:Q8RXG3 STRING:Q8RXG3 PRIDE:Q8RXG3 EnsemblPlants:AT3G21220.1 GeneID:821676 KEGG:ath:AT3G21220 NMPDR:fig|3702.1.peg.14356 GeneFarm:832 TAIR:At3g21220 InParanoid:Q8RXG3 OMA:SAISTNI PhylomeDB:Q8RXG3 ArrayExpress:Q8RXG3 Genevestigator:Q8RXG3 GermOnline:AT3G21220 Uniprot:Q8RXG3

MKPIQSPSGVASPMKNRLRKRPDLSLPLPHRDVALAVPLPLPPPSSSSSAPASSSAISTNISAAKSLSEL
ERVNRIGSGAGGTVYKVIHTPTSRPFALKVIYGNHEDTVRRQICREIEILRSVDHPNKCHDMFDHNG
EIQVLLEFMDQGSLEGAHIWQEQELADLSRQILSGLAYLHRRHIVHRDIKPSNLLINSAKNVKIADFG
VSRILAQTMDPCNSSVGTIAYMSPERINTDLNHGRYDGYAGDVWSLGVIEFYLGRFPFAVSRQGD
WASLMCAICMSQPPEAPATASQEFRHFVSCCLQSDPPKRWSAQQLLQHPFILKATGGPNLRQMLP
PPRPLPSAS

>TAIR|locus:2118116 symbol:WRKY19 species:3702 "Arabidopsis thaliana" Pfam:PF00560 InterPro:IPR000157 InterPro:IPR001611 InterPro:IPR000719 InterPro:IPR000767 InterPro:IPR002182 InterPro:IPR002290 InterPro:IPR003593 InterPro:IPR003657 InterPro:IPR003822 InterPro:IPR006210 InterPro:IPR011009 Pfam:PF00069 Pfam:PF00931 Pfam:PF02671 Pfam:PF03106 PRINTS:PR00364 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 PROSITE:PS50811 PROSITE:PS51477 SMART:SM00181 SMART:SM00220 SMART:SM00382 SMART:SM00774 InterPro:IPR017442 GO:GO:0005524 EMBL:CP002687 GenomeReviews:CT486007_GR GO:GO:0005634 GO:GO:0007165 GO:GO:0005515 GO:GO:0006952 SUPFAM:SSF56112 GO:GO:0004674 GO:GO:0043565 GO:GO:0003700 GO:GO:0006351 GO:GO:0043531 GO:GO:0009941 GO:GO:0017111 EMBL:AL049638 EMBL:AL161533 GeneTree:EPGT00070000028175 InterPro:IPR011713 Pfam:PF07725 Gene3D:G3DSA:1.20.1160.11 SUPFAM:SSF47762 SUPFAM:SSF52200 Gene3D:G3DSA:2.20.25.80 SUPFAM:SSF118290 IPI:IPI00519247 PIR:T06609 RefSeq:NP_001118968.1 UniGene:At.3076 ProteinModelPortal:Q9SZ67 SMR:Q9SZ67 IntAct:Q9SZ67 PRIDE:Q9SZ67 EnsemblPlants:AT4G12020.2 GeneID:826810 KEGG:ath:AT4G12020 GeneFarm:1664 TAIR:At4g12020 InParanoid:Q9SZ67 PhylomeDB:Q9SZ67 ProtClustDB:CLSN2690875 ArrayExpress:Q9SZ67 Genevestigator:Q9SZ67 Uniprot:Q9SZ67

MSEKEELPLTLTSIGAATATSDYHQRVGSSGEGISSSSSDVDPRFMQNSPTGLMISQSSSMCTVPPG
MAATPPISSGSGLSQQLNNSSSSKLCQVEGCQKGARDASGRCISHGGGRRCQKPDCQKGAKTVYC
KAHGGGRRCEYLGCTKGAEGSTDFCIAHGGGRRCNHEDCTRSAWGRTEFCVKHGGGARCKTYGC
GKSASGPLPFCRAHGGGKKCSHEDCTGFARGRSGLCLMHGGGKRCQRENCTKSAEGLGCISHGGG
RRCQSIGCTKGAKGSKMFCKACITKRPLTIDGGGNMGGVTTGDALNYLKAVKDKFEDSEKYDTFLEV
LNDCKHQGVDTSGVIARLKDLFKGHDDLLLGFNTYLSKEYQITILPEDDFPDFDKVEGPYEMTYQQA
QTVQANANMQPQTEYPSSSAVQSFSSGQPQIPTSAPDSSLLAKSNTSGITIIEHMSQQPLNVDKQV
NDGYNWQKYGQKKVKGSKFPLSYYKCTYLGCPSKRKVERSLDGQAEIYKDRHNHEPPNQGKDGST
TYLSGSSTHINCMSSELTASQFSSNKTKIEQQEAASLATTIEYMSEASDNEEDSNGETSEGEKDEDEPE
PKRRITEVQVSELADASDRTVREPRVIFQTTSEVDNDDGYWRKYGQKVVKGNPYPRFSSSKDYDVVI
RYGRADISNEDFISHLRASLCRRGISVYEKFNEVDALPKCRVLIIVLTSTYVPSNLLNILEHQHTEDRVVY
PIFYRLSPYDFVCNSKNYERFYLQEPKKWAALKEITQMPGYTLTDKSESELIDEIVRDALKVLCSADKV
NMIGMDMQVEEILSLLCIESLDVRSIGIWGTVGIGKTTIAEEIFRKISVQYETCVVLKDLHKEVEVKGH
DAVRENFLSEVLVEPHVIISDIKTSFLRSRLQRKRILVILDDVNDYRDVDTFLGTLNYFGPGSRIIMTSR
NRRVFVLCKIDHVYEVKPLDIPKSLLLLDRGTCQIVLSPEVYKTLSLELVKFSNGNPQVLQFLSSIDRWN
KLSQEKTTSPIYIPGIFEKSCCGLDDNERGIFLDIACFFNRIDKDNVAMLLDGCGFSAHVGFRGLVDKS
LLTISQHNLVDMLSFIQATGREIVRQESADRPGDRSRLWNADYIRHVFINDTGTSIEGIFLDMNLKFD
ANPNVFEKMCNLRLLKLYCSKAEEKHGVSFPQGLEYLPSKLRLLHWEYYPLSSLPKSFNPENLVELNLP
SSCAKKLWKGKKARFCTTNSSLEKLKKMRLSYSDQLTKIPRLSSTNLEHIDLECNSLLSLSQSISYLKKLV
FLNLKGCSKLENIPSMVDLESLEVLNLSGCSKLGNFPEISPNVKELYMGGTMIQEIPSSIKNLVLLEKLD
LENSRHLKNLPTSIYKLKHLETLNLSGCILERFPDSSRRKCLRFLDLSRTDIKELPSSISYLTALDELLFVDS
RRNSPVVTNPNANSTELMPSESSKLEILGTPADNEVVVGGTVEKTRGIERTPTILVKSREYLIPDDVVA
VGGDIKGLRPPVLLQPAMKLSHIPGSTWDFVTHFAPPETVAPPSSSSEAREEEVETEETGAMFIPLGD
KETCSFTVNKGDSSRTISNTSPIYASEGSFITCWQKGQLLGRGSLGSVYEGISADGDFFAFKEVSLLDQ
GSAHEWIQQVEGGILLSQLQHQNIVRYRGTTKDESNLYIFLELVTQGSLRKLYQRNQLGDSVVSLYTR
QILDGLKYLHDKGFIHRNIKCANVLVDANGTVKLADFGLAKVMSLWRTPYWNWMAPEVILPKDYD
GYGTPADISLGCTVLEMLTGQIPYSDLEIGTALYNIGTGKLPKIPDILSLDARDFILTCLKVNPEERPTAA
ELLNHPFVNMPLPSSGSGSVSSLLRG

>TAIR|locus:2120855 symbol:MEK1 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 EMBL:CP002687 GenomeReviews:CT486007_GR GO:GO:0042742 GO:GO:0005515 GO:GO:0009611 EMBL:AL161564 EMBL:AL049483 SUPFAM:SSF56112 GO:GO:0004674 HOGENOM:HBG755340 GO:GO:0009414 GO:GO:0042542 GO:GO:0002237 GO:GO:0004708 KO:K04368 GO:GO:0009814 EMBL:AF000977 EMBL:AB004796 EMBL:AY050774 EMBL:BT001935 EMBL:AY087065 IPI:IPI00532526 IPI:IPI00532754 PIR:T04262 RefSeq:NP_194337.1 RefSeq:NP_849446.1 RefSeq:NP_974619.1 UniGene:At.21332 UniGene:At.223 ProteinModelPortal:Q94A06 SMR:Q94A06 IntAct:Q94A06 STRING:Q94A06 PRIDE:Q94A06 EnsemblPlants:AT4G26070.2 EnsemblPlants:AT4G26070.3 GeneID:828713 KEGG:ath:AT4G26070 NMPDR:fig|3702.1.peg.20524 GeneFarm:883 TAIR:At4g26070 eggNOG:KOG0581 GeneTree:EPGT00070000029225 InParanoid:Q94A06 OMA:HHERRII PhylomeDB:Q94A06 ProtClustDB:CLSN2685391 Genevestigator:Q94A06 GermOnline:AT4G26070 Uniprot:Q94A06

MNRGSLCPNPICLPPLEQSISKFLTQSGTFKDGDLRVNKDGIQTVSLSEPGAPPPIEPLDNQLSLADLE
VIKVIGKGSSGNVQLVKHKLTQQFFALKVIQLNTEESTCRAISQELRINLSSQCPYLVYQSFYHNGLVSI
ILEFMDGGSLADLLKKVGKVPENMLSAICKRVLRGLCYIHHERRIIHRDLKPSNLLINHRGEVKITDFG
VSKILTSTSSLANSFVGTYPYMSPERISGSLYSNKSDIWSLGLVLEATGKFPYTPPEHKKGWSSVYELV
DAIVENPPPCAPSNLFSPEFCSFISQCVQKDPRDRKSAKELLEHKFVKMFEDSDTNLSAYFTDAGSLIP
PLAN

>TAIR|locus:2123909 symbol:MKK2 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005886 GO:GO:0005524 EMBL:CP002687 GenomeReviews:CT486007_GR GO:GO:0005737 GO:GO:0005515 SUPFAM:SSF56112 GO:GO:0004674 HOGENOM:HBG755340 GO:GO:0009651 EMBL:AL050352 EMBL:AL161575 GO:GO:0000165 OMA:KVIQLNI GO:GO:0004708 GO:GO:0009631 KO:K04368 GO:GO:0009814 GeneTree:EPGT00070000029225 ProtClustDB:CLSN2685391 EMBL:AB015313 EMBL:AJ006871 EMBL:AF067792 EMBL:AF385688 EMBL:AY078009 IPI:IPI00520140 IPI:IPI00656994 PIR:T08542 PIR:T51735 RefSeq:NP_001031751.1 RefSeq:NP_194710.1 UniGene:At.1001 UniGene:At.24272 ProteinModelPortal:Q9S7U9 SMR:Q9S7U9 IntAct:Q9S7U9 STRING:Q9S7U9 PRIDE:Q9S7U9 ProMEX:Q9S7U9 EnsemblPlants:AT4G29810.1 GeneID:829103 KEGG:ath:AT4G29810 NMPDR:fig|3702.1.peg.20954 GeneFarm:887 TAIR:At4g29810 InParanoid:Q9S7U9 PhylomeDB:Q9S7U9 Genevestigator:Q9S7U9 GermOnline:AT4G29810 Uniprot:Q9S7U9

MKKGGFSNNLKLAIPVAGEQSITKFLTQSGTFKDGDLRVNKDGVRIISQLEPEVLSPIKPADDQLSLSD
LDMVKVIGKGSSGVVQLVQHKWTGQFFALKVIQLNIDEAIRKAIAQELKINQSSQCPNTSYQSFYDN
GAISLILEYMDGGSLADFLKSVKAIPDSYLSAIFRQVLQGLIYLHHDRHIIHRDLKPSNLLINHRGEVKIT
DFGVSTVMTNTAGLANTFVGTYNYMSPERIVGNKYGNKSDIWSLGLVECATGKFPYAPPNQEETW
TSVFELMEAIVDQPPPALPSGNFSPELSSFISTCLQKDPNSRSSAKELMEHPFLNKYDYSGINLASYFT
DAGSPLATLGNLSGTFSV

>TAIR|locus:2124943 symbol:MPK4 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008271 InterPro:IPR008351 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PRINTS:PR01772 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005829 GO:GO:0005524 GO:GO:0009737 EMBL:CP002687 GenomeReviews:CT486007_GR GO:GO:0005634 GO:GO:0005515 SUPFAM:SSF56112 HOGENOM:HBG755340 GO:GO:0009409 GO:GO:0009555 GO:GO:0006972 GO:GO:0009620 GO:GO:0005874 GO:GO:0007112 GO:GO:0043622 GO:GO:0042539 BRENDA:2.7.11.24 EMBL:AL161491 GO:GO:0009862 GO:GO:0004707 KO:K04371 EMBL:AF007269 GeneTree:EPGT00050000000049 EMBL:D21840 EMBL:EF470667 EMBL:EF470668 EMBL:EF470669 EMBL:EF470670 EMBL:EF470671 EMBL:EF470672 EMBL:EF470673 EMBL:EF470674 EMBL:EF470675 EMBL:EF470676 EMBL:EF470677 EMBL:EF470678 EMBL:EF470679 EMBL:EF470680 EMBL:EF470681 EMBL:EF470682 EMBL:EF470683 EMBL:EF470684 EMBL:EF470685 EMBL:EF470686 EMBL:DQ112072 EMBL:AF360231 EMBL:AY040031 EMBL:AY088537 IPI:IPI00521890 PIR:S40470 RefSeq:NP_192046.1 UniGene:At.19915 ProteinModelPortal:Q39024 SMR:Q39024 IntAct:Q39024 STRING:Q39024 PRIDE:Q39024 EnsemblPlants:AT4G01370.1 GeneID:828151 KEGG:ath:AT4G01370 NMPDR:fig|3702.1.peg.17922 GeneFarm:827 TAIR:At4g01370 InParanoid:Q39024 OMA:PRRENFN PhylomeDB:Q39024 ProtClustDB:CLSN2915881 ArrayExpress:Q39024 Genevestigator:Q39024 GermOnline:AT4G01370 GO:GO:0009868 Uniprot:Q39024

MSAESCFGSSGDQSSSKGVATHGGSYVQYNVYGNLFEVSRKYVPPLRPIGRGAYGIVCAATNSETGE
EVAIKKIGNAFDNIIDAKRTLREIKLLKHMDHENVIAVKDIIKPPQRENFNDVYIVYELMDLHQIIRSNQ
PLTDDHCRFFLYQLLRGLKYVHSANVLHRDLKPSNLLLNANCDLKLGDFGLARTKSETDFMTEYVVT
RWYRAPELLLNCSEYTAAIDIWSVGCILGETMTREPLFPGKDYVHQLRLTLIGSPDDSSLGFLRSDNA
RRYVRQLPQYPRQNFAARFPNMSAGAVDLLEKMLVFDPSRRITVDEALCHPYLAPLHDINEEPVCV
RPFNFDFEQPTLTEENIKELIYRETVKFNPQDSV

>TAIR|locus:2128263 symbol:MPK5 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008271 InterPro:IPR008351 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PRINTS:PR01772 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 EMBL:CP002687 GenomeReviews:CT486007_GR EMBL:AL096882 EMBL:AL161531 SUPFAM:SSF56112 HOGENOM:HBG755340 BRENDA:2.7.11.24 GO:GO:0004707 KO:K04371 EMBL:D21841 EMBL:AK176361 IPI:IPI00517830 PIR:S40471 PIR:T13024 RefSeq:NP_567378.4 UniGene:At.264 ProteinModelPortal:Q39025 SMR:Q39025 IntAct:Q39025 STRING:Q39025 PRIDE:Q39025 EnsemblPlants:AT4G11330.1 GeneID:826735 KEGG:ath:AT4G11330 GeneFarm:826 TAIR:At4g11330 InParanoid:Q39025 PhylomeDB:Q39025 ProtClustDB:CLSN2927402 ArrayExpress:Q39025 Genevestigator:Q39025 GermOnline:AT4G11330 Uniprot:Q39025

MAKEIESATDLGDTNIKGVLVHGGRYFQYNVYGNLFEVSNKYVPPIRPIGRGAYGFVCAAVDSETHE
EIAIKKIGKAFDNKVDAKRTLREIKLLRHLEHENVVVIKDIIRPPKKEDFVDVYIVFELMDLHQIIRSNQS
LNDDHCQYFLYQILRGLKYIHSANVLHRDLKPSNLLLNSNCDLKITDFGLARTTSETEYMTEYVVTRW
YRAPELLLNSSEYTSAIDVWSVGCIFAEIMTREPLFPGKDYVHQLKLTLIGSPDGASLEFLRSANARKY

VKELPKFPRQNFSARFPSMNSTAIDLLEKMLVFDPVKRITVEEALCYPYLSALHDLNDEPVCSNHFSF
HFEDPSSTEEEIKELVWLESVKFNPLPSI

>TAIR|locus:2133529 symbol:MEKK3 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 EMBL:CP002687 SUPFAM:SSF56112 GO:GO:0004674 EMBL:AL161511 HSSP:Q13153 GeneTree:EPGT00070000029130 EMBL:BT021102 IPI:IPI00543410 PIR:D85084 RefSeq:NP_192587.1 UniGene:At.28670 ProteinModelPortal:Q9M0T3 SMR:Q9M0T3 STRING:Q9M0T3 PRIDE:Q9M0T3 EnsemblPlants:AT4G08470.1 GeneID:826406 KEGG:ath:AT4G08470 NMPDR:fig|3702.1.peg.18502 TAIR:At4g08470 InParanoid:Q9M0T3 PhylomeDB:Q9M0T3 Genevestigator:Q9M0T3 Uniprot:Q9M0T3

MDVTAIFAGDILVQSREYLIPNDVVDVDGGIKAVRPPIIQPPPGRKLPLIDFPGSSWDFLTYFAPSKTV
KRQSSSSSDNTSDKEEVETEETRGMFVQLGDTAHEACPFATNEADSSSTVSIISPSYAGSIVPSWLKR
KFLGRVSLGFVYEGSSGSSVGSESTCSLMTPSLEFPDRISFRKKDFSEKGPSRHVWEKRKLTRAKLIEN
FCNPEDIEPVTSWLKGQLLGEESFASVYEAISDSSVGSESTCSLMTPMFPDRISFRKRDFSEEGPSGRV
KEKRKLMRNKLIENFRKPEDITSWLKGQLLGRGSYASVYEAISEDGDFFAVKEVSLLDKGIQAQECIQ
QLEGEIALLSQLQHQNIVRYRGTAKDVSKLYIFLELTQSVQKLYERYQLSYTVVSLYTRQILAGLNYLHD
KGFVHRDIKCANMLVDANGTVKLADFGLAEASKFNDIMSCKGTLFWMAPEVINRKDSDGNGSPA
DIWSLGCTVLEMCTGQIPYSDLKPIQAAKIGGTLPDVPDTLSLDARHFILTCLKVNPEERPTAAELLHH
PFVINL

>TAIR|locus:2133539 symbol:MAPKKK9 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR011009 Pfam:PF00069 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 EMBL:CP002687 GenomeReviews:CT486007_GR SUPFAM:SSF56112 GO:GO:0004674 eggNOG:KOG0198 EMBL:AL161511 EMBL:AF076275 HSSP:Q13153 GeneTree:EPGT00070000029130 HOGENOM:HBG593886 ProtClustDB:CLSN2685974 IPI:IPI00546846 PIR:T01835 RefSeq:NP_192588.1 UniGene:At.33748 ProteinModelPortal:O81472 SMR:O81472 STRING:O81472 PRIDE:O81472 EnsemblPlants:AT4G08480.1 GeneID:826407 KEGG:ath:AT4G08480 NMPDR:fig|3702.1.peg.18503 TAIR:At4g08480 InParanoid:O81472 OMA:IERKPTI PhylomeDB:O81472 ArrayExpress:O81472 Genevestigator:O81472 Uniprot:O81472

MKKSSDKSPVRQHDTATQINSDAVSSSTSFTDSDSTCSFLTPSMEFPDRISFRRIDFSEAAPTGVVLPS
TSSELTRSNSSENKIPNEDISVSTSSRYLVFDKILALMKKSPGRRGDKTSPARRLDRSVRRNIDYDAGE
DSSSLLITRSLDFPNRTSFRVDGVDDGEIDRIYQYIGVSGPEDFAISSDAWKARMEHERSSSDVVNKL
KSLDLDSREAGPSGGVVASSSMNHKFQGHDLSEAGSIGVVVASNFTLENKIENLNSLRDKEIVDGD
MVENRCGIERKPTILVKSRGYLVHNDDVGVGGGIKGVRPPVLNVPRADKEVVDGGTVESKSGIEWK
PTILVKSKGYLVSNDGGIKGVTSPVLNLRPTDKEVVDSGTVNRGIKGVRPSVLKPPPVMKLPPVDLPG
SSWDILTHFAPDSEIVRRPSSSSSSENGCDEEEAEDDKVEKEETGDMFIQLEDTTDEACSFTTNEGDS
SSTVSNTSPICVSGGSINTSWQKGQLLRQGSGSVEAISEDGDFFAVKEVSLLDQGSQAQECIQQLEG
EIALLSQLEHQNILRYRGTDKDGSNLYIFLELVTQGSLLELYRRYQIRDSLISLYTKQILDGLKYLHHKGFI
HRDIKCATILVDANGTVKADFGAKVSKLNDIKSRKETLFWMAPEVINRKDNDGYRSPADIWSLGCTV
LEMCTGQIPYSDLEPVEALFRIRRGTLPEVPDTLSLDARHFILKCLKLNPEERPTATELLNHPFVRRPLP
SSGSGSTPLIRR

>TAIR|locus:2133559 symbol:MEKK1 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 EMBL:CP002687 GenomeReviews:CT486007_GR GO:GO:0005634 GO:GO:0009611 GO:GO:0019900 GO:GO:0003677 SUPFAM:SSF56112 GO:GO:0046777 GO:GO:0009409 GO:GO:0009651 eggNOG:KOG0198 GO:GO:0004709 EMBL:AL161511 GO:GO:0000165 BRENDA:2.7.11.25 EMBL:AF076275 EMBL:D50468 EMBL:AY062459 EMBL:BT000116 EMBL:L43125 IPI:IPI00521547 PIR:T01833 RefSeq:NP_192590.1 UniGene:At.21066 ProteinModelPortal:Q39008 SMR:Q39008 IntAct:Q39008 STRING:Q39008 PRIDE:Q39008 EnsemblPlants:AT4G08500.1 GeneID:826409 KEGG:ath:AT4G08500 NMPDR:fig|3702.1.peg.18504 GeneFarm:859 TAIR:At4g08500 GeneTree:EPGT00070000029130 HOGENOM:HBG593886 InParanoid:Q39008 OMA:ARNINYD PhylomeDB:Q39008 ProtClustDB:CLSN2685974 Genevestigator:Q39008 GermOnline:AT4G08500 KO:K13414 Uniprot:Q39008

MDRILARMKKSTGRRGGDKNITPVRRLERRDAARNINYDAASCSSSSAEDLSVSTSSLMTRSLEFPEP
TSFRIGGGVGEMDRIYRSLGVSGPDDLAISFDAWEACKKRSSSDVVNRFKSFDLDKVRDLSEEGPSG
VVVGSDSMNHKVQGQDLSEAGPSGGIVTELSEIGNLITPVDRLVADGVVENRRVMERTPTIVKSKG
YLVPNNVVAVGVGVGGGIKGLRPPVLKPPPAMKRPPIDHRGSSWDFLTHFAPEVKRPSSSSSSSED
GCDEEEGKEEEAEAEEMGARFIQLGDTADETCSFTTNEGDSSSTVSNTSPIYPDGGAIITSWQKGQLL
GRGSFGSVYEGISGDGDFFAVKEVSLLDQGSQAQECIQQLEGEILLQLQHQNIVRYRGTAKDGSNLY
IFLELVTQGSLLKLYQRYQLRDSVVSLYTRQILDGLKYLHDKGFIHRDIKCANILVDANGAVKLADFGL
AKVSKFNDIKSCKGTPFWMAPEVINRKDSDGYGSADISLGCTVLEMCTGQIPYSDLEPVQALFRIGR
GTLPEVPDTLSLDARLFILKCLKVNPEERPTAAELLNHPFVRRPLPSVGSGGSGSASPLLRR

>TAIR|locus:2164981 symbol:MKK6 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 EMBL:CP002688 GenomeReviews:BA000015_GR GO:GO:0005515 SUPFAM:SSF56112 GO:GO:0004674 HOGENOM:HBG755340 GO:GO:0004708 EMBL:AB013392 eggNOG:KOG0581 ProtClustDB:CLSN2685391 EMBL:AB104460 IPI:IPI00537754 RefSeq:NP_200469.1 UniGene:At.29375 ProteinModelPortal:Q9FJV0 SMR:Q9FJV0 IntAct:Q9FJV0 MINT:MINT-1206105 STRING:Q9FJV0 PRIDE:Q9FJV0 EnsemblPlants:AT5G56580.1 GeneID:835759 KEGG:ath:AT5G56580 NMPDR:fig|3702.1.peg.27598 GeneFarm:876 TAIR:At5g56580 GeneTree:EPGT00070000031255 InParanoid:Q9FJV0 OMA:FIKKFED PhylomeDB:Q9FJV0 Genevestigator:Q9FJV0 GermOnline:AT5G56580 Uniprot:Q9FJV0

MVKIKSNLKQLKLSVPAQESPISSFLTASGTFHDGDFLLNQKGLRLTSDEKQSRQSDSKELDFEITAED
LETVKVIGKGSGGVVQLVRHKWVGKFFAMKVIQMNIQEEIRKQIVQELKINQASSQCPVVCYHSFY
HNGAFSLVLEYMDRGSLADVIRQVKTILEPYLAVVCKQVLLGLVYLHNERHVIHRDIKPSNLLVNHKG
EVKISDFGVSASLASSMGQRDTFVGTYNYMSPERISGSTYDYSSDIWSLGSLECAIGRFPYLESEDQQ
NPPSFYELLAAIVENPPPTAPSDQFSPEFCSFVSACIQKDPPARASSLDLLSHPFIKKFEDKDIDLGILVG
TLEPPVNYLR

>TAIR|locus:2206885 symbol:MKK9 species:3702 "Arabidopsis thaliana" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 EMBL:CP002684 GenomeReviews:CT485782_GR GO:GO:0005524 GO:GO:0045893 GO:GO:0005515 GO:GO:0009693 GO:GO:0009611 GO:GO:0009873 SUPFAM:SSF56112 GO:GO:0004674 GO:GO:0046777 GO:GO:0030295 HOGENOM:HBG755340 GO:GO:0009651 HSSP:P49137 GO:GO:0004708 GO:GO:0010120 EMBL:AC012396 eggNOG:KOG0581 GeneTree:EPGT00070000028134 EMBL:AY084571 EMBL:BT005300 EMBL:AK118530 IPI:IPI00544496 PIR:G96761 RefSeq:NP_177492.1 UniGene:At.27674 UniGene:At.67792 ProteinModelPortal:Q9FX43 SMR:Q9FX43 IntAct:Q9FX43 STRING:Q9FX43 PRIDE:Q9FX43 EnsemblPlants:AT1G73500.1 GeneID:843685 KEGG:ath:AT1G73500 NMPDR:fig|3702.1.peg.6851 TAIR:At1g73500 InParanoid:Q9FX43 OMA:SSKRWTA PhylomeDB:Q9FX43 ProtClustDB:CLSN2914344 Genevestigator:Q9FX43 Uniprot:Q9FX43

MALVRERRQLNLRLPLPPISDRRFSTSSSSATTTTVAGCNGISACDLEKLNVLGCGNGGIVYKVRHKT
TSEIYALKTVNGDMDPIFTRQLMREMEILRRTDSPYVVKCHGIFEKPVVGEVSILMEYMGTLESLRG
GVTEQKLAGFAKQILKGLSYLHALKIVHRDIKPANLLLNSKNEVKIADFGVSKILVRSLDSCNSYVGTCA
YMSPERFDSESSGGSSDIYAGDIWSFGLMMLELLVGHFPLLPPGQRPDALMCAVCFGEPPRAPEGC
SEEFRSFVECCLRKDSSKRWTAPQLLAHPFLREDL

>UNIPROTKB|B4DEQ4 symbol:MKNK2 species:9606 "Homo sapiens" InterPro:IPR000719 InterPro:IPR008271 InterPro:IPR011009 Pfam:PF00069 PROSITE:PS00108 PROSITE:PS50011 InterPro:IPR017442 SUPFAM:SSF56112 HOVERGEN:HBG106949 UniGene:Hs.515032 HGNC:HGNC:7111 EMBL:AC007136 EMBL:AK293742 IPI:IPI01015106 ProteinModelPortal:B4DEQ4 SMR:B4DEQ4 STRING:B4DEQ4 Ensembl:ENST00000541165 Bgee:B4DEQ4 Uniprot:B4DEQ4

MLYQCQGHRNVLELIEFFEEEDRFYLVFEKMRGGSILSHIHKRRHFNELEASVVVQDVASALDFLHN
KGIAHRDLKPENILCEHPNQVSPVKICDFDLGSGIKLNGDCSPISTPELLTPCGSAEYMAVVEAFSEEA
SIYDKRCDLWSLGVILYILLSGYPPFVGRCGSDCGWDRGEACPACQNMLFESIQEGKYEFPDKDWA
HISCAAKDLISKLLVRDAKQRLSAAQVLQHPWVQGCAPENTLPTPMVLQRNCKDLTSFAAEAIAMN
RQLAQHDEDLAEEEAAGQGQPVLVRATSRCLQLSPPSQSKLAQRRQRASLSSAPVVLVGDHA

>UNIPROTKB|B4DEW2 symbol:MAPK4 species:9606 "Homo sapiens" InterPro:IPR000719 InterPro:IPR008350 InterPro:IPR011009 Pfam:PF00069 PRINTS:PR01771 PROSITE:PS50011 InterPro:IPR017442 GO:GO:0005524 SUPFAM:SSF56112 GO:GO:0004707 EMBL:AC012433 EMBL:AC090395 UniGene:Hs.433728 HGNC:HGNC:6878 HOVERGEN:HBG104376 EMBL:AC090638 EMBL:AK293818 IPI:IPI01012827 ProteinModelPortal:B4DEW2 SMR:B4DEW2 STRING:B4DEW2 Ensembl:ENST00000540640 Bgee:B4DEW2 Uniprot:B4DEW2

MWAAGCILAEMLTGRMLFAGAHELEQMQLILETIPVIREEDKDELLRVMPSFVSSTWEVKRPLRKLL
PEVNSEAIDFLEKILTFNPMDRLTAEMGLQHPYMSPYSCPEDEPTSQHPFRIEDEIDDIVAANQSQLS
NWDTCSSRYPVSLSSDLEWRPDRCQDASEVQRDPRAGSAPLAEDVQVDPRKDSHSSSERFLEQSHS
SMERAFEADYGRSCDYKVGSPSYLDKLLWRDNKPHHYSEPKLILDLSHWKQAGPPTATGLADTGAR
EDEPASLFLEIAQWVKSTQGGPEHASPPADDPERRLSASPPGRPAPVDGGASPQFDLDVFISRALKL
CTKPEDLPDNKLGDLNGACIPEHPGDLVQTEAFSKERW

>UNIPROTKB|P27448 symbol:MARK3 species:9606 "Homo sapiens" InterPro:IPR000719 InterPro:IPR001772 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 Pfam:PF02149 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 PROSITE:PS50032 SMART:SM00220 InterPro:IPR017442 GO:GO:0005886 GO:GO:0005524 GO:GO:0005515 SUPFAM:SSF56112 GO:GO:0004674 InterPro:IPR015940 SMART:SM00165 PROSITE:PS50030 Gene3D:G3DSA:3.30.310.80 SUPFAM:SSF103243 HOVERGEN:HBG052453 KO:K08798 EMBL:U64205 EMBL:AF159295 EMBL:AF387637 EMBL:AF465413 EMBL:M80359 EMBL:AL133367 EMBL:BC024773 EMBL:AF170723 IPI:IPI00183118 IPI:IPI00220505 IPI:IPI00220506 IPI:IPI00220507 IPI:IPI00220508 IPI:IPI00220509 PIR:S27966 RefSeq:NP_001122390.1 RefSeq:NP_001122391.1 RefSeq:NP_001122392.1 RefSeq:NP_001122393.1 RefSeq:NP_002367.4 UniGene:Hs.35828 PDB:2QNJ PDB:3FE3 PDBsum:2QNJ PDBsum:3FE3 ProteinModelPortal:P27448 SMR:P27448 DIP:DIP-34637N IntAct:P27448 MINT:MINT-272697 STRING:P27448 PhosphoSite:P27448 DMDM:281185502 PRIDE:P27448 Ensembl:ENST00000335102 GeneID:4140 KEGG:hsa:4140 UCSC:uc001ymw.2 UCSC:uc001ymx.2 UCSC:uc001yna.2 UCSC:uc010awp.1 CTD:4140 GeneCards:GC14P103851 HGNC:HGNC:6897 HPA:HPA024652 MIM:602678 neXtProt:NX_P27448 PharmGKB:PA30640 eggNOG:prNOG08718 InParanoid:P27448 OMA:DGIPSRK PhylomeDB:P27448 ArrayExpress:P27448 Bgee:P27448 CleanEx:HS_MARK3 Genevestigator:P27448 GermOnline:ENSG00000075413 Uniprot:P27448

MSTRTPLPTVNERDTENHTSHGDGRQEVTSRTSRSGARCRNSIASCADEQPHIGNYRLLKTIGKGNF
AKVKLARHILTGREVAIKIIDKTQLNPTSLQKLFREVRIMKILNHPNIVKLFEVIETEKTLIMEYASGGEV
FDYLVAHGRMKEKEARSKFRQIVSAVQYCHQKRIVHRDLKAENLLLDADMNIKIADFGFSNEFTVG
GKLDTFCGSPPYAAPELFQGKKYDGPEVDVWSLGVILYTLVSGSLPFDGNKELRERVLRGKYRIPFYM
STDCENLLKRFLVLNPIKRGTLEQIMKDRWINAGHEEDELKPFVEPELDISDQKRIDIMVGMGYSQEE
IQESLSKMKYDEITATYLLLGRKSSELDASDSSSSSNLSAKRPSSDLNNSTGQSPHHKVQRSVFSSQKQ
RRYSDHAGPAIPSVVAYPKRSQTSTADSDLKEDGISSRKSSGSAVGGKGIAPASPMLGNASNPNKAD
IPERKKSSTVPSSNTASGGMTRRNTYVCSRTTDRHSVIQNGKENSTIPDQRTPVASTHSISSAATPDRI
RFPRGTASRSTFHGQPRERRTATYNGPPASPSLSHEATPLSQTRSRGSTNLFSKLTSKLTRRNMSFRFI
KRLPTEYERNGRYEGSSNVSAQKDENKEAKPRSLRFTWSMKTTSSMDPGDMMREIRKVLDANNC
DYEQRERFLLFCVHGDGHAENLVQWEMEVCKLPRLSLNGVRFKRISGTSIAFKNIASKIANELKL

>UNIPROTKB|P49136 symbol:MAPKAPK2 species:10030 "Cricetulus longicaudatus" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 SUPFAM:SSF56112 GO:GO:0004674 EMBL:X82220 PIR:S49490 ProteinModelPortal:P49136 SMR:P49136 HOVERGEN:HBG106948 Uniprot:P49136

LGINGKVLRIFDKRTQQKFALKMLQDCPKARREVELHWRASQCPHIVDIVDVYENLYAGRKCLLIVM
ECLDGGELFSRIQDRGDQAFTEREASEIMKSIGEAIQYLHSINIAHRDVKPENLLYTSKRAILKLTDFGF
AKETTSHNSLTTPCYTPYYVAPEVLGPEKYDKSCDMWSLGVIMYILLCGYPPFYSNHGLAISPGMKTR
IRMGQYEFPNPEWSEVSEEVKMLIRNLLKTEPTQRMTITEFMNHPWIMQSTKVPQTPLHTSRVLKE
DKERWEDVKEEMTSALMRVDYEQIKIKKIEDASNPLLLKRRKKARAVEAAALAH

>UNIPROTKB|P49137 symbol:MAPKAPK2 species:9606 "Homo sapiens" Reactome:REACT_111217 InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005829 GO:GO:0005524 Pathway_Interaction_DB:p38_mk2pathway Reactome:REACT_111102 Reactome:REACT_6900 GO:GO:0048011 GO:GO:0007265 GO:GO:0005654 GO:GO:0005515 EMBL:CH471100 Pathway_Interaction_DB:il2_1pathway Reactome:REACT_22258 Pathway_Interaction_DB:p38alphabetadownstreampathway SUPFAM:SSF56112 GO:GO:0004674 GO:GO:0045087 GO:GO:0000187 HOGENOM:HBG755340 BRENDA:2.7.11.1 GO:GO:0004871 GO:GO:0019370 GO:GO:0051403 GO:GO:0002755 GO:GO:0002756 GO:GO:0008063 GO:GO:0034130 GO:GO:0034134 GO:GO:0034138 GO:GO:0034142 GO:GO:0048010 Pathway_Interaction_DB:mapktrkpathway GO:GO:0006692 EMBL:AL591846 HOVERGEN:HBG106948 OMA:NGKVVQC KO:K04443 EMBL:U12779 EMBL:BC036060 EMBL:BC052584 EMBL:X75346 IPI:IPI00026054 IPI:IPI00215763 PIR:JC2204 PIR:S39793 RefSeq:NP_004750.1 RefSeq:NP_116584.2 UniGene:Hs.643566 UniGene:Hs.713747 PDB:1KWP PDB:1NXK PDB:1NY3 PDB:2JBO PDB:2JBP PDB:2OKR PDB:2ONL PDB:2OZA PDB:2P3G PDB:2PZY PDB:3A2C PDB:3FPM PDB:3FYJ PDB:3FYK PDB:3GOK PDB:3KA0 PDB:3KC3 PDB:3KGA PDB:3M2W PDB:3M42 PDB:3R2B PDB:3R2Y PDB:3R30 PDBsum:1KWP PDBsum:1NXK PDBsum:1NY3 PDBsum:2JBO PDBsum:2JBP PDBsum:2OKR PDBsum:2ONL PDBsum:2OZA PDBsum:2P3G PDBsum:2PZY PDBsum:3A2C PDBsum:3FPM PDBsum:3FYJ PDBsum:3FYK PDBsum:3GOK PDBsum:3KA0 PDBsum:3KC3 PDBsum:3KGA PDBsum:3M2W PDBsum:3M42 PDBsum:3R2B PDBsum:3R2Y PDBsum:3R30 ProteinModelPortal:P49137 SMR:P49137 IntAct:P49137 MINT:MINT-1539725 STRING:P49137 PhosphoSite:P49137 DMDM:1346538 PRIDE:P49137 Ensembl:ENST00000367103 GeneID:9261 KEGG:hsa:9261 UCSC:uc001hem.1 CTD:9261 GeneCards:GC01P206858 H-InvDB:HIX0023634 HGNC:HGNC:6887 HPA:CAB010297 MIM:602006 neXtProt:NX_P49137 PharmGKB:PA30631 eggNOG:prNOG06010 GeneTree:ENSGT00550000074510 InParanoid:P49137 PhylomeDB:P49137 NextBio:34715 ArrayExpress:P49137 Bgee:P49137 CleanEx:HS_MAPKAPK2 Genevestigator:P49137 GermOnline:ENSG00000162889 Uniprot:P49137

MLSNSQGQSPPVPFPAPAPPPQPPTPALPHPPAQPPPPPPQQFPQFHVKSGLQIKKNAIIDDYKVTS
QVLGLGINGKVLQIFNKRTQEKFALKMLQDCPKARREVELHWRASQCPHIVRIVDVYENLGRKCLLI
VMECLDGGELFSRIQDRGDQAFTEREASEIMKSIGEAIQYLHSINIAHRDVKPENLLYTSKRPNAILKL
TDFGFAKETTSHNSLTTPCYTPYYVAPEVLGPEKYDKSCDMWSLGVIMYILGYPPFYSNHGLAISPG
MKTRIRMGQYEFPNPEWSEVSEEVKMLIRNLLKTEPTQRMTITEFMNHPWIMQSTKVPQTPLHTS
RVLKEDKERWEDVKEEMTSALATMRVDYEQIKIKKIEDASNPLLKRKKARALEAAALAH

>UNIPROTKB|P49139 symbol:MAPKAPK2 species:9986 "Oryctolagus cuniculus" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 SUPFAM:SSF56112 GO:GO:0004674 HOVERGEN:HBG106948 EMBL:X75345 EMBL:AAGW02025411 PIR:S39794 UniGene:Ocu.3281 eggNOG:maNOG08085 Uniprot:P49139

PPPPPPQQFPQFHVRSGLQIKKNAIIDDYKVTSQVLGLGINGKVLQIFSKKTQEKFALKMLQDCPKAR REVELHWRASQCPHIVRIVDVYENLYAGRKCLLIVMECLDGGELFSRIQDRGDQAFTERSEIMKSIGE AIQYLHSINIAHRDVKPENLLYTSKRPKAILKLTDFGFAKETTSHNSLTTPCYTPYYVAPEVLGPEKYDKS CDMWSLGVIMYILLCGYPPFYSNHGLAISPGMKTRIRMGQYEFPNPWEVSEEVKMLIRNLLKTEPT QRMTITEFMNHPWIMQSTKVPQTPLHTSRVLKEDKERWEDVKEEMTSALATMRVDYEQIKIKKKIE DASNPLLLKRRKKARALEAAALAH

>UNIPROTKB|Q16644 symbol:MAPKAPK3 species:9606 "Homo sapiens" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005829 GO:GO:0005524 Pathway_Interaction_DB:p38_mk2pathway Reactome:REACT_111102 Reactome:REACT_6900 GO:GO:0048011 GO:GO:0007265 GO:GO:0005654 GO:GO:0005515 Pathway_Interaction_DB:p38alphabetadownstreampathway SUPFAM:SSF56112 GO:GO:0004674 GO:GO:0045087 GO:GO:0000187 HOGENOM:HBG755340 EMBL:CH471055 GO:GO:0051403 GO:GO:0002755 GO:GO:0002756 GO:GO:0008063 GO:GO:0034130 GO:GO:0034134 GO:GO:0034138 GO:GO:0034142 GO:GO:0004708 HOVERGEN:HBG106948 GeneTree:ENSGT00550000074510 OrthoDB:EOG4HQDJP CTD:7867 OMA:IRMGQYG KO:K04444 EMBL:U43784 EMBL:U09578 EMBL:AB451303 EMBL:BC001662 EMBL:BC007591 EMBL:BC010407 IPI:IPI00005777 PIR:JC6094 RefSeq:NP_001230854.1 RefSeq:NP_001230855.1 RefSeq:NP_004626.1 UniGene:Hs.234521 PDB:3FHR PDB:3FXW PDB:3R1N PDBsum:3FHR PDBsum:3FXW PDBsum:3R1N ProteinModelPortal:Q16644 SMR:Q16644 IntAct:Q16644 STRING:Q16644 PhosphoSite:Q16644 DMDM:74762148 PeptideAtlas:Q16644 PRIDE:Q16644 Ensembl:ENST00000357955 Ensembl:ENST00000446044 GeneID:7867 KEGG:hsa:7867 UCSC:uc003day.1 GeneCards:GC03P050624 H-InvDB:HIX0003305 HGNC:HGNC:6888 MIM:602130 neXtProt:NX_Q16644 PharmGKB:PA30632 eggNOG:prNOG16541 InParanoid:Q16644 PhylomeDB:Q16644 NextBio:30313 ArrayExpress:Q16644 Bgee:Q16644 CleanEx:HS_MAPKAPK3 Genevestigator:Q16644 GermOnline:ENSG00000114738 Uniprot:Q16644

MDGETAEEQGGPVPPPVAPGGPGLGGAPGGRREPKKYAVTDDYQLSKQVLGLGVNGKVLECFHR RTGQKCALKLLYDSPKARQEVDHHWQASGGPHIVCILDVYENMHHGKRCLLIIMECMEGGELFIQE RGDQAFTEREAAEIMRDIGTAIQFLHSHNIAHRDVKPENLLYTSKEKDAVLKLTDFGFAKETTQNALQ TPCYTPYYVAPEVLGPEKYDKSCDMWSLGVIMYILLCGFPPFYSNTGQAISPGMKRRLGQYGFPNPE WSEVSEDAKQLIRLLLKTDPTERLTITQFMNHPWINQSMVVPQTPLHTARVLQEDKDHWDEVKEE MTSALATMRVDYDQVKIKDLKTSNNRLLNKRRKKQAGSSSASQGCNNQ

>UNIPROTKB|Q291K8 symbol:Sin1 species:46245 "Drosophila pseudoobscura pseudoobscura" GO:GO:0005829 GO:GO:0006915 EMBL:CM000071 GenomeReviews:CM000071_GR InterPro:IPR008828 PANTHER:PTHR13335 GO:GO:0045767 Pfam:PF05422 OrthoDB:EOG4RN8QM RefSeq:XP_001360529.2 GeneID:4803881 KEGG:dpo:Dpse_GA10075 FlyBase:FBgn0070134 InParanoid:Q291K8 Uniprot:Q291K8

MATYSNQHWLLSHIRNSFISTDDTGMCETVMLSDDMPKHYLRKFNSSAGVESHRRRPLKPPLASAL
PDRNTRHPDAPMQEVDFMCYPGLDLSDDEEDMSTHSFDIQMYPEVGAHRFRSNTAQKLEKLAKR
RAARIKSINYNEEVQPPEDKDFFMRKEIPNIKPTIPKEKKANDDELSDEGVQSMLTEQLAKSPKQTQN
KFIEFARFDGTSQVGMQTKRINVYLNMLPEPDRNYPLKVCVLSTAKIQEVIGFVCKSLQYPDVPLKSL
QHYGLYMTEDNDDMEDFPPLDNREPCSKFGFSHLTLAERRPLAPVTRVDYPGQLGNKSMTSEDDK
ATLADAALRALKNITLNGGAADPGGGAVGGGEGDGDGDDSPHDNVKEYKRLNHNDMLEAPMHR
SFRLNIIDKRFFKSDVTLGISGERIEIDQYKNAKFWPQKKPVSTPIDLVAHCEIVERRHLKALLRIWLKS
NSSSSSLPSGCTSAPINASVTTLNTGTGSSSAGIAHSPSSPNSFFFMTSNIRFKHYDFDTDTHTAEQIN
SKLNCILEMRSSELRREFLQQRERKQERQQVKKQLKL

>UNIPROTKB|Q3SYZ2 symbol:MAPKAPK3 species:9913 "Bos taurus" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 GO:GO:0005634 GO:GO:0005737 SUPFAM:SSF56112 GO:GO:0004674 HOVERGEN:HBG106948 GeneTree:ENSGT00550000074510 OrthoDB:EOG4HQDJP EMBL:BT026197 EMBL:BC103321 IPI:IPI00707891 RefSeq:NP_001029951.1 UniGene:Bt.43984 ProteinModelPortal:Q3SYZ2 SMR:Q3SYZ2 STRING:Q3SYZ2 PRIDE:Q3SYZ2 Ensembl:ENSBTAT00000021983 GeneID:615215 KEGG:bta:615215 CTD:7867 eggNOG:maNOG10802 InParanoid:Q3SYZ2 OMA:IRMGQYG PhylomeDB:Q3SYZ2 KO:K04444 Uniprot:Q3SYZ2

MDVETAEEQGGPAPPSGVPCGPCSAGAPALGGRREPKKYAVTDDYQLSKQVLGLGVNGKVLECFH
RRTGQKCALKLLYDSPKARQEVDHHWQASGGPHIVRILDVYENMHHSKRCLLIIMECMEGGESRIQ
ERGDQAFTEREAAEIMRDIGTAIQFLHSRNIAHRDVKPENLLYTSKDKDAVLKLTDFGFAKETTQNAL
QTPCYTPYYVAPEVLGPEKYDKSCDMWSLGVIMYILLCGFPPFYSNTGQAISPGKRIRLGQYGFPSPE
WSEVSEDAKQLIRLLLKTDPTERLTITQFMNHPWINQSMVVPQTPLHTARVLQEDRDHWDEVKEE
MTSALATMRVDYDQVKIKDLKTSNNRLLNKRRKKQAGSSSGSQGCNN

>UNIPROTKB|Q58D94 symbol:MKNK1 species:9913 "Bos taurus" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 GO:GO:0006417 SUPFAM:SSF56112 GO:GO:0004674 GeneTree:ENSGT00550000074510 EMBL:BT021703 EMBL:BC111299 IPI:IPI00718398 IPI:IPI00742625 RefSeq:NP_001030435.1 UniGene:Bt.21055 ProteinModelPortal:Q58D94 SMR:Q58D94 STRING:Q58D94 PRIDE:Q58D94 GeneID:525647 KEGG:bta:525647 CTD:8569 eggNOG:maNOG14839 HOVERGEN:HBG106949 InParanoid:Q58D94 KO:K04372 Uniprot:Q58D94

MGSSEPIPIAESDKRKKKKRKARATDSLPGKFEDVYKLTSELLGEGANAKVQVAVSLQNGNEYAVKII
EKHAGHSRSRVFREVETLYQCQGNKHILELIEFFEDDTRFYLVFEKLQGGSILAHIQKQFNEREASRVV
RDVAAALDFRHTKGIAHRDLKPENILCESPEKVSPVKICDFDLGSGVKLNNSCTPITTPELTTPCGSAE

YMAPEVVEVFTDEATFYDKRCDLWSLGVVLYIMLSGYPPFVGHCGADGDRGEVCTVCQNKLFESIQ
KGKYEFPDKDWAHISNEAKDLISKLLVRDAKQRLSAAQVLQHPWVQGQAPERGLPTPQVLQRNSS
TMDLTLFAAEAIALNRQLSQHEENEQNKLAEESEVLAEGLCSKLPPSKSRLARRRALAQAGRSGDAP
PSPTPTTPAP

>UNIPROTKB|Q7Z319 symbol:DKFZp686E14208 species:9606 "Homo sapiens" InterPro:IPR000719 InterPro:IPR008271 InterPro:IPR011009 Pfam:PF00069 PROSITE:PS00108 PROSITE:PS50011 InterPro:IPR017442 GO:GO:0005524 SUPFAM:SSF56112 GO:GO:0004674 HSSP:P49137 EMBL:AL136373 GeneTree:ENSGT00550000074510 HOVERGEN:HBG106949 UniGene:Hs.371594 HGNC:HGNC:7110 EMBL:BX538193 IPI:IPI01014049 ProteinModelPortal:Q7Z319 SMR:Q7Z319 STRING:Q7Z319 Ensembl:ENST00000371944 UCSC:uc001cpz.1 ArrayExpress:Q7Z319 Bgee:Q7Z319 Uniprot:Q7Z319

MAKSMPSKSSRNKQGTVGVGCFERWRRCISVRETSSILAHIQKQKHFNEREASRVVRDVAAALDFL
HTKGIAHRDLKPENILCESPEKVSPVKICDFDLGSGMKLNNSCTPITTPELTTPCGSAEYMEVVEVFTD
QATFYDKRCDLWSLGVVLYIMLSGYPPFVGHCGADCGWDRGEVCRVCQNKLFESIQEGKYEFPDK
DWAHISSEAKDLISKLLVRDAKQRLSAAQVLQHPWVQGQAPEKGLPTPQVLQRSTMDLTLFAAEAI
ALNRQLSQHEENELAEEPEALADGLCSMKLSPPCKSRLARRRALAQAGRGEDRSPPTAL

>UNIPROTKB|Q8IW41 symbol:MAPKAPK5 species:9606 "Homo sapiens" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 GO:GO:0005634 GO:GO:0005737 GO:GO:0007165 GO:GO:0005515 Pathway_Interaction_DB:p38alphabetadownstreampathway SUPFAM:SSF56112 GO:GO:0004674 EMBL:CH471054 HOGENOM:HBG755340 GO:GO:0004708 HOVERGEN:HBG106948 GeneTree:ENSGT00550000074510 EMBL:AF032437 EMBL:AK122767 EMBL:BC000833 EMBL:BC041049 EMBL:BC047284 EMBL:AL110301 IPI:IPI00160672 IPI:IPI00217131 PIR:T34519 RefSeq:NP_003659.2 RefSeq:NP_620777.1 UniGene:Hs.413901 ProteinModelPortal:Q8IW41 SMR:Q8IW41 IntAct:Q8IW41 STRING:Q8IW41 PhosphoSite:Q8IW41 DMDM:52000829 PRIDE:Q8IW41 Ensembl:ENST00000202788 GeneID:8550 KEGG:hsa:8550 UCSC:uc001tsz.1 UCSC:uc001tta.1 CTD:8550 GeneCards:GC12P112282 HGNC:HGNC:6889 HPA:CAB004546 HPA:HPA015515 MIM:606723 neXtProt:NX_Q8IW41 PharmGKB:PA30633 eggNOG:prNOG06554 InParanoid:Q8IW41 OMA:QVTKQIA OrthoDB:EOG43JC4K PhylomeDB:Q8IW41 NextBio:32036 ArrayExpress:Q8IW41 Bgee:Q8IW41 CleanEx:HS_MAPKAPK5 Genevestigator:Q8IW41 GermOnline:ENSG00000089022 KO:K04442 Uniprot:Q8IW41

MSEESDMDKAIKETSILEEYSINWTQKLGAGISGPVRVCVKKSTQERFALKILLDRPKARNEVRLHM
MCATHPNIVQIIEVFANSVQFPHESSPRARLLIVMEMMEGGELFHRISQHRHFTEKQASQKQIALAL
RHCHLLNIAHRDLKPENLLFKDNSLDAPVKLCDFGFAKIDQGDLMTPQFTPYYVAPQVLEAQRRHQ
KEKSGIIPTSPTPYTYNKSCDLWSLGVIIYVMLCGYPPFYSKHHSRTIPKDMRKMTGSFEFPEEEWSQI
SEMAKDVVRKLLKVKPEERLTIEGVLDHPWLNSTEALDNVLPSAQLMMDKAVVAGIQQAHAEQLA
NMRIQDLKVSLKPLHSVNNPILRKRKLLGTKPKDSVYIHDHENGADSVALEKLRDVIAQCILPQAGKG
ENEDEKLNEVMQEAWKYNRECKLLRDTLQSFSWNGRGFTDKVDRLKLAEIVKQVIEEQTTSHESQ

>UNIPROTKB|Q96L34 symbol:MARK4 species:9606 "Homo sapiens" InterPro:IPR000449 InterPro:IPR000719 InterPro:IPR001772 InterPro:IPR002290 InterPro:IPR008271

InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 Pfam:PF00627 Pfam:PF02149 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 PROSITE:PS50032 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 GO:GO:0005813 GO:GO:0007399 SUPFAM:SSF56112 GO:GO:0004674 GO:GO:0043005 GO:GO:0050321 InterPro:IPR015940 SMART:SM00165 PROSITE:PS50030 GO:GO:0008017 GO:GO:0043130 GO:GO:0001578 GO:GO:0043068 GO:GO:0043015 Gene3D:G3DSA:3.30.310.80 SUPFAM:SSF103243 GeneTree:ENSGT00600000084258 HOGENOM:HBG315019 HOVERGEN:HBG052453 KO:K08798 EMBL:AY057448 EMBL:AB049127 EMBL:AB088047 EMBL:AY120867 EMBL:AB058763 EMBL:AK027619 EMBL:AK075272 IPI:IPI00064797 IPI:IPI00297959 RefSeq:NP_001186796.1 RefSeq:NP_113605.2 UniGene:Hs.34314 ProteinModelPortal:Q96L34 SMR:Q96L34 IntAct:Q96L34 STRING:Q96L34 PhosphoSite:Q96L34 DMDM:29840797 PRIDE:Q96L34 Ensembl:ENST00000262891 GeneID:57787 KEGG:hsa:57787 UCSC:uc002pbb.1 CTD:57787 GeneCards:GC19P045754 HGNC:HGNC:13538 HPA:HPA039186 MIM:606495 neXtProt:NX_Q96L34 PharmGKB:PA30641 InParanoid:Q96L34 OMA:TERPGSE OrthoDB:EOG4TB49R PhylomeDB:Q96L34 NextBio:64721 ArrayExpress:Q96L34 Bgee:Q96L34 CleanEx:HS_MARK4 Genevestigator:Q96L34 GermOnline:ENSG00000007047 Uniprot:Q96L34

MSSRTVLAPGNDRNSDTHGTLGSGRSSDKGPSWSSRSLGARCRNSIASCPEEQPHVGNYRLLRTIG
KGNFAKVKLARHILTGREVAIKIIDKTQLNPSSLQKLFREVRIMKGLNHPNIVKLFEVIETTLYLVMEYA
SAGEVFDYLVSHGRMKEKEARAKFRQIVSAVHYCHQKNIVHRDLKAENLLLDAEANIKIADFGFSNE
FTLGSKLDTFCGSPPYAAPELFQGKKYDGPEVDIWSLGVILYTLVSGSLPDHNLKELRERVLRGKYRVP
FYMSTDCESILRRFLVLNPAKRCTLEQIMKDKWINIGYEGEELKPYTEPEEDFGDTKRIEVMVGMGYT
REEIKESLTSQKYNEVTATYLLLGRKTEEGGDRGAPGLAARRAPSDTTNGTSSSKGTSHSKGQRSSSS
TYHRQRRHSDFCGPSPAPLHPKRSPTSTGEAELKEERLPGRKASCSTAGSGSRGLPPSSPMVSSAHN
PNKAEIPERRKDSTSTPNNLPPSMMTRRNTVCTRPGAERPSLLPNGKENSSGTPRVPPASPSSHSLA
PPSGERSRLARGSTIRSTFHGGQVRDRRAGGGGGGVQNGPPASPTLAHEAAPLPAGRPRPTTNLF
TKLTSKLTRRVADEPERIGGPEVSCHLWDQTETAPRLLRFPWSVKLTSSRPPEALMAALRQATAAAR
CRCRQPQPFLLACLHGGAGGPEPLSHFEVEVCQLPRPGLRGVLFRRVAGTALAFRTLVTRISNDLEL

>UNIPROTKB|Q9BUB5 symbol:MKNK1 species:9606 "Homo sapiens" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 GO:GO:0005634 GO:GO:0005737 Reactome:REACT_111102 GO:GO:0005515 GO:GO:0006417 Pathway_Interaction_DB:mtor_4pathway EMBL:CH471059 Pathway_Interaction_DB:p38alphabetadownstreampathway SUPFAM:SSF56112 GO:GO:0004674 GO:GO:0007243 HOGENOM:HBG755340 GO:GO:0018105 EMBL:AL136373 GeneTree:ENSGT00550000074510 CTD:8569 HOVERGEN:HBG106949 KO:K04372 EMBL:AB000409 EMBL:AY355461 EMBL:BC002755 IPI:IPI00187091 IPI:IPI00304048 IPI:IPI00412417 RefSeq:NP_001129025.1 RefSeq:NP_003675.2 RefSeq:NP_945324.1 UniGene:Hs.371594 PDB:2HW6 PDBsum:2HW6 ProteinModelPortal:Q9BUB5 SMR:Q9BUB5 IntAct:Q9BUB5 MINT:MINT-85533 STRING:Q9BUB5 PhosphoSite:Q9BUB5 DMDM:30316115 PRIDE:Q9BUB5 Ensembl:ENST00000371946 GeneID:8569 KEGG:hsa:8569 UCSC:uc001cqa.1 UCSC:uc001cqb.1 UCSC:uc001cqc.1 GeneCards:GC01M047023 H-InvDB:HIX0000552 HGNC:HGNC:7110 MIM:606724 neXtProt:NX_Q9BUB5 eggNOG:prNOG07605

InParanoid:Q9BUB5 OMA:HEENELA OrthoDB:EOG4GTKD2 PhylomeDB:Q9BUB5 NextBio:32143 ArrayExpress:Q9BUB5 Bgee:Q9BUB5 CleanEx:HS_MKNK1 Genevestigator:Q9BUB5 GermOnline:ENSG00000079277 Uniprot:Q9BUB5

MVSSQKLEKPIEMGSSEPLPIADGDRRRKKKRRGRATDSLPGKFEDMYKLTSELLGEGAYAKVQGAV
SLQNGKEYAVKIIEKQAGHSRSRVFREVETLYQCQGNKNILELIEFFEDDTRFYLVFEKLGSILAHIQKQ
KHFNEREASRVVRDVAAALDFLHTKDKVSLCHLGWSAMAPSGLTAAPTSLGSSDPPTSASQVAGTT
GIAHRDLKPENILCESPEKVSPVKICDFDLGSGMKLNNSCTPITTPELTTCSAEYMAPEVVEVFTDQAT
FYDKRCDLWSLGVVLYIMLSGYPPFVGHCGADCGWDRGEVCRVCQNKLFESIQEGKYEFPDKDWA
HISSEAKDLISKLLVRDAKQRLSAAQVLQHPWVQGQAPEKGLTPVLQRNSSTMDLTLFAAEAIALNR
QLSQHEENELAEEPEALADGLCSMKLSPPCKSRLARRRALAQAGRGEDRSPPTAL

>UNIPROTKB|Q9HBH9 symbol:MKNK2 species:9606 "Homo sapiens" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 GO:GO:0006417 GO:GO:0046872 SUPFAM:SSF56112 GO:GO:0004674 GO:GO:0007243 GO:GO:0007166 GO:GO:0030097 GO:GO:0071243 GeneTree:ENSGT00550000074510 HOVERGEN:HBG106949 KO:K04372 EMBL:AF237775 EMBL:AF237776 EMBL:AF125532 EMBL:BC073140 IPI:IPI00396114 IPI:IPI00479444 RefSeq:NP_060042.2 RefSeq:NP_951009.1 UniGene:Hs.515032 PDB:2AC3 PDB:2AC5 PDB:2HW7 PDBsum:2AC3 PDBsum:2AC5 PDBsum:2HW7 ProteinModelPortal:Q9HBH9 SMR:Q9HBH9 IntAct:Q9HBH9 STRING:Q9HBH9 PhosphoSite:Q9HBH9 DMDM:90102033 PRIDE:Q9HBH9 Ensembl:ENST00000250896 GeneID:2872 KEGG:hsa:2872 UCSC:uc002lus.2 CTD:2872 GeneCards:GC19M002037 HGNC:HGNC:7111 HPA:HPA021875 MIM:605069 neXtProt:NX_Q9HBH9 InParanoid:Q9HBH9 OMA:VQKKTAE PhylomeDB:Q9HBH9 NextBio:11333 ArrayExpress:Q9HBH9 Bgee:Q9HBH9 CleanEx:HS_MKNK2 Genevestigator:Q9HBH9 GermOnline:ENSG00000099875 Uniprot:Q9HBH9

MVQKKPAELQGFHRSFKGQNPFELAFSLDQPDHGDSDFGLQCSARPDMPASQPIDIPDAKKRGKK
KKRGRATDSFSGRFEDVYQLQEDVLGEGAHARVQTCINLITSQEYAVKIIEKQPGHIRSRVFVEMLYQ
CQGHRNVLELIEFFEEEDRFYLVFEKMRGGSILSHIHKRRHFNELEASVVVQDVASALDFLHNKGIAH
RDLKPENILCEHPNQVSPVKICDFDLGSGIKLNGDCSPISTPELLTPCGSAEMPEVVEAFSEEASIYDKR
CDLWSLGVILYILLSGYPPFVGRCGSDCGWDRGEACPACQNMLFESIQEGKYEFPDKDWAHISCAA
KDLISKLLVRDAKQRLSAAQVLQHPWVQGCAPENTLPTPMVLRNCAKDLTSFAAEAIAMNRQLAQ
HDEDLAEEEAAGQGQPVLVRATSRCLQLSPPSQSKLAQRRQRASLSSAPVVLVGDHA

>UNIPROTKB|Q9UQ07 symbol:MOK species:9606 "Homo sapiens" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 GO:GO:0005524 GO:GO:0005737 GO:GO:0007165 SUPFAM:SSF56112 HOGENOM:HBG755340 GO:GO:0004693 GeneTree:ENSGT00600000084046 EMBL:AB022694 EMBL:U46191 EMBL:U46192 EMBL:U46193 EMBL:U46194 EMBL:BC053536 IPI:IPI00398648 IPI:IPI00398649 IPI:IPI00413657 IPI:IPI00472352 RefSeq:NP_055041.1 UniGene:Hs.104119 ProteinModelPortal:Q9UQ07 SMR:Q9UQ07 IntAct:Q9UQ07 STRING:Q9UQ07 PhosphoSite:Q9UQ07 DMDM:41017258 PRIDE:Q9UQ07 Ensembl:ENST00000361847

GeneID:5891 KEGG:hsa:5891 UCSC:uc001ylm.1 CTD:5891 GeneCards:GC14M102692 H-InvDB:HIX0011985 HGNC:HGNC:9833 HPA:HPA027282 HPA:HPA027292 MIM:605762 neXtProt:NX_Q9UQ07 PharmGKB:PA34187 HOVERGEN:HBG106271 PhylomeDB:Q9UQ07 NextBio:22916 ArrayExpress:Q9UQ07 Bgee:Q9UQ07 CleanEx:HS_RAGE Genevestigator:Q9UQ07 GermOnline:ENSG00000080823 KO:K08830 Uniprot:Q9UQ07

MKNYKAIGKIGEGTFSEVMKMQSLRDGNYYACKQMKQRFESIEQVNNLREIQALRRLNPHPNILM
LHEVVFDRKSGSLALICELMDMNIYELIRGRRYPLSEKKIMHYMYQLCKSLDHIHRNGIFHRKPENILI
KQDVLKLGDFGSCRSVYSKQPYTEYISTRWYRAPECLLTDGFYTYKMDLWSAGCVFYEIASLQPLFPG
VNELDQISKIHDVIGTPAQKILTKFKQSRAMNFDFPFKKGSGIPLLTTNLSQLSLLHAMVAYDPDERIA
AHQALQHPYFQEQRKTEKRALGSHRKAGFPEHPVAPEPLSNSCQISKEGRKQKQSLKQEEDRPKRR
GPAYVMELPKLKLSGVVRLSSYSSPTLQSVLGSGTNGRVPVLPLCIPASKKTDPQKDLKPAPQQCRLP
TIVRKGGR

>ZFIN|ZDB-GENE-030131-6099 symbol:mknk2a species:7955 "Danio rerio" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 ZFIN:ZDB-GENE-030131-6099 GO:GO:0005524 SUPFAM:SSF56112 GO:GO:0004674 HSSP:P49137 GeneTree:ENSGT00550000074510 HOVERGEN:HBG106949 KO:K04372 EMBL:BC045391 IPI:IPI00507047 RefSeq:NP_997888.1 UniGene:Dr.6680 ProteinModelPortal:Q7ZVV9 SMR:Q7ZVV9 STRING:Q7ZVV9 PRIDE:Q7ZVV9 GeneID:334167 KEGG:dre:334167 CTD:334167 eggNOG:fiNOG07216 InParanoid:Q7ZVV9 ArrayExpress:Q7ZVV9 Bgee:Q7ZVV9 Uniprot:Q7ZVV9

MVQNKITEVTGFHRSFKGQNPFKTDEFIDSDSHLESSFILERSTRPAMPSSQPIDIPDAKKRNKKKKR
CRATDSFSGRFEDVYKLQNEVLGEGAYAVVQTCINLITNKEYAVKIIEKRPGHSRSRVFVEMLYQCQG
HRNILELVEYFEEEDKFYLVFEKLRGGSILTHIHRRQHFNEQEASIVVQDIASALDFLHNKGMAHRDLK
PENILCEHSDRISPVKICDFDLGSGIKLNSDSSPISTPELLTPCGSAEMPEVVEAFNEEASIYDKRCDLW
SLGVILYIMLSGYPPFVGRCGTDCGWDWGEPCQACQSMLFESIQEGKYEFPEKDWAHISPAAKDLI
TKLLVRDAKDRLSAAQVLQHPWVKGCAPNTVSASILHQGGAQDLTFFAGQAVAMNRQLAEREESE
DLSLSSPLLSSSSGSMLLSPPSRSKLAHRRKTASSQHRGPVCAAELRQLLAPLVIVGDCA

>ZFIN|ZDB-GENE-030131-6232 symbol:mark3 species:7955 "Danio rerio" InterPro:IPR000719 InterPro:IPR001772 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 Pfam:PF02149 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 PROSITE:PS50032 SMART:SM00220 InterPro:IPR017442 ZFIN:ZDB-GENE-030131-6232 GO:GO:0005524 SUPFAM:SSF56112 GO:GO:0004674 InterPro:IPR015940 SMART:SM00165 PROSITE:PS50030 HSSP:P24941 Gene3D:G3DSA:3.30.310.80 SUPFAM:SSF103243 GeneTree:ENSGT00600000084258 HOVERGEN:HBG052453 KO:K08798 CTD:4140 EMBL:BC047179 IPI:IPI00810064 RefSeq:NP_956179.1 UniGene:Dr.77067 ProteinModelPortal:Q802W0 SMR:Q802W0 STRING:Q802W0 GeneID:334300 KEGG:dre:334300 InParanoid:Q802W0 PhylomeDB:Q802W0 ArrayExpress:Q802W0 Bgee:Q802W0 Uniprot:Q802W0

MSTTRAPLPTVNERKAENHTTNGHGRSEVTSRSVRSSGRNRNSGSGLDDVHPVIGNYRLLKTIGKG
NFAKVKLARHILTGSEVAIKMIDKTQLNPTSLQKLSREVTIMKNLNHPNIVKLFEVIETEKFLVMEYAS
GGEVFDYLVAHGRMKEKEARAKFRQIVSAVQYCHQKRIVHRDLKAENLLLDGDMNIKIADFGFSNE

FMVGSKLDTFCGSPPYAAPELFQGKKYDGPEVDVWSLGVILYTLVSGSLPFDQLKELRERVLRGKYRI
PFYMSTDCENLLKRFLVLNPAKRGTLEQIMKERWIDSGFEDDELKPFTEPDADISDQKRIDVIVGMG
FSKEKIHESLFKMNYDEVTAIYLLLGRKTHEEVSDSSSNSNLSAKRPSSEMNSQSPSHLKVQRSISSSES
RKSRRHSEQVGVVANNALSNSKRVVPVTADSEVKQEGGVIARKLPNHSPPSPLLGNANNPNKTEIP
DRKKGNSITSNNISGSGSMSRRNTYVCTERNNTDRLSVIPNGKENSVSLSPSSRDPGASTHSISTSVTP
DKARFPRGSASRSTFHGQVRDRRTATYNGPPASPAQPRSRANANNLLTKLTSKLTRSRSGDQQKDE
GKDGKDGKPRSLRFTWSMNTTSTMEPADIINEIRTVLDANSCSYQQRECFLLLCAHGDSHTDSLVQ
WEMEVCKLPRLSLNGVRFKRISGNSIAFKNIASKIAGELKL

>ZFIN|ZDB-GENE-030829-2 symbol:mknk2b species:7955 "Danio rerio" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 ZFIN:ZDB-GENE-030829-2 GO:GO:0005524 SUPFAM:SSF56112 GO:GO:0004674 HSSP:P49137 GeneTree:ENSGT00550000074510 HOVERGEN:HBG106949 KO:K04372 eggNOG:fiNOG07216 EMBL:BC044375 IPI:IPI00492599 RefSeq:NP_919383.1 UniGene:Dr.76090 ProteinModelPortal:Q803R1 SMR:Q803R1 STRING:Q803R1 GeneID:373121 KEGG:dre:373121 CTD:373121 InParanoid:Q803R1 ArrayExpress:Q803R1 Bgee:Q803R1 Uniprot:Q803R1

MVQNKITEVTGFHRSFKGQNPFETEEFSKTGSHLLESAFNFDCSARPDMPSSQPIDIPDSKKRNKKK
KRCRATDSFSGRFEDVYKLQDEVLGEGAYARVQTCISQITQKEYAVKIIEKRPGHSRSRVEVEMLYQC
QGHRSILELVEFFEEEDKFYLVFEKLRGGSILAHIHKRRYFGEQEASIVVQDVASALDFLHNKGMAHR
DLKPENILCEHEHRISPVKICDFDLGSGIKLNSDSSPISTPELLTPCGSAYAPEVVEAFNEEATIYDKRCD
LWSLGVILYIMLSGYPPFVGRCGSDCGWENGEPCQACQNMLFESIQEGKYEFPEKEWAHISSSAKD
LISKLLVRDAKKRLSAAQVLQHPWVQGGAFDCLPSSNLPRNSTKDLTFFAGKAVAMNRQLAQQDD
LEEQQQQDSPQVITASSTSMRLSPPSNSKLAKRRQRSSLLKGAPVSASELRQLLAPLVIVGDCA

>ZFIN|ZDB-GENE-040426-933 symbol:tab2 species:7955 "Danio rerio" InterPro:IPR001876 InterPro:IPR003892 Pfam:PF02845 PROSITE:PS01358 PROSITE:PS50199 PROSITE:PS51140 SMART:SM00547 ZFIN:ZDB-GENE-040426-933 GO:GO:0005622 GO:GO:0007507 GO:GO:0008270 GO:GO:0060027 EMBL:CR536610 EMBL:BC065982 IPI:IPI00497931 IPI:IPI00637926 RefSeq:NP_001009900.1 UniGene:Dr.82175 ProteinModelPortal:Q5RFW2 SMR:Q5RFW2 STRING:Q5RFW2 Ensembl:ENSDART00000017791 Ensembl:ENSDART00000064436 Ensembl:ENSDART00000136669 Ensembl:ENSDART00000137031 GeneID:494163 KEGG:dre:494163 CTD:23118 eggNOG:fiNOG09285 GeneTree:ENSGT00530000063642 HOGENOM:HBG714653 HOVERGEN:HBG056952 InParanoid:Q5RFW2 OMA:LQSQNVY OrthoDB:EOG41JZBR PhylomeDB:Q5RFW2 Bgee:Q5RFW2 Uniprot:Q5RFW2

MAQGNQQIDNQVLHHLRQKFPEVPEDVVCECVLQNKSDLAACCEYLTKVSPRFLYSEGSQSLTDLR
NHMTQLNLGVSQNTHGAVQRDAVGMNGSRTLAPSVSDGPLNVPSALSEFYQPETPSVPTHTSLS
MESTRKPQPPQHLGLYQVGGKGHAPPQAPRFNPITVTLAPNTGRNTPTSLHIHGGPQSGLNSPNSI
YIRPYVTQPGSTRQVQCRAQYSPTSQPAQQIYQITHPAAPQSSWSQHQTSHVYMPISPNTQAPSIP
SAVASQAVSSSPLPSSGSSFSQYNIQNISTGPRKNQIEIKLESPQRGSGSSSLLRSSSAPRSACSSTSSSC
PSSCTSLASSSGSSTPISIGGAGLSRSQPTVYISPSPPTAATAPSECAVPNTPRSQPKIYFSANTSADDG
GGRNPPTVYISANPALQGPAGLRALGSQMSMGPAYIHHHPPKSRPSVGAGGTATSPRVVVTQPNT
KYTFKITVSPNKPPSVSPGVVSPTFEPNNMLSLPADHYAEEISQPDPMRDKAVEPRRLSMGADDAA

YTQALLVHQRARMERLWHELELKKRKLEKLKEEVNEMESDLTRRRLQRSNAFCQIPSIEEMQQLRCK
NRLLQIDIDCLTKEIDLLQTRGPDFNPIAINFYDLGFLGPVPPKPLKGPTKAEVSRTDAGVRVLSEPEED
DGVQWSCTACTFLNHPALNRCEECEFPRNF

>ZFIN|ZDB-GENE-060503-408 symbol:tab3 species:7955 "Danio rerio" InterPro:IPR001876 InterPro:IPR003892 Pfam:PF02845 PROSITE:PS01358 PROSITE:PS50199 SMART:SM00547 ZFIN:ZDB-GENE-060503-408 GO:GO:0005622 GO:GO:0008270 EMBL:BX247907 GeneTree:ENSGT00530000063642 HOVERGEN:HBG056952 CTD:257397 OMA:QGPVPHY KO:K12793 IPI:IPI00609738 RefSeq:NP_001038570.1 UniGene:Dr.82674 ProteinModelPortal:Q1LY04 SMR:Q1LY04 STRING:Q1LY04 GeneID:566547 KEGG:dre:566547 InParanoid:Q1LY04 Bgee:Q1LY04 Uniprot:Q1LY04

MMAQGGPQLDYQILQDLRQRFPEIPETVVSQYLLQNNNNADLCYHLLAQESNRYLYEEYHSPDDL
HLNRNHMLRISVGYPVPDGVKNNPGGRALVHSSSDGHIEHPRSGFSEPLSAPATMAPSPGYNFKTD
QSRSNIPTPPPSIPGMSPTYHPVSRYMTPITVTLSQNMPSAPQALQIPPGTYCTSGNTVYMRPSPSQ
SPQPTPWSTSGTSMYQQSPYATPTYQSPYSSPQHQVQQPPQVFLPISPPTLPGLSQTPVSQRPFISS
KGPMKNQIEITLEGQRPRSNSPVHTPQGALYMATSPSPSSPSRAISMAGPPGASIHQGMYAHQAV
ARPRPTSSPQPAPSAFIKIKVSPRQVQGSSNSPPVETESLLNIVDQGERGAPPILPISALPGSIANQINC
MPRRSSSGSDDYAYTQALLLHQRARMERLMKELMLERQKLDQLKAEVNEMEFDALQRRFRRVNS
TSLIPRPEEMTKIRSQNRQLQIDIDCTLKETDLLQSRGKFDRTMNFYDNIQPGPVVPPRAKPTAVQR
DEDFEGAQWNCESCTFLNHPALHRCEQCEMPRNT

>ZFIN|ZDB-GENE-070626-2 symbol:mark1 species:7955 "Danio rerio" InterPro:IPR000719 InterPro:IPR001772 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 Pfam:PF02149 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 PROSITE:PS50032 SMART:SM00220 InterPro:IPR017442 ZFIN:ZDB-GENE-070626-2 GO:GO:0005524 SUPFAM:SSF56112 GO:GO:0004674 InterPro:IPR015940 SMART:SM00165 PROSITE:PS50030 Gene3D:G3DSA:3.30.310.80 SUPFAM:SSF103243 CTD:4139 HOVERGEN:HBG052453 KO:K08798 EMBL:BC155559 IPI:IPI00495094 RefSeq:NP_001107948.1 UniGene:Dr.80328 UniGene:Dr.89844 ProteinModelPortal:A9JR88 SMR:A9JR88 GeneID:100003170 KEGG:dre:100003170 eggNOG:veNOG12734 Uniprot:A9JR88

MSTRTPLPTVNERDAENHTSVDGYTDTPAAPTKSSSRQSLPRSRNSVASITDEQPHVGNYRLLKTIG
KGNFAKVKLARHVLTGREVAVKIIDKTQLNPTSLQKLFREVRIMKVLNHPNIVKLFEVIEKTLYLIMEYA
SGGEVFDYLVAHGRMKEKEARAKFRQIVSAVQYCHQKRIVHRDLKAENLLLDADMNIKIADFGFSN
EFTLGSKLDTFCGSPPYAAPELFQGKKYDGPEVDVWSLGVILYTLVSGSLPFDGQNLKELRERVLRGK
YRIPFYMSTDCENLKLLVLNPGKRGSLEQIMKDHWINVGHEEEELKPYTEPEPDFSDTKRIELMITMG
FPKDEITEALVGQKYDEVMATYLLLGRKPPEFEGSDSLSTTNLCQRSRPSSDLNNSSSQSPAHSKVQR
SISAQQRRFSDHVAPSIPPAVSYTKRSQANSVEGEKKEEWDASRKLPSSSSKGDMAASPLAAQERRK
SSTASGNSAAGGMTRRNTYVCERSSTDRYSAIPNGKDSSLTEMSTSGSGTSSVSPGASALSSTPRVKS
MSASGHPNKSPLPPIEDNTEFKGSGSRAPSTSPSAHSISSMTPDRTRFPRGTSSRSTFHGAQLRDRRS
ATYNGPPASPTLSHDTGALAQARRGTSSGFISKLTSKFVRRSGSGEPKEDGRDKPRLRFTWSMKTTS
SLEPGDMMREIRKVLDANNCDYEQRERFLLFCVHGDARHDSLVQWEMEVCKLPRLSLNGVRFKRIS
GTSIAFKNIASKIANELKL

>ZFIN|ZDB-GENE-080220-11 symbol:mknk1 species:7955 "Danio rerio" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009

InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 ZFIN:ZDB-GENE-080220-11 GO:GO:0005524 SUPFAM:SSF56112 GO:GO:0004674 HOGENOM:HBG755340 InterPro:IPR020636 PANTHER:PTHR24347 GeneTree:ENSGT00550000074510 HOVERGEN:HBG106949 OrthoDB:EOG4GTKD2 EMBL:BC154477 IPI:IPI00614231 UniGene:Dr.99488 ProteinModelPortal:A8WFW0 SMR:A8WFW0 STRING:A8WFW0 eggNOG:fiNOG09894 Bgee:A8WFW0 Uniprot:A8WFW0

MESSQPISITDPNSRRKKKRRRAGDSFTGKFCDLYRLTDELLGQGAYAKVQGCVSLQNGTEYAVKIIE
KNAGHSRSRVFREVETLYQCQGNKNILELIQFFEDDSCFYLVFEKLRGGSILTHIQSRKDEREASRVVR
DIANALDFLHNKGIAHRDLKPENILCEYTDKVSPVKICDFDLGSGVKLNSACTPITTPELTTPCGSAEY
MAPEVVEVFTDEASFYDKRCDLWSLGVILYILLSGSPPFTGHCGTNCWRGETCRSCQNNLFERIQEG
KYEFSNGVWTQISADAKDLISRLLVRDATLRLSAAQVLQHPWVQGNAPERVLPTPRVLQRNCSTKD
LTQFAAEAIAFNRQLSQQEEEQEDFGAVVCSMRLSPPSNSLARRAQSQALRNNT

>DICTYBASE|DDB_G0269152 symbol:mekA species:44689 "Dictyostelium discoideum" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 dictyBase:DDB_G0269152 GO:GO:0005524 GO:GO:0005634 GO:GO:0005737 EMBL:AAFI02000005 GenomeReviews:CM000150_GR GO:GO:0046872 SUPFAM:SSF56112 GO:GO:0004674 GO:GO:0006935 KO:K00924 GeneTree:EPrGT00050000001059 GO:GO:0031152 eggNOG:KOG0581 EMBL:U87912 RefSeq:XP_646465.1 HSSP:P36507 ProteinModelPortal:Q55CL6 EnsemblProtists:DDB0191164 GeneID:8617426 KEGG:ddi:DDB_G0269152 InParanoid:Q55CL6 OMA:TILECAI PhylomeDB:Q55CL6 Uniprot:Q55CL6

MNTNTNTNTNISSSGNNIINTPTTNNNNKNNNNNNNNNNNSNNSNNNSSNNNNNNNNAVGV
KTGKKVNLKVETPVQNNENSYSLTTSGTFKEGDLLINKKGLLIKGESPKNSSVNDRNKNKSLHSNLQL
LASPTSSESMDFNQGFYNNNNNNNNNNNNNNLNNFNNLMNNGIDSPQLSGISISTPTSSHSFNN
TFTNYYNNNNNYNNYNNNNNSNNNNNNYNNSNNNFNNFNNYNNYGNNNNFNNFNALQSSSS
FDISSSGSSNNYLNNSANNHPHYDTNLSYDLKDLKIIRVLGRGAGGVVKLAYHETSGTYIALKVITLDI
QENIRKQIILELKTLHKTSYPYIVSFYDAFYTEGSIFIALEFMELGSLSDIMKKTSIPPVLGKIAFQVLQGL
VYLHRKLHLIHRDIKPSNILVNNKGEAKIADFGVSGQLQHTLSKAVTWVGTVTYMSPERISGRSYSFD
SEIWSLGLTILECAIGKFPYGSNLPHQQQQPLQQQQQQQQQQQPLQQQQQQQQQQQPLQLQL
QNLDINNSNNNIRNSNNNNNNNNNNNNNNNNNNNNNNVLDISNGGLVDSGSSVPEGMGFWVL
LDCIVKEEVPILPSTFSKEFRSFISECLQKEPTERPTASNLLNHEVKKYNFNVEKWTANLKQQQ

>DICTYBASE|DDB_G0283903 symbol:erkB species:44689 "Dictyostelium discoideum" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008271 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 dictyBase:DDB_G0283903 GO:GO:0005829 GO:GO:0005524 GO:GO:0005515 GO:GO:0007067 GenomeReviews:CM000153_GR GO:GO:0051301 GO:GO:0019933 SUPFAM:SSF56112 GO:GO:0007190 GO:GO:0030819 HOGENOM:HBG755340 GO:GO:0006935 GO:GO:0051344 GO:GO:0031152 EMBL:AAFI02000058 GeneTree:EPrGT00050000000232 HSSP:P24941 GO:GO:0004707 eggNOG:KOG0660 EMBL:L33043 PIR:A56492 RefSeq:XP_638833.1

ProteinModelPortal:Q54QB1 IntAct:Q54QB1 PRIDE:Q54QB1 EnsemblProtists:DDB0191457 GeneID:8624357 KEGG:ddi:DDB_G0283903 OMA:REIMFLH PhylomeDB:Q54QB1 ProtClustDB:CLSZ2728958 KO:K08293 Uniprot:Q54QB1

MSSEDIDKHVLRKYEVLQKIGKGAYGIVWKAIDKKTKQTVALKKIFDAFQNATDAQRTFREIMFLQE
LHGHENIIKLLNVIKADNDRDIYLVFEHMETDLHAVIRAKILEEIHKQYTIYQLLKALKYSANVLHRDIKP
SNLLLNSECLVKVADFGLARSITSLESIAEANPVLTEYVATRWYRAPEILLGSTKYTKGVDMWSIGCIL
GELLGEKAMFPGNSTMNQLDLIIEVTGRPSAEDIEAIKSPFAGTMLSPPSNPRSLSDMYPSASVDAL
DLLKKLLQFNPDKRITAEEALAHPFVTQFHNPAEEPHFDRIIKISIDDGQKFPIAEYRNRLYNDIIKKKKE
ERKKQTNPTKPDTTAPTLST

>DICTYBASE|DDB_G0286353 symbol:erkA species:44689 "Dictyostelium discoideum" InterPro:IPR000719 InterPro:IPR002290 InterPro:IPR003527 InterPro:IPR008271 InterPro:IPR008352 InterPro:IPR011009 InterPro:IPR017441 Pfam:PF00069 PRINTS:PR01773 PROSITE:PS00107 PROSITE:PS00108 PROSITE:PS01351 PROSITE:PS50011 SMART:SM00220 InterPro:IPR017442 dictyBase:DDB_G0286353 GO:GO:0005524 GO:GO:0007067 GenomeReviews:CM000153_GR GO:GO:0051301 SUPFAM:SSF56112 HOGENOM:HBG755340 GO:GO:0030587 EMBL:AAFI02000085 GeneTree:EPrGT00050000000232 BRENDA:2.7.11.24 GO:GO:0004707 KO:K04371 EMBL:U11077 PIR:A56042 RefSeq:XP_637704.1 ProteinModelPortal:P42525 SMR:P42525 EnsemblProtists:DDB0201635 GeneID:8625569 KEGG:ddi:DDB_G0286353 eggNOG:KOG0660 OMA:LRRAFWD PhylomeDB:P42525 Uniprot:P42525

MEPEFDHFQSQMDSDNTHQSTMFNVQDNNAILMSGMENVLQSPRQLQAAAQAQQQAAAQA
QQQQVQAQQVQAQQAQQQQQQQQNQQQQQQQQNQQNQQQQQNQQQQSQQMTQQQL
QQLMPPPPTSDTFNDNISYFVYGSQFTVPRRYSIVKCIGHGAYGVVCSAKDNLTGEKVAIKKISKAFD
NLKDTKRTLREIHLLRHFKHENLISIKDILKPNSKEQFEDVYIVSELMDTDLHQIITSPQPLSDDHCQYFY
MLRGLKHIHSANVLHRDLKPSNLLINEDCLLKICDLGLARVEDATHQGFMTEYVATRWYRAPEVILS
WNKYTKAIDIWSVGCIFAELLGRKPLFQGKDYIHQITLIIETIGSPSEEDICNIANEQRQIRNMGNQPK
VNFANMFPKANPDAIDLLERMLYFDPSKRLTVEEALAHPYFQSLHDPSDEPICLHKFSLNFEAWDLN
RDLLKELIYNEMLAYHPEDPQAPYYTDLNNPNFNLSRIQSSSELFNLLQQKQIHQQVNQQSIKN

Appendix III. Setup parameters for proteomic analysis using the software SIEVE v1.3.

Parameters	Value
Alignment	
Tile increment	150
Tile maximum	300
Tile size	300
Tile threshold	0.6
Framing	
Maximum frames	35000
Mz start	360 Da
Mz stop	1800 Da
MZwidth	0.02 Da
PRMaxCharge	5
RTstart	20 min
RTstop	61 min
Threshold	1000

Appendix IV. Target in-house-built metabolite library

Monoisotopic mass	Metabolite identity	Molecular Formula
72.0211	Methylglyoxal	$C_3H_4O_2$
74.0004	Glyoxylate	$C_2H_2O_3$
74.0844	1,3-Diaminopropane	$C_3H_{10}N_2$
75.032	Glycine	$C_2H_5NO_2$
75.0684	(R)-1-Aminopropan-2-ol	C_3H_9NO
87.032	Dehydroalanine	$C_3H_5NO_2$
87.0684	4-Aminobutyraldehyde	C_4H_9NO
88.0160	Pyruvate	$C_3H_4O_3$
88.0524	acetoin	$C_4H_8O_2$
88.1000	Putrescine	$C_4H_{12}N_2$
90.0317	D-glyceraldehyde	$C_3H_6O_3$
104.0222	Urea-1-carboxylate	$C_2H_4N_2O_3$
117.0426	L-2-Amino-3-oxobutanoic acid ; L-Aspartic 4-semialdehyde	$C_4H_7NO_3$
102.0317	(S)-Methylmalonatesemialdehyde ; 2-Oxobutanoate ; Acetoacetate	$C_4H_6O_3$
103.0633	(S)-3-amino-2-methylpropanoate ; 4-Aminobutanoate ; Dimethylglycine	$C_4H_9NO_2$
104.0109	Hydroxypyruvate	$C_3H_4O_4$
106.0266	D-Glycerate	$C_3H_6O_4$
113.0477	(S)-1-Pyrroline-5-carboxylate	$C_5H_7NO_2$
116.0109	Fumarate	$C_4H_4O_4$

116.0473	3-Methyl-2-oxobutanoic acid	$C_5H_8O_3$
117.0578	Indole	C_8H_7N
118.0266	Methylmalonate ; Succinic acid	$C_4H_6O_4$
1187.8257	Trichopolyn	$C_{61}H_{109}N_{11}O_{12}$
119.9881	Mercaptopyruvate	$C_3H_4O_3S$
120.0059	2-hydroxymalonic acid	$C_3H_4O_5$
120.0245	3-(Methylthio) propionic acid	$C_4H_8O_2S$
122.0367	p-Toluquinone	$C_7H_6O_2$
122.0731	2-phenylethanol	$C_8H_{10}O$
124.0524	Toluquinol	$C_7H_8O_2$
128.1201	1-octen-3-ol ; 3-Octanon	$C_8H_{16}O$
129.079	N4-Acetylaminobutanal	$C_6H_{11}NO_2$
130.1106	N-Acetylputrescine	$C_6H_{14}N_2O$
131.0219	2-Oxosuccinamate	$C_4H_5NO_4$
131.0582	5-Amino-2-oxopentanoic acid; 5-Aminolevulinate; cis-4-Hydroxy-D-proline; L-Glutamate-5-semialdehyde	$C_5H_9NO_3$
131.1059	N-Carbamoylputrescine	$C_5H_{13}N_3O$
131.1422	Norspermidine	$C_6H_{17}N_3$
132.0059	Oxaloacetate	$C_4H_4O_5$
132.0899	L-Ornithine	$C_5H_{12}N_2O_2$
134.0731	Chroman	$C_9H_{10}O$
136.0524	2,5-Dimethylquinone ; phenylacetate	$C_8H_8O_2$
138.0317	4-Hydroxybenzoate	$C_7H_6O_3$
139.9875	Acetylphosphate	$C_2H_5O_5P$

140.9827	Carbamoyl phosphate	CH_4NO_5P
142.0742	Ectoine	$C_6H_{10}N_2O_2$
144.0422	Pentenomycin I	$C_6H_8O_4$
145.0375	4-Oxoglutaramate	$C_5H_7NO_4$
145.1579	Spermidine	$C_7H_{19}N_3$
146.0215	2-Oxoglutarate	$C_5H_6O_5$
146.0579	2-Dehydropantoate	$C_6H_{10}O_4$
146.0691	L-Glutamine	$C_5H_{10}N_2O_3$
147.0532	2-Oxo-4-hydroxy-5-aminovalerate; Glutamic acid; L-4-Hydroxyglutamatesemialdehyde; O-Acetyl-L-serine	$C_5H_9NO_4$
148.0194	4-Methylthio-2-oxobutanoic acid	$C_5H_8O_3S$
149.0324	L-threo-3-hydroxyaspartate	$C_4H_7NO_5$
149.0476	homothallin II	$C_8H_7NO_2$
150.0528	a-D-xylose; a-L-arabinofuranose; beta-D-ribofuranose; beta-D-xylopyranose	$C_5H_{10}O_5$
152.0334	Xanthine	$C_5H_4N_4O_2$
152.0473	mandelic acid;2-hydroxy-2-phenylacetic acid	$C_8H_8O_3$
154.0266	Gigantin; Patulin	$C_7H_6O_4$
154.0378	Imidazol-5-yl-pyruvate	$C_6H_6N_2O_3$
154.11061	Loline;Festuline	$C_8H_{14}N_2O$
156.0422	Epoxydon	$C_7H_8O_4$
158.0691	5-Hydroxyectoine	$C_6H_{10}N_2O_3$
158.1307	nonanoic acid	$C_9H_{18}O_2$
160.0372	2-Oxoadipate	$C_6H_8O_5$
160.0848	N-gamma-Acetyldiaminobutyrate	$C_6H_{12}N_2O_3$

161.0324	N-Formyl-L-aspartate	$C_5H_7NO_5$
161.0688	L-2-Aminoadipate; O-Acetyl-L-homoserine	$C_6H_{11}NO_4$
163.0633	3-(3-isocyanocyclopent-2-enylidene) propionic acid	$C_9H_9NO_2$
164.0473	4-Coumarate; Phenylpyruvate	$C_9H_8O_3$
164.0685	L-rhamnofuranose	$C_6H_{12}O_5$
164.0837	Ethyl 2-phenylacetate	$C_{10}H_{12}O_2$
166.0491	3-Methylxanthine	$C_6H_6N_4O_2$
166.0993	6-pentyl-2H-pyran-2-one	$C_{10}H_{14}O_2$
167.9729	3-Sulfopyruvate	$C_3H_4O_6S$
167.9824	Phosphoenolpyruvate	$C_3H_5O_6P$
168.0423	Homogentisic acid ; p-Vanillic acid	$C_8H_8O_4$
168.115	Massoilactone	$C_{10}H_{16}O_2$
169.998	D-glyceraldehyde-3-phosphate	$C_3H_7O_6P$
173.0688	N-Acetyl-L-glutamate-5-semialdehyde	$C_7H_{11}NO_4$
173.1051	Swainsonine	$C_8H_{15}NO_3$
174.0528	Shikimate	$C_7H_{10}O_5$
174.0641	N-Formimino-L-glutamate	$C_6H_{10}N_2O_4$
175.0481	N-Formyl-L-glutamate	$C_6H_9NO_5$
175.1321	Carboxynorspermidine	$C_7H_{17}N_3O_2$
176.0433	N-Carbamoyl-L-aspartate	$C_5H_8N_2O_5$
178.0477	3-keto-b-D-galactose	$C_6H_{10}O_6$
179.0582	dermadin	$C_9H_9NO_3$
180.0423	4-hydroxyphenylpyruvate	$C_9H_8O_4$
180.0456	5-Methylthio-D-ribose	$C_6H_{12}O_4S$

180.0634	D-galactose; D-glucose; D-fructofuranose; L-sorbose	$C_6H_{12}O_6$
180.0786	Clavatol	$C_{10}H_{12}O_3$
182.079	D-galactitol; L-iditol ; Mannitol	$C_6H_{14}O_6$
182.1671	Geosmin	$C_{12}H_{22}O$
183.0532	trichoviridin	$C_8H_9NO_4$
184.1463	Chokol G	$C_{11}H_{20}O_2$
185.0089	O-Phospho-L-serine	$C_3H_8NO_6P$
185.9929	2-Phospho-D-glycerate	$C_3H_7O_7P$
186.0528	Pentenomycin II	$C_8H_{10}O_5$
189.0637	L-2-Amino-6-oxoheptanedioate; N-Acetyl-L-glutamate	$C_7H_{11}NO_5$
189.0823	S-prenyl-L-cysteine	$C_8H_{15}NO_2S$
192.0786	Harzialactone A	$C_{11}H_{12}O_3$
194.0579	Ferulic acid	$C_{10}H_{10}O_4$
196.1211	N-Acetylloline ; cyclo(S-Pro-S-Val)	$C_{10}H_{16}N_2O_2$
197.0688	L-dopa; N-hydroxy-L-tyrosine	$C_9H_{11}NO_4$
197.1164	Hercynine	$C_9H_{15}N_3O_2$
198.1368	Slaframine	$C_{10}H_{18}N_2O_2$
198.1619	ChokolA	$C_{12}H_{22}O_2$
199.0246	O-Phospho-L-homoserine	$C_4H_{10}NO_6P$
200.0086	D-Erythrose-4-phosphate	$C_4H_9O_7P$
200.9766	S-Sulfo-L-cysteine	$C_3H_7NO_5S_2$
202.1106	Nb-acetyltryptamine	$C_{12}H_{14}N_2O$
202.2157	Spermine	$C_{10}H_{26}N_4$
204.0899	L-tryptophan	$C_{11}H_{12}N_2O_2$

204.1878	Valencene	$C_{15}H_{24}$
206.0427	Homocitrate	$C_7H_{10}O_7$
208.0848	Kynurenine	$C_{10}H_{12}N_2O_3$
210.1368	cyclo(S-Pro-S-Leu)	$C_{11}H_{18}N_2O_2$
211.0481	betalamate	$C_9H_9NO_5$
212.1201	Acorenone	$C_{15}H_{16}O$
213.0038	L-aspartyl-4-phosphate	$C_4H_8NO_7P$
213.0637	N,N-dihydroxy-L-tyrosine	$C_9H_{11}NO_5$
214.0242	1-deoxy-D-xylulose-5-phosphate	$C_5H_{11}O_7P$
216.111	gamma-Glutamyl-gamma-aminobutyraldehyde	$C_9H_{16}N_2O_4$
217.1426	g-L-Glutamylputrescine	$C_9H_{19}N_3O_3$
219.0743	O-Succinyl-L-homoserine	$C_8H_{13}NO_6$
219.0769	N-hydroxy-L-tryptophan	$C_{11}H_{11}N_2O_3$
219.1107	Pantothenate	$C_9H_{17}NO_5$
221.0899	N-acetyl-D-glucosamine	$C_8H_{15}NO_6$
221.0908	8-methylthiooctylhydroximate	$C_9H_{19}NOS_2$
222.0528	2-Succinylbenzoate	$C_{11}H_{10}O_5$
222.0674	L-Cystathionine	$C_7H_{14}N_2O_4S$
222.0892	ferulic acid, ethyl ester	$C_{12}H_{14}O_4$
226.0993	benzyl 2-phenylacetate	$C_{15}H_{14}O_2$
227.0195	L-Glutamyl 5-phosphate	$C_5H_{10}NO_7P$
227.0794	L-Arogenate	$C_{10}H_{13}NO_5$
228.0399	(R)-4-Phosphopantoate	$C_6H_{13}O_7P$
229.0884	Ergothioneine	$C_9H_{15}N_3O_2S$

230.0192	a-D-xylose-1-phosphate; b-D-arabinose-1-phosphate; D-ribose-5-phosphate; D-xylulose-5-phosphate	$C_5H_{11}O_8P$
231.0743	N-Acetyl-L-2-amino-6-oxopimelate; N-Succinyl-L-glutamate 5-semialdehyde	$C_9H_{13}NO_6$
232.1059	N2-succinyl-L-ornithine; N6-Acetyl-LL-2,6-diaminoheptanedioate	$C_9H_{16}N_2O_5$
232.1099	Sorbicillin	$C_{14}H_{16}O_3$
232.1211	Melatonin; Melatonine; N-Acetyl-5-methoxytryptamine	$C_{13}H_{16}N_2O_2$
232.14633	Botrydienal	$C_{15}H_{20}O_2$
234.0892	Pyrenochaetic acid A	$C_{13}H_{14}O_4$
234.1368	p-Coumaroylputrescine	$C_{13}H_{18}N_2O_2$
235.1895	Hypusine	$C_{10}H_{25}N_3O_3$
236.1048	Pyrenochaetic acid C	$C_{13}H_{16}O_4$
238.1469	Agroclavine; Lysergine	$C_{16}H_{18}N_2$
238.1932	Chokol B; Chokol C; Chokol D	$C_{15}H_{26}O_2$
240.0238	L-Cystine	$C_6H_{12}N_2O_4S_2$
240.115	2-phenylethyl 2-phenylacetate	$C_{16}H_{16}O_2$
240.1626	Pyroclavine	$C_{16}H_{20}N_2$
240.1725	Chokol F	$C_{14}H_{24}O_3$
240.2089	Cyclonerodiol	$C_{15}H_{28}O_2$
242.0192	6-Deoxy-5-ketofructose-1-phosphate	$C_6H_{11}O_8P$
243.0855	gamma-Glutamyl-beta-cyanoalanine	$C_9H_{13}N_3O_5$
246.1328	D-Octopine	$C_9H_{18}N_4O_4$
246.1619	Geranylhydroquinone	$C_{16}H_{22}O_2$
247.0692	N-Succinyl-L-glutamate	$C_9H_{13}NO_7$

247.1056	Linamarin	$C_{10}H_{17}NO_6$
247.1433	Peramine	$C_{12}H_{17}N_5O$
248.1048	Pyriculariol	$C_{14}H_{16}O_4$
250.0623	L-gamma-glutamylcysteine	$C_8H_{14}N_2O_5S$
250.0841	Paecilospirone	$C_{13}H_{14}O_5$
250.1568	Roridan C; Trichodermol	$C_{15}H_{22}O_3$
252.0997	Pyrenochaetic acid B	$C_{13}H_{16}O_5$
252.1725	Arthrosporone	$C_{15}H_{24}O_3$
254.0192	Shikimate-3-phosphate	$C_7H_{11}O_8P$
254.078	L-Arginine phosphate	$C_6H_{15}N_4O_5P$
254.1419	Lysergol	$C_{16}H_{18}N_2O$
256.0736	Emodin anthrone	$C_{15}H_{12}O_4$
256.1575	Chanoclavine-I	$C_{16}H_{20}N_2O$
256.2038	Chokol E	$C_{15}H_{28}O_3$
258.0528	Alternariol	$C_{14}H_{10}O_5$
259.0457	D-Glucosamine-6-phosphate	$C_6H_{14}NO_8P$
259.1168	Linatine	$C_{10}H_{17}N_3O_5$
259.1208	Ampullicin	$C_{15}H_{17}NO_3$
260.0119	5-methylthioribulose-1-phosphate	$C_6H_{13}O_7PS$
260.0119	S-Methyl-5-thio-D-ribose-1-phosphate	$C_6H_{13}O_7PS$
260.0297	D-galactose-1-phosphate; D-mannose-1-phosphate; D-glucose-1-phosphate; D-fructose-1-phosphate; D-hexose-6-phosphate	$C_6H_{13}O_9P$
261.101	Carboxyspermidine	$C_8H_{21}Cl_2N_3O_2$
261.1212	Lotaustralin	$C_{11}H_{19}NO6$

262.0453	D-mannitol-1-phosphate; D-sorbitol-6-phosphate	$C_6H_{15}O_9P$
262.1205	Harziphilone	$C_{15}H_{18}O_4$
264.1362	Trichothecolone ; Alliacol A/B	$C_{15}H_{20}O_4$
264.1474	Feruloylputrescine	$C_{14}H_{20}N_2O_3$
266.1518	7-a-Hydroxytrichodermol ; Verrucarol ; Alliacolide	$C_{15}H_{22}O_4$
267.0777	S-Ribosyl-L-homocysteine	$C_9H_{17}NO_6S$
269.0301	N-acetylglutamyl-phosphate	$C_7H_{12}NO_8P$
269.0449	Emodin	$C_{15}H_9O_5$
270.1368	Penniclavine	$C_{16}H_{18}N_2O_2$
272.1525	4-L-DMAT	$C_{16}H_{20}N_2O_2$
274.0477	Altenuisol	$C_{14}H_{10}O_6$
274.1277	N2-Succinyl-L-arginine	$C_{10}H_{18}N_4O_5$
274.1569	Geranyl-hydroxybenzoate	$C_{17}H_{22}O_3$
274.1932	1-Menthyl phenylacetate	$C_{18}H_{26}O_2$
275.1117	N-Succinyl-L-citrulline	$C_{10}H_{17}N_3O_6$
276.0633	Norjavanicin	$C_{14}H_{12}O_6$
276.1321	Saccharopine	$C_{11}H_{20}N_2O_6$
280.131	Heptelidic acid	$C_{15}H_{20}O_5$
281.1263	Harzianopyridone	$C_{14}H_{19}NO_5$
282.0951	Xylobiose	$C_{10}H_{18}O_9$
284.1623	Botryaloic acid	$C_{15}H_{24}O_5$
286.0841	Aflatoxin D1; Dehydroherbarin	$C_{16}H_{14}O_5$
289.0798	N-Succinyl-2-L-amino-6-oxoheptanedioate	$C_{11}H_{15}NO_8$
290.1114	N-Succinyl-LL-2;6-diaminoheptanedioate	$C_{11}H_{18}N_2O_7$

290.1226	L-Argininosuccinate	$C_{10}H_{18}N_4O_6$
292.0946	Altenuene	$C_{15}H_{16}O_6$
292.16746	Trichodermin	$C_{17}H_{24}O_4$
296.1259	Deoxynivalenol	$C_{15}H_{20}O_6$
298.0477	Aflatoxin P1	$C_{16}H_{10}O_6$
298.0841	Trichoflectin	$C_{17}H_{14}O_5$
298.1681	Fumigaclavine A	$C_{18}H_{22}N_2O_2$
299.077	D-4'-Phosphopantothenate	$C_9H_{18}NO_8P$
300.1936	Achaetolide	$C_{16}H_{28}O_5$
301.0563	N-acetyl-D-glucosamine-6-phosphate	$C_8H_{16}NO_9P$
302.1742	Aurantiamine	$C_{16}H_{22}N_4O_2$
302.2245	6-Hydroxydolaballa-3.8.12-trien-14-one	$C_{20}H_{30}O_2$
304.0946	Herbarin	$C_{16}H_{16}O_6$
306.0739	Fusarubin; Oxyjavanicin	$C_{15}H_{14}O_7$
307.0838	Glutathione	$C_{10}H_{17}N_3O_6S$
308.0896	Dihydrofusarubin	$C_{15}H_{16}O_7$
310.0477	Sterigmatin	$C_{17}H_{10}O_6$
310.178	Botrydial	$C_{17}H_{26}O_5$
312.0633	Aflatoxin B; Dihydrodemethylsterigmatocystin ; BE 23372M	$C_{17}H_{12}O_6$
312.1209	Nivalenol	$C_{15}H_{20}O_7$
312.1936	Dihydrobotrydial	$C_{17}H_{28}O_5$
314.0684	Geranyldiphosphate	$C_{10}H_{20}O_7P_2$
314.079	Aflatoxicol Ro ; Aflatoxicol B; aflatoxin B2	$C_{17}H_{14}O_6$
316.1885	Achaetolidone	$C_{16}H_{28}O_6$

318.1579	Phomamide	$C_{17}H_{22}N_2O_4$
318.2194	3,4-Epoxy-6-hyroxy-dolabella-7,12-diene-one ; Cyathin A3	$C_{20}H_{30}O_3$
321.1477	Neoechinulin B	$C_{19}H_{19}N_3O_2$
322.0688	Altenuic acid	$C_{15}H_{14}O_8$
322.0841	Desmethoxyviridin	$C_{19}H_{14}O_5$
323.1368	Acremoauxin A	$C_{16}H_{21}NO_6$
323.1633	NeoechinulinA	$C_{19}H_{21}N_3O_2$
324.0633	Sterigmatocystin	$C_{18}H_{12}O_6$
324.0997	Desmethoxyviridiol	$C_{19}H_{16}O_5$
326.0394	Gliotoxin	$C_{13}H_{14}N_2O_4S_2$
326.1729	Botryaloic Acid Acetate	$C_{17}H_{26}O_6$
328.0583	Aflatoxin Q1; Aflatoxin G1; Aflatoxin M1	$C_{17}H_{12}O_7$
328.1885	Botryoloic Acid	$C_{17}H_{28}O_6$
330.0739	Aflatoxin G2; Aflatoxin M2	$C_{17}H_{14}O_7$
332.0896	Rhizoctonic acid	$C_{17}H_{16}O_7$
332.1624	Trichothecin	$C_{19}H_{24}O_5$
335.1329	N4-(acetyl-beta-D-glucosaminyl) asparagine	$C_{12}H_{21}N_3O_8$
338.0426	Versicolorin A	$C_{18}H_{10}O_7$
338.1366	15-O-Acetyl-4-deoxynivalenol	$C_{17}H_{22}O_7$
339.996	Fructose-2,6-bisphosphate	$C_6H_{14}O_{12}P_2$
340.0583	Versicolorin B;Versicolorin C	$C_{18}H_{12}O_7$
340.1006	3-Ketolactose	$C_{12}H_{20}O_{11}$
342.1162	a-D-mannosyl-(1-6)-D-mannose;galactinol;lactose;maltose;melibiose;sucrose;trehalose	$C_{12}H_{22}O_{11}$

348.111	Camptothecin	$C_{20}H_{16}N_2O_4$
350.1729	4,15-Diacetylverrucarol	$C_{19}H_{26}O_6$
352.0946	Viridin	$C_{20}H_{16}O_6$
354.1103	Viridiol	$C_{20}H_{18}O_6$
357.0995	Deacetoxycephalosporin C	$C_{14}H_{19}N_3O_6S$
358.0688	Versiconal	$C_{18}H_{14}O_8$
360.0845	Versiconol	$C_{18}H_{16}O_8$
360.1321	Betaxanthin	$C_{18}H_{20}N_2O_6$
360.23005	Dihydrosorgoleone	$C_{22}H_{32}O_4$
363.1464	delta-(L-2-Aminoadipyl)-L-cysteinyl-D-valine	$C_{14}H_{25}N_3O_6S$
365.1838	Harzianic acid	$C_{19}H_{27}NO_6$
366.2307	Fumigaclavine C	$C_{23}H_{30}N_2O_2$
373.0944	Deacetylcephalosporin C	$C_{14}H_{19}N_3O_7S$
382.1991	T-2 Triol	$C_{20}H_{30}O_7$
384.0845	1'-Hydroxyversicolorone	$C_{20}H_{16}O_8$
384.0977	S-inosyl-L-homocysteine	$C_{14}H_{18}N_5O_6S$
384.1216	S-Adenosyl-L-homocysteine	$C_{14}H_{20}N_6O_5S$
385.2253	Spirodihydrobenzofuranlactam 1	$C_{23}H_{31}NO_4$
386.2093	Stachybotrylactone	$C_{23}H_{30}O_5$
386.2457	Atrarone D/E	$C_{24}H_{34}O_4$
388.2249	L671 776	$C_{23}H_{32}O_5$
389.2103	Isoechinulin B	$C_{24}H_{27}N_3O_2$
389.9518	5-phosphoribosyl-1-pyrophosphate	$C_5H_{13}O_{14}P_3$
391.1895	Neoechinulin	$C_{23}H_{25}N_3O_3$

391.2259	Isoechinulin A	$C_{24}H_{29}N_3O_2$
396.3392	3-Keto-4-methylzymosterol ; 5,7,24(28)-Ergostatrienol ; 5-Dehydroepisterol ; Ergosterol ; Vitamin D2 ; Lichesterol	$C_{28}H_{44}O$
398.3548	Fecosterol ; Ignosterol; 22.23-Dihydroergosterol; 4 alpha-Methylzymosterol ; 24-Methylenecholesterol ; Episterol	$C_{28}H_{46}O$
399.145	S-Adenosyl-L-methionine	$C_{15}H_{23}N_6O_5S$
400.0794	Versiconal hemiacetal acetate	$C_{20}H_{16}O_9$
400.1885	Harzianum A	$C_{23}H_{28}O_6$
400.3705	Campesterol; Fungisterol; Ergost-5-en-3b-ol	$C_{28}H_{48}O$
401.2202	Stachybotrin A	$C_{23}H_{31}NO_5$
402.0862	(R)-4-Phosphopantothenoyl-L-cysteine	$C_{12}H_{23}N_2O_9PS$
402.095	Versiconol acetate	$C_{20}H_{18}O_9$
402.1328	Tryptoquivaline F	$C_{22}H_{18}N_4O_4$
404.2198	Atranone J	$C_{23}H_{32}O_6$
404.2562	Monacolin K; Lovastatin	$C_{24}H_{36}O_5$
406.2719	Dolabellane diterpene	$C_{24}H_{38}O_5$
410.19407	Alternaric acid	$C_{21}H_{30}O_8$
414.0733	(7R)-7-(5-Carboxy-5-oxopentanoyl)aminocephalosporinate	$C_{16}H_{18}N_2O_9S$
414.0971	Cephalosporin C	$C_{16}H_{20}N_3O_8S$
416.1002	O-Carbamoyl-deacetylcephalosporin C	$C_{15}H_{20}N_4O_8S$
416.2198	Atrarone A/C	$C_{24}H_{32}O_6$
416.3654	gamma-Tocopherol	$C_{28}H_{48}O_2$
418.1277	Tryptoquivaline E	$C_{22}H_{18}N_4O_5$
420.0668	Sucrose-6-phosphate ; Trehalose 6-phosphate	$C_{12}H_{21}O_{14}P$
420.2148	Trichoverrol A/B	$C_{23}H_{32}O_7$

421.298	Aspernomine ; Paspaline	$C_{28}H_{39}NO_2$
422.0825	Trehalose 6-phosphate	$C_{12}H_{23}O_{14}P$
422.3548	Glochidone	$C_{30}H_{46}O$
424.2097	HT-2 Toxin	$C_{22}H_{32}O_8$
424.3705	Alnusenone	$C_{30}H_{48}O$
425.0449	Thiamindiphosphate	$C_{12}H_{19}N_4O_7P_2S$
426.0879	S-Glutathionyl-L-cysteine	$C_{13}H_{22}N_4O_8S_2$
426.3861	Lanosterol ; Friedelin ; Obtusifoliol ; Parkeol ; 24-Ethylidenelophenol ; Cycloartenol ; (S)-2,3-Epoxysqualene	$C_{30}H_{50}O$
428.1471	Wortmannin	$C_{23}H_{24}O_8$
428.329	Peroxyergosterol; Ergosterol-5,8-peroxide	$C_{28}H_{44}O_3$
428.4018	24,25-Dihydrolanosterol ; Epi-friedelinol	$C_{30}H_{52}O$
429.2515	Spirodihydrobenzofuranlactam 2	$C_{25}H_{35}NO_5$
430.3447	Cerevisterol	$C_{28}H_{46}O_3$
430.3811	alpha-Tocopherol	$C_{29}H_{50}O_2$
432.1168	Trichodermamide A	$C_{20}H_{20}N_2O_9$
432.2148	Atrarone F	$C_{24}H_{32}O_7$
434.2311	Glutathionylspermidine	$C_{17}H_{34}N_6O_5S$
437.2929	Dihydroxyaflavinine	$C_{28}H_{39}NO_3$
445.1709	Tetrahydrofolate	$C_{19}H_{23}N_7O_6$
446.2304	Atrarone B	$C_{25}H_{34}O_7$
448.2097	Atranone H	$C_{24}H_{32}O_8$
45.0215	Formamide	CH_3NO
450.0829	Trichodermamide B	$C_{20}H_{19}ClN_2O_8$

451.2722	Cytochalasin Opho ; Deacetylcytochalasin H	$C_{28}H_{37}NO_4$
458.3032	Ergokonin B	$C_{28}H_{42}O_5$
462.2253	Atranone G	$C_{25}H_{34}O_8$
465.2515	Zygosporin D	$C_{28}H_{35}NO_5$
466.2202	Insariotoxin (T-2 toxin)	$C_{24}H_{34}O_9$
469.2828	Cytochalasin S	$C_{28}H_{39}NO_5$
477.2515	1'-O-Acetylpaxilline ; Cytochalasin A	$C_{29}H_{35}NO_5$
477.2879	Cytochalasin	$C_{30}H_{39}NO_4$
479.2420	Fumitremorgin B; Lanosulin	$C_{27}H_{33}N_3O_5$
479.2671	Cytochalasin B; Phomin	$C_{29}H_{37}NO_5$
480.0661	Gliovirin	$C_{20}H_{20}N_2O_8S_2$
484.2097	Verrucarin J	$C_{27}H_{32}O_8$
488.1695	Tryptoquivalone	$C_{26}H_{24}N_4O_6$
490.1213	L-2-Aminoadipateadenylate	$C_{16}H_{23}N_6O_{10}P$
493.2828	Epoxycytochalasin H	$C_{30}H_{39}NO_5$
496.2097	Trichodimerol; Bisvertinolone	$C_{28}H_{32}O_8$
498.2253	Bisvertinol	$C_{28}H_{34}O_8$
500.2046	Verrucarin B	$C_{27}H_{32}O_9$
502.2202	Verrucarin A	$C_{27}H_{34}O_9$
504.169	Maltotriose ; Raffinose	$C_{18}H_{32}O_{16}$
508.2308	Acetyl-T-2 toxin	$C_{26}H_{36}O_{10}$
511.2318	Verruculogen	$C_{27}H_{33}N_3O_7$
511.2933	Cytochalasin Ppho	$C_{30}H_{41}NO_6$
512.2159	Raucaffricine	$C_{27}H_{32}N_2O_8$

512.241	Roridine H	$C_{29}H_{36}O_8$
512.2675	Chaetoglobosin J	$C_{32}H_{36}N_2O_4$
514.2566	Roridine E	$C_{29}H_{38}O_8$
514.3294	Officinalic acid	$C_{31}H_{46}O_6$
516.2008	Deoxynortryptoquivaline	$C_{28}H_{28}N_4O_6$
520.2474	Okaramine A	$C_{32}H_{32}N_4O_3$
523.257	19,20-Epoxycytochalasin Q	$C_{30}H_{37}NO_7$
528.2359	Satratoxin H	$C_{29}H_{36}O_9$
528.2624	Chaetoglobosin D	$C_{32}H_{36}N_2O_5$
530.2165	Deoxytryptoquivaline	$C_{29}H_{30}N_4O_6$
530.2515	Roridin L2 ; Hydroxy-Roridin E	$C_{29}H_{38}O_9$
530.278	Chaetoglobosin E ; Chaetoglobosin F	$C_{32}H_{38}N_2O_5$
530.2879	Stemphone	$C_{30}H_{42}O_8$
532.1958	Nortryptoquivaline; Tryptoquivaline D	$C_{28}H_{28}N_4O_7$
532.2672	Trichoverrin A/B ; Roridine A	$C_{29}H_{40}O_9$
532.3036	Cochlioquinone A	$C_{30}H_{44}O_8$
533.2638	Ergovaline	$C_{29}H_{35}N_5O_5$
534.1526	Cercosporin	$C_{29}H_{26}O_{10}$
542.2152	Satratoxin F	$C_{29}H_{34}O_{10}$
543.3559	Ergokonin C	$C_{32}H_{49}NO_6$
544.2308	Satratoxin G	$C_{29}H_{36}O_{10}$
545.2333	Dihydrozeatin-9-N-glucoside-O-glucoside	$C_{22}H_{35}N_5O_{11}$
546.1526	Hypocrellin ; Shiraiachrome A ; Shiraiachrome B	$C_{30}H_{26}O_{10}$
547.2795	Ergosinine	$C_{30}H_{37}N_5O_5$

548.0444	UDP-L-rhamnose	$C_{15}H_{22}N_2O_{16}P_2$
550.1434	Gomphrenin I ; Betanine	$C_{24}H_{26}N_2O_{13}$
552.4331	Cryptoxanthin	$C_{40}H_{56}O$
561.2951	Ergoptine	$C_{31}H_{39}N_5O_5$
564.0393	UDP-D-galactose	$C_{15}H_{22}N_2O_{17}P_2$
564.3967	Canthaxanthin	$C_{40}H_{52}O_2$
566.2529	Okaramine B	$C_{33}H_{34}N_4O_5$
568.428	Zeaxanthin	$C_{40}H_{56}O_2$
570.2729	19-O-Acetylchaetoglobosin B	$C_{34}H_{38}N_2O_6$
575.3107	alpha-Ergocryptine	$C_{32}H_{41}N_5O_5$
577.0108	UDP-D-glucuronate	$C_{15}H_{19}N_2O_{18}P_2$
581.2638	Ergotamin	$C_{33}H_{35}N_5O_5$
583.3297	Penitrem B	$C_{37}H_{45}NO_5$
584.2468	Citrafungin A	$C_{28}H_{40}O_{13}$
585.3454	Janthitrem B	$C_{37}H_{47}NO_5$
587.0665	Adenosine diphosphoglucose	$C_{16}H_{23}N_5O_{15}P_2$
595.2794	Ergostinine	$C_{34}H_{37}N_5O_5$
596.3866	Astaxanthin	$C_{40}H_{52}O_4$
601.2958	Penitrem C	$C_{37}H_{44}ClNO_4$
603.0615	GDP-L-gulose	$C_{16}H_{23}N_5O_{16}P_2$
603.3559	Janthitrem E	$C_{37}H_{49}NO_6$
606.3768	Fusapyrone	$C_{34}H_{54}O_9$
609.2951	Ergocristinine	$C_{35}H_{39}N_5O_5$
629.3716	Janthitrem G	$C_{39}H_{51}NO_6$

633.2857	Penitrem A ; Pennigritrem	$C_{37}H_{44}ClNO_6$
645.3665	Janthitrem F	$C_{39}H_{51}NO_7$
666.2219	Maltotetraose ; Stachyose	$C_{24}H_{42}O_{21}$
667.339	Ergokonin A	$C_{34}H_{53}NO_{10}S$
670.1533	Alterporriol D ; Alterporriol E	$C_{32}H_{30}O_{16}$
680.3771	Fusicoccin A	$C_{36}H_{56}O_{12}$
685.3978	Lolitrem B	$C_{42}H_{55}NO_7$
690.2888	Zaragozic acid A	$C_{35}H_{46}O_{14}$
692.3111	Ditryptophenaline	$C_{42}H_{40}N_6O_4$
719.0043	1-(5-Phospho-D-ribosyl)-ATP	$C_{15}H_{25}N_5O_{20}P_4$
790.5066	Solanesyl diphosphate	$C_{45}H_{76}O_7P_2$
828.2747	Maltopentaose ; Verbascose	$C_{30}H_{52}O_{26}$
882.503	Stachybocin A	$C_{52}H_{70}N_2O_{10}$
914.4928	Stachybocin D	$C_{52}H_{70}N_2O_{12}$

Appendix V. Detected metabolic biomarkers applying direct infusion Orbitrap MS analyses in positive (ESI^+) and negative (ESI^-) electrospray modes in *R. solani* monoculture and during interaction after 120 h of growth. Biomarkers were selected based on their PLS-DA regression coefficients ($P < 0.05$). Putative molecular formulae were assigned after searches against five biological databases (KEGG, PlantCyc, LIPID MAPS, YMDB, and KNApSAcK) and an in house fungal metabolic library with a mass accuracy (Δppm < 3 ppm).

Detected m/z	Putative Molecular Formula	Monoisotopic mass	Adduct
R. solani			
89.0248	$C_3H_6O_3$	90.0316	$[M-H]^-$
121.0295	$C_7H_6O_2$	122.0367	$[M-H]^-$
143.1060	$C_8H_{14}O_2$	142.0993	$[M+H]^+$
149.0969	$C_{10}H_{14}O$	150.1044	$[M-H]^-$
155.0677	$C_6H_{12}O_3$	132.0786	$[M+Na]^+$
157.1234	$C_9H_{18}O_2$	158.1306	$[M-H]^-$
165.0520	$C_7H_{10}O_3$	142.0629	$[M+Na]^+$
171.1387	$C_{10}H_{20}O_2$	172.1463	$[M-H]^-$
179.1063	$C_{11}H_{14}O_2$	178.0993	$[M+H]^+$
185.9652	$C_4H_5NO_2S_2$	162.9761	$[M+Na]^+$
191.1038	$C_{10}H_{16}O_2$	168.115	$[M+Na]^+$
195.1386	$C_{12}H_{20}O_2$	196.1463	$[M-H]^-$
205.1229	$C_{13}H_{18}O_2$	206.1306	$[M-H]^-$
217.1564	$C_{13}H_{22}O$	194.167	$[M+Na]^+$
217.1588	$C_{15}H_{20}O$	216.1514	$[M+H]^+$
219.1387	$C_{14}H_{20}O_2$	220.1463	$[M-H]^-$
221.1543	$C_{14}H_{22}O_2$	222.1619	$[M-H]^-$
228.1356	$C_{13}H_{19}NO$	205.1466	$[M+Na]^+$
241.2165	$C_{15}H_{30}O_2$	242.2245	$[M-H]^-$
245.1149	$C_{10}H_{13}NO_5$	227.0793	$[M+NH_4]^+$
259.1303	$C_{14}H_{20}O_3$	236.1412	$[M+Na]^+$
267.2323	$C_{17}H_{32}O_2$	268.2402	$[M-H]^-$
269.2480	$C_{17}H_{34}O_2$	270.2558	$[M-H]^-$
271.1699	$C_{18}H_{24}O_2$	272.1776	$[M-H]^-$
271.2270	$C_{16}H_{32}O_3$	272.2351	$[M-H]^-$
275.2010	$C_{18}H_{28}O_2$	276.2089	$[M-H]^-$
277.2132	$C_{16}H_{30}O_2$	254.2245	$[M+Na]^+$
277.2166	$C_{18}H_{30}O_2$	278.2245	$[M-H]^-$

281.1147	$C_{16}H_{18}O_3$	258.1255	$[M+Na]^+$
283.1338	$C_{18}H_{18}O_3$	282.1255	$[M+H]^+$
299.2585	$C_{18}H_{36}O_3$	300.2664	$[M-H]^-$
307.0949	$C_{17}H_{16}O_4$	284.1048	$[M+Na]^+$
307.2249	$C_{17}H_{32}O_3$	284.2351	$[M+Na]^+$
313.1228	$C_{14}H_{20}N_2O_4S$	312.1143	$[M+H]^+$
313.2376	$C_{18}H_{34}O_4$	314.2457	$[M-H]^-$
329.1392	$C_{19}H_{20}O_5$	328.131	$[M+H]^+$
333.2039	$C_{18}H_{30}O_4$	310.2144	$[M+Na]^+$
339.1724	$C_{20}H_{28}O_2$	300.2089	$[M+K]^+$
341.2122	$C_{22}H_{28}O_3$	340.2038	$[M+H]^+$
341.2129	$C_{22}H_{30}O_3$	342.2194	$[M-H]^-$
349.1990	$C_{18}H_{30}O_5$	326.2093	$[M+Na]^+$
361.1314	$C_{20}H_{22}N_2O_2$	322.1681	$[M+K]^+$
362.9837	$C_6H_{14}O_{12}P_2$	339.996	$[M+Na]^+$
371.2559	$C_{22}H_{36}O_3$	348.2664	$[M+Na]^+$
381.2596	$C_{20}H_{38}O_5$	358.2719	$[M+Na]^+$
401.2660	$C_{23}H_{38}O_4$	378.277	$[M+Na]^+$
437.2439	$C_{26}H_{38}O_3$	398.282	$[M+K]^+$
439.0852	$C_{12}H_{23}NO_9S_3$	421.0534	$[M+NH_4]^+$
Interaction			
87.0435	$C_4H_6O_2$	86.0367	$[M+H]^+$
115.0750	$C_6H_{10}O_2$	114.068	$[M+H]^+$
148.0749	C_9H_9NO	147.0684	$[M+H]^+$
179.1075	$C_{11}H_{16}O_2$	180.115	$[M-H]^-$
189.0518	$C_9H_{10}O_3$	166.0629	$[M+Na]^+$
193.0868	$C_{11}H_{14}O_3$	194.0942	$[M-H]^-$
291.2682	$C_{20}H_{34}O$	290.2609	$[M+H]^+$
299.1642	$C_{19}H_{22}O_3$	298.1568	$[M+H]^+$
304.2608	$C_{18}H_{35}NO$	281.2718	$[M+Na]^+$
309.2391	$C_{17}H_{34}O_3$	286.2507	$[M+Na]^+$
417.2277	$C_{24}H_{34}O_6$	418.2355	$[M-H]^-$

Appendix VI. Relative intensities of detected metabolic biomarkers applying direct infusion Orbitrap MS analyses in positive (ESI^+) and negative (ESI^-) electrospray modes in *R. solani* monoculture and during interaction after 120 h of growth. Biomarkers were selected based on their PLS-DA regression coefficients ($P < 0.05$). Putative molecular formulae were assigned after searches against five biological databases (KEGG, PlantCyc, LIPID MAPS, YMDB, and KNApSAcK) and an in house fungal metabolic library with a mass accuracy (Δppm < 3 ppm).

Detected m/z	Putative Molecular Formula	Monoisotopic mass	Adduct	RI* in *R. solani*	RI during interaction	Fold change
190.1434	$C_9H_{16}O_3$	172.1099	$[M+NH_4]^+$	0.001181	0.001825	1.5
248.1286	$C_{14}H_{19}NO_3$	249.1364	$[M-H]^-$	0.000814	0.00232	2.8
295.1873	$C_{15}H_{28}O_4$	272.1987	$[M+Na]^+$	0.00158	0.00217	1.4
341.1878	$C_{20}H_{30}O_2$	302.2245	$[M+K]^+$	0.00193	0.0012	0.6

*RI: Relative intensity

Appendix VII. Mass to charge ratios (m/z) of metabolic biomarkers detected during the interaction after 120 h of growth applying direct infusion Orbitrap MS analyses in positive (ESI^+) electrospray mode. Biomarkers were selected based on their PLS-DA regression coefficients ($P < 0.05$).

88.2224; 88.2355; 88.2396; 88.2410; 88.3158; 89.5899; 93.9423; 99.0437; 101.0081; 115.0365; 116.9855; 117.4403;; 133.0343;; 147.9546; 147.9957; 148.0620; 148.0666; 148.0685; 148.0707; 153.6996; 153.7049; 153.7062; 155.1063; 161.0932; 161.0936; 166.0853; 171.0624; 181.0832; 183.0989; 185.9830; 187.2244; 187.6501; 193.0723; 198.7101; 200.2365; 212.1252; 227.0682; 227.1264; 259.0949; 285.1775; 289.8685; 289.8803; 291.2011; 314.0161; 314.0272; 314.0408; 314.0461; 314.0927; 314.0953; 325.2343; 327.9019; 332.3306; 333.8471; 334.8638; 338.2170; 347.0739; 347.2915; 355.0694; 360.3234; 372.1000; 378.6280; 379.5434; 379.5576; 379.5603; 379.5611; 379.5634; 394.0820; 394.0827; 395.0792; 407.1343; 409.2409; 410.0559; 410.0593; 420.2802; 424.7904; 437.7445; 453.2403; 459.2400; 480.2791; 481.1536; 490.3305; 490.6493; 490.6564; 490.6659; 490.6692; 490.6774; 490.6891; 491.0714; 516.6247; 535.0210; 553.2107; 585.2873; 630.6935; 737.4573; 774.4664; 793.9993; 794.0058; 794.0117; 794.0205; 794.0984; 794.1316; 859.5368; 872.2641; 872.2964; 872.3102; 872.3364; 872.3426; 872.3493; 872.4536; 1159.4061

Appendix VIII. Mass to charge ratios (m/z) of metabolic biomarkers detected during the interaction after 120 h of growth applying direct infusion Orbitrap MS analyses in negative (ESI$^-$) electrospray mode. Biomarkers were selected based on their PLS-DA regression coefficients ($P < 0.05$).

96.9224; 119.9700; 146.9348; 146.9715; 146.9744; 146.9969; 221.0451; 234.8589; 259.0949; 260.9098; 261.0586; 276.8838; 292.8302; 304.9390; 305.0223; 313.1013; 316.8712; 318.8684; 324.8350; 332.8451; 333.8405; 350.7980; 378.0654; 389.8756; 403.8178; 502.8486; 529.7376; 762.8226

Appendix IX. Mass to charge ratios (m/z) of metabolic biomarkers detected in the monoculture of *R. solani* after 120 h of growth applying direct infusion Orbitrap MS analyses in positive (ESI^+) electrospray mode. Biomarkers were selected based on their PLS-DA regression coefficients ($P < 0.05$).

88.2101; 88.2215; 93.9423; 98.9181; 117.4291; 147.9728; 148.0633; 148.0700; 151.0421; 174.0275; 175.0198;; 186.1179; 194.9464; 195.0629; 198.4802; 198.4855; 198.4868; 198.4900; 198.5281; 199.8704; 206.5130; 209.9000; 217.1316; 229.1411; 232.1021; 232.9400; 233.9984; 234.0227; 247.1670; 249.9070; 253.1774; 255.1558; 265.1463; 269.1181; 275.1421; 275.1440; 277.0651; 280.1200; 281.8349; 289.8461; 289.8798; 291.1666; 291.175; 291.208; 291.2155; 291.2366; 291.2447; 294.2122; 297.1669; 297.2398; 299.1078; 310.1860; 310.2522; 311.1829; 313.1602; 313.4598; 313.6449; 313.6547; 319.1725; 327.9035; 333.8466; 336.2222; 337.2230; 338.2376; 341.2668; 343.8769; 345.0092; 347.0097; 349.0583; 349.1083; 349.8415; 352.1966; 353.2651; 357.1858; 359.1808; 379.5188; 379.5242; 379.5273; 379.5648; 380.2733; 385.1810; 385.2909; 385.8002; 390.0095; 393.2094; 395.2766; 396.3258; 401.1269; 410.2877; 414.2681; 423.1125; 427.2674; 430.2419; 435.8158; 436.2539; 437.8394; 437.8530; 437.8630; 437.8741; 437.9113; 453.2095; 458.4201; 461.8168; 473.3447; 483.1786; 489.3170; 493.2774; 497.1264; 507.1840; 516.6381; 516.6478; 516.6509; 520.7933; 533.3459; 535.0599; 535.1257; 545.7772; 561.3975; 563.7863; 577.3707; 610.3661; 611.3464; 628.3218; 630.5515; 630.6161; 641.3287; 656.3851; 665.4233; 683.4320; 683.4334; 704.4785; 717.4520; 717.4546; 733.4284; 744.4360; 771.4871; 793.7483; 793.7540; 793.8635; 793.8699; 793.8759; 793.8811; 793.9104; 793.9176; 859.5385

Appendix X. Mass to charge ratios (m/z) of metabolic biomarkers detected in the monoculture of *R. solani* after 120 h of growth applying direct infusion Orbitrap MS analyses in negative (ESI^-) electrospray mode. Biomarkers were selected based on their PLS-DA regression coefficients ($P < 0.05$).

89.1053; 145.9956; 157.0117; 161.0969; 172.9887; 175.9599; 191.9371; 194.0942; 194.9464; 197.0275; 198.9175; 200.0536; 206.0067; 228.1237; 232.9400; 254.8747; 257.1285; 266.1506; 268.8130; 275.8820; 278.8580; 280.9414; 285.1596; 292.8448; 294.8319; 299.9262; 306.8216; 311.7934; 314.8083; 315.1879; 318.1314; 319.0744; 326.1938; 330.8658; 332.1469; 333.1596; 335.8376; 343.1189; 347.0653; 350.0401; 354.8271; 356.8891; 357.2038; 357.8016; 362.8572; 367.2267; 367.2635; 371.9043; 372.1810; 375.1909; 376.8333; 378.1526; 389.1927; 393.7779; 395.2218; 395.7756; 397.7787; 422.2288; 423.7888; 426.8048; 435.7752; 458.7518; 460.7498; 466.7817; 469.8818; 476.7643; 485.8557; 496.8170; 521.0031; 522.1764; 529.7117; 529.7301; 529.7347; 529.7485; 529.7660; 537.7216; 750.2476; 762.7960; 762.8056; 762.8217

Appendix XI. Relative intensities of mass to charge ratios (m/z) of detected metabolic biomarkers applying direct infusion Orbitrap MS analyses in positive (ESI^+) and negative (ESI^-) electrospray modes in *R. solani* monoculture and during interaction after 120 h of growth. Biomarkers were selected based on their PLS-DA regression coefficients ($P < 0.05$).

Detected m/z	Relative intensity in *R. solani*	Relative intensity during interaction	Fold change	ESI
172.2052	0.00101	0.00316	3	+
181.0832	0.00175	0.00305	1.7	+
183.0983	0.001813	0.001515	0.83	+
187.0568	0.00205	0.00248	1.2	+
214.1057	0.003332	0.002352	0.7	-
278.0432	0.000402	0.002581	6.4	-
291.1178	0.00256	0.00289	1.12	+
291.1565	0.00173	0.00237	1.4	+
293.1514	0.00237	0.00386	1.6	+
296.2582	0.00172	0.00254	1.5	+
323.2547	0.00284	0.00424	1.5	+
334.8627	0.00142	0.00283	2	+
335.8374	0.001502	0.002281	1.5	-
365.1054	0.00348	0.00277	0.8	+
378.5757	0.00131	0.00304	2	+
404.1036	0.010031	0.004742	0.47	-
519.2778	0.00786	0.0024	0.3	+
666.0579	0.000425	0.003306	7.7	-