

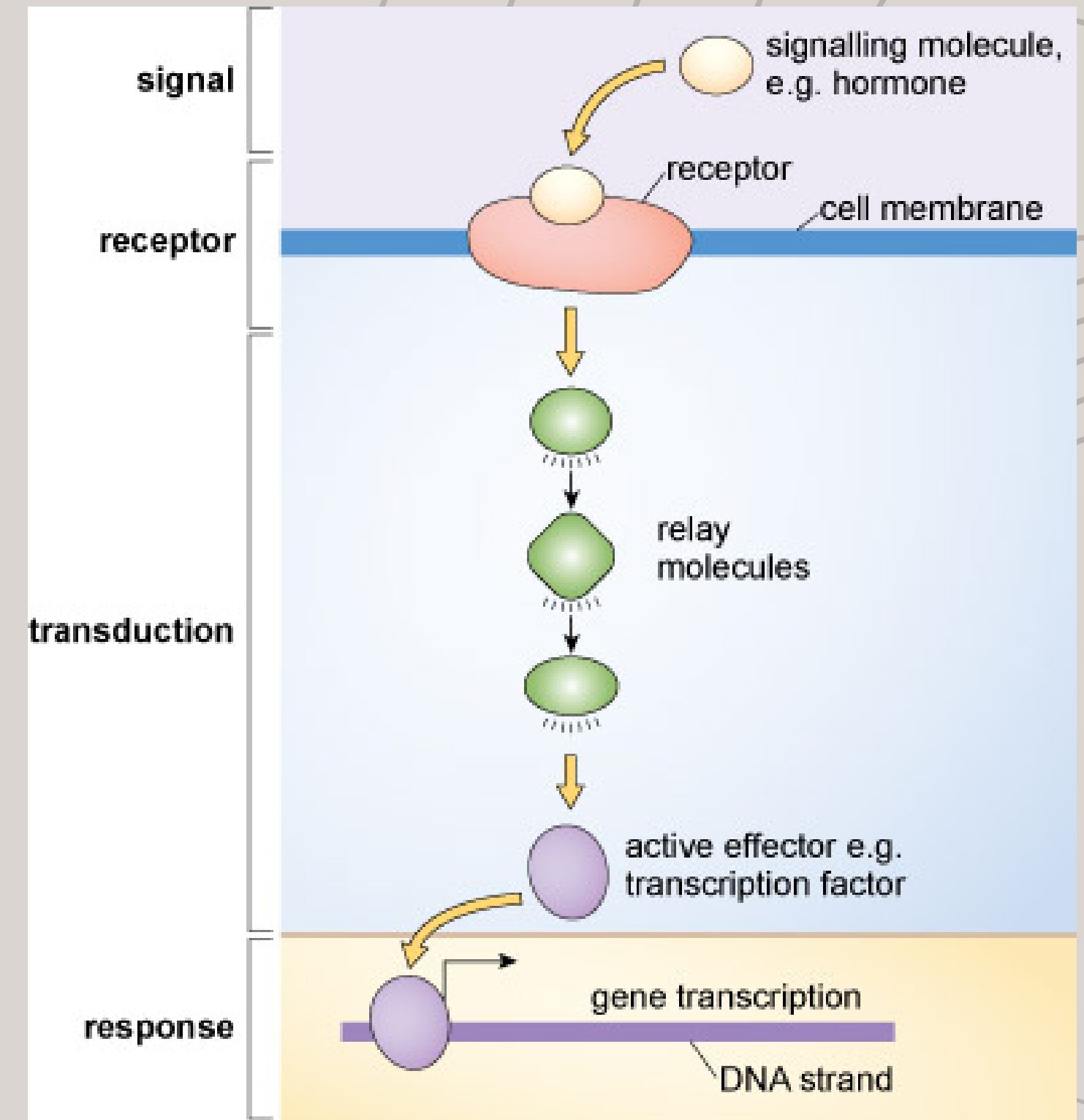
BCHM521 Final Project

# **Evolution of Mitogen- Activated Protein Kinase Gene in fungi, animals, and plants**

Presented by Julie Li

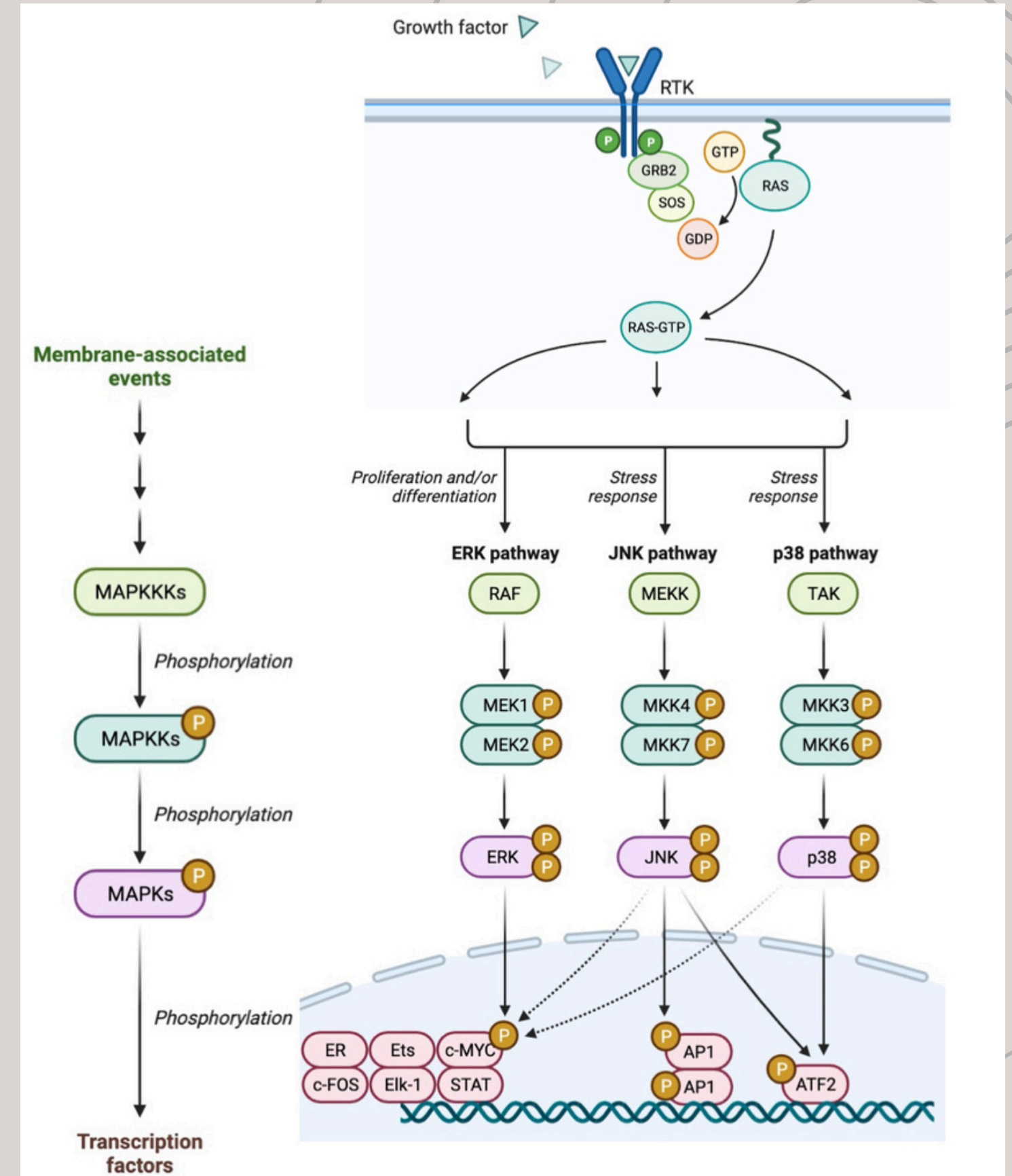
# Intro/Background

- Living organisms rely on communication networks to sense and respond to changes in their environment.
- Mitogen-activated protein kinase (MAPK) signaling pathways



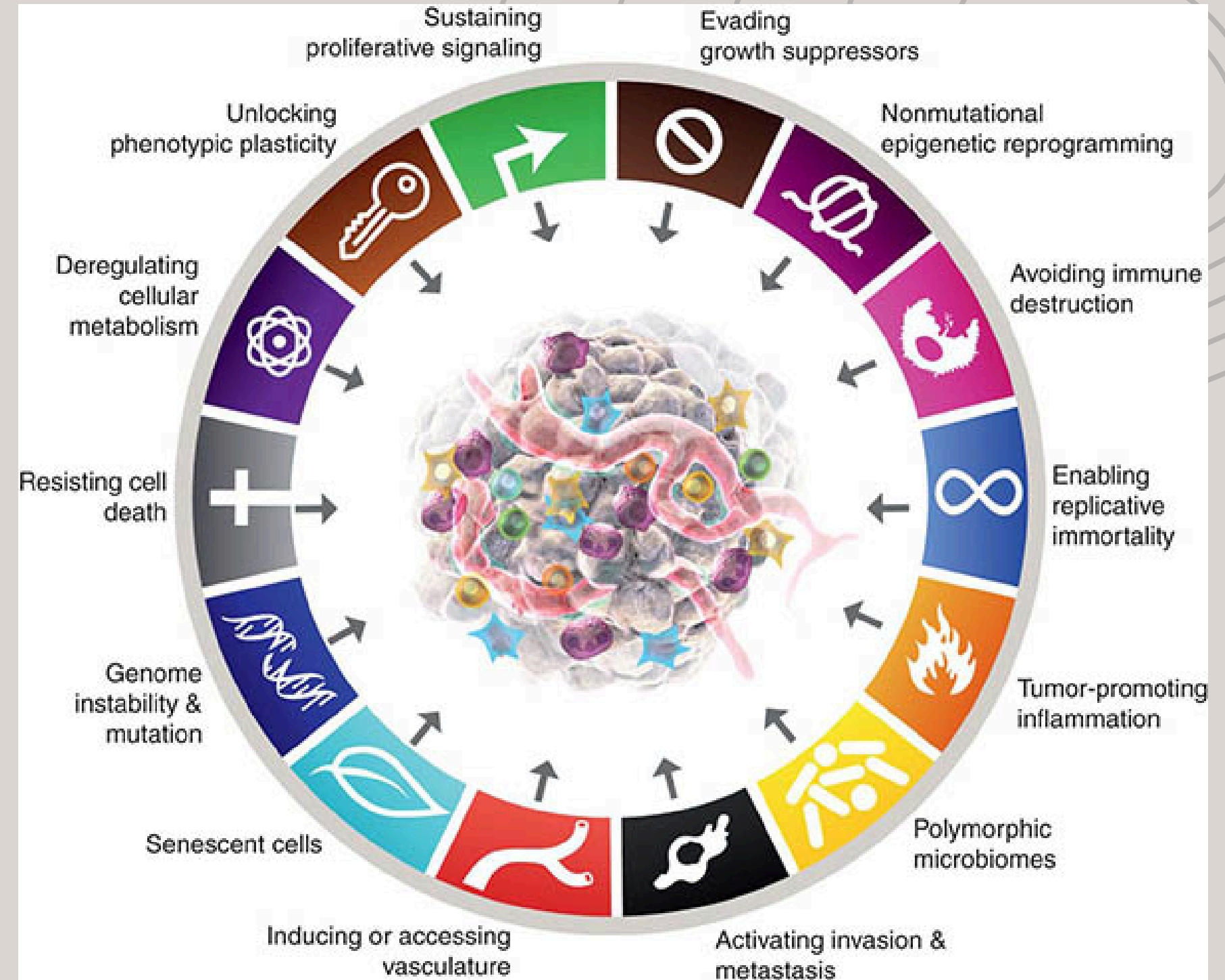
# Intro/Background

- Mitogen-activated protein kinases (MAPKs) belong to a family of protein Ser/Thr kinase that play a key role in signal transduction
- Converts signals from outside the cell into a series of phosphorylation events within the cell.
- MAPKs regulate a diverse range of cellular processes.
  - Gene expression
  - Cell division
  - Survival
  - Apoptosis
  - Differentiation



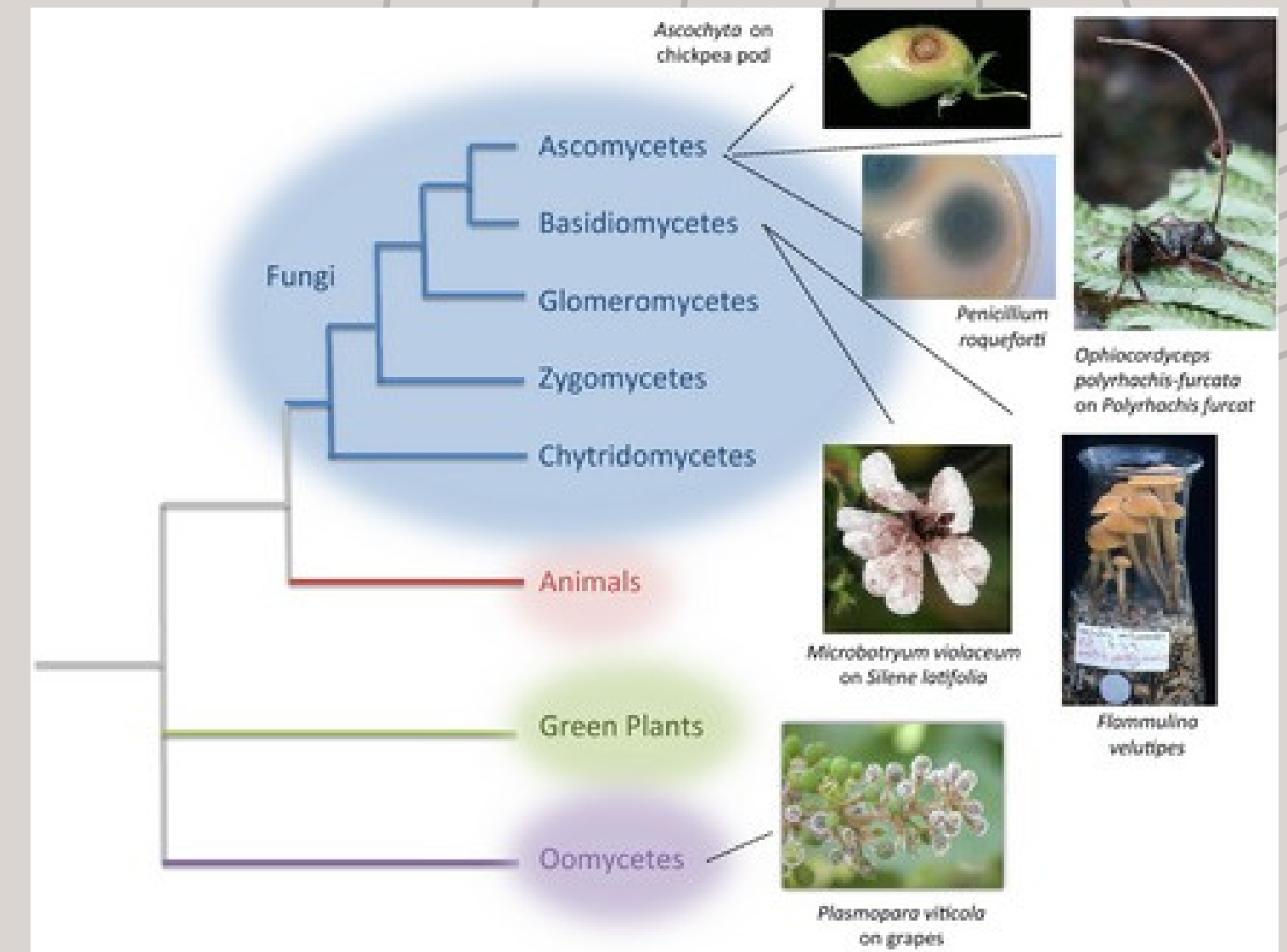
# Intro/Background

- Disruptions in MAPK signaling
  - uncontrolled cellular processes such as sustaining proliferative signaling
  - become oncogenic



# Rationale and Hypothesis

- Conservation of MAPK signaling across eukaryotes suggests a **fundamental pathway** connecting diverse life forms.
- If this is true:
  - Fungi and animals share a closer evolutionary relationship than plants on the species tree
- Is this also true? (hypothesis)
  - Fungal MAPKs are more similar to animal MAPKs than plant MAPKs



(Gladieux et al., 2013)



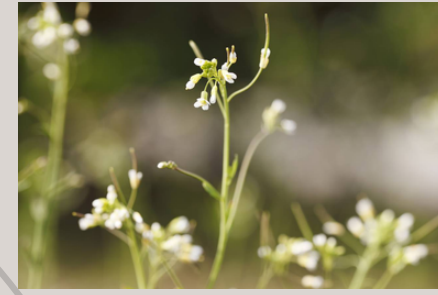
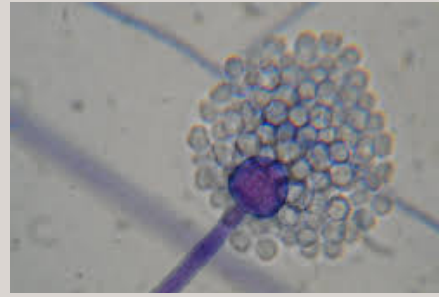
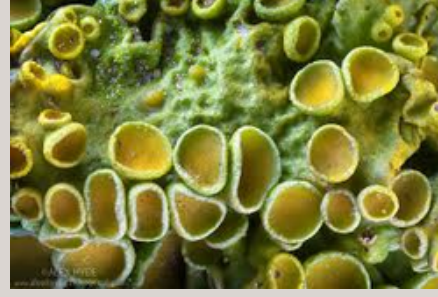
# Application

- By knowing fungal MAPKs are more similar to animal MAPKs than plant MAPKs....
- Conserved MAPK signaling pathway
- Target the specific features of fungal MAPKs that differ from animal MAPKs, we could potentially create drugs that are effective against fungal infections with minimal side effects on animals and humans.





# 15 annotated genomes and outgroup



# 15 annotated genomes and outgroup list

Kingdom	Species	Classes or Common Name
Fungus	<i>Saccharomyces cerevisiae</i>	Ascomycota
Fungus	<i>Xanthoria parietina</i>	Ascomycota
Fungus	<i>Bjerkandera adusta</i>	Basidiomycota
Fungus	<i>Rhizophagus irregularis</i>	Glomeromycetes
Fungus	<i>Backusella circina</i>	Mucoromycotina
Fungus	<i>Gonapodya prolifera</i>	Monoblepharidomycetes
Fungus	<i>Conidiobolus coronatus</i>	Entomophthoromycota
Animal	<i>Drosophila melanogaster</i>	fruit fly
Animal	<i>Danio rerio</i>	zebrafish
Animal	<i>Caenorhabditis elegans</i>	Roundworm
Animal	<i>Mus musculus</i>	house mouse
Plant	<i>Oryza sativa</i>	rice
Plant	<i>Arabidopsis thaliana</i>	thale cress
Plant	<i>Lotus japonicus</i>	-
Plant	<i>Zea mays</i>	corn
Protista	<i>Chlamydomonas reinhardtii</i>	-



# Work Flow



**select 15 annotated genomes and outgroup**



**run OrthoFinder**

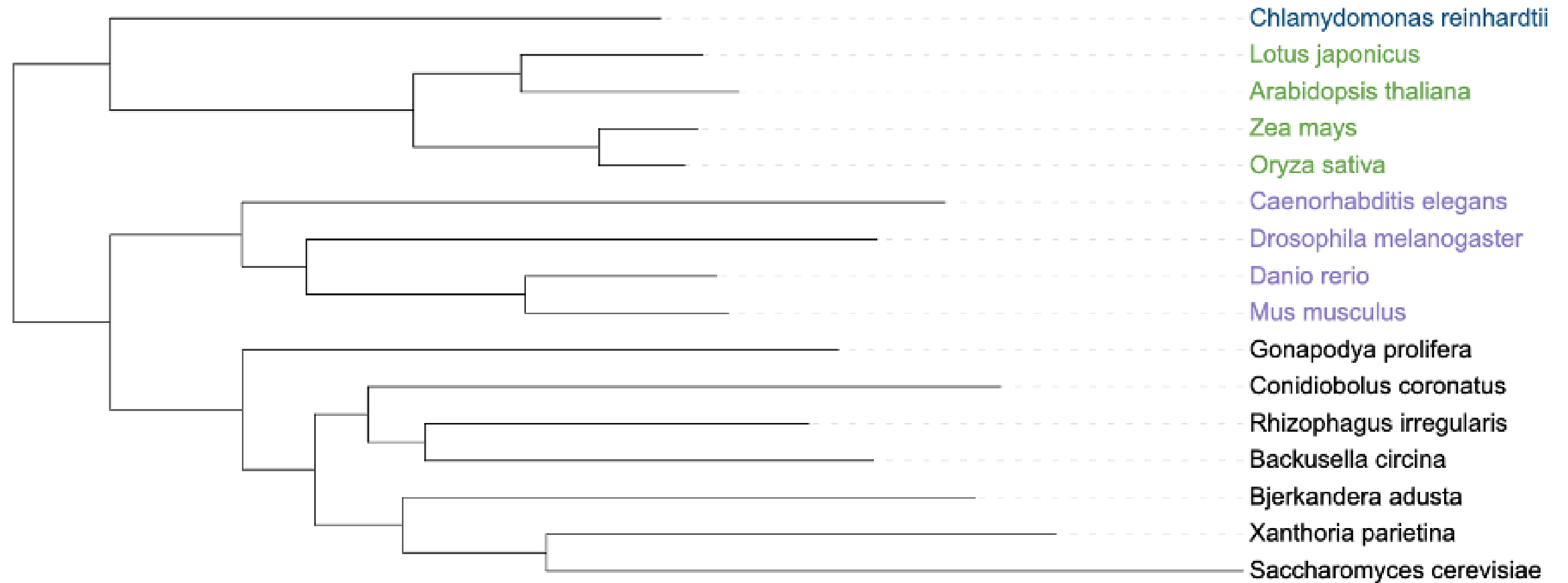


**run MAFFT Multiple Sequence Alignment**



**Notung gene tree-species tree reconciliation**

# OrthoFinder Species Tree



# MAFFT Multiple Sequence Alignment

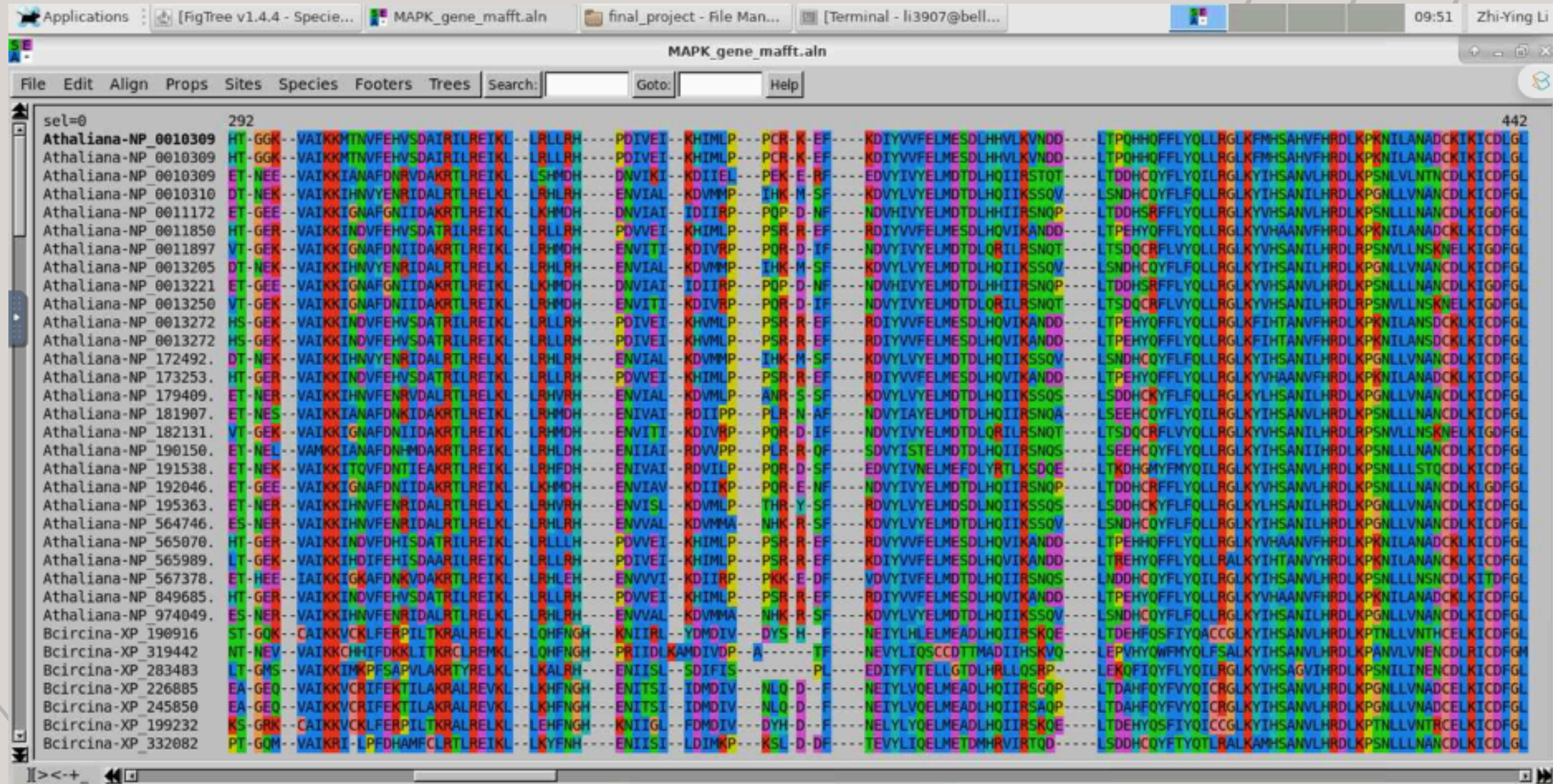
- At1g10210 and At3g45640 sequences were identified in previous studies as MAPK protein sequences of Arabidopsis thaliana and search on NCBI
- Retrieve protein sequence from GenBank
- Search on BLASTp to get top accession number
- Grep in Orthogroup result file to find to identify the relevant MAPK orthogroup
- GO term: OG0000053 orthogroup

```
grep "NP_181907.1" Orthogroups.txt
```

```
OG0000053: Athaliana-NP_001030939.1 Athaliana-NP_0  
liana-NP_001117210.1 Athaliana-NP_001185027.1 Atha  
112.1 Athaliana-NP_001325006.1 Athaliana-NP_001327  
_173253.1 Athaliana-NP_179409.1 Athaliana-NP_18190  
38.1 Athaliana-NP_192046.1 Athaliana-NP_195363.1 A  
Athaliana-NP_567378.4 Athaliana-NP_849685.1 Athali  
800 Badusta-XP_43732 Badusta-XP_57610 Badusta-XP_7  
rcina-XP_233019 Bcirculara-XP_245850 Bcirculara-XP_283  
ronatus-XP_51740 Ccoronatus-XP_78330 Ccoronatus-XP  
66708.1 Celegans-NP_494947.2 Celegans-NP_501365.1  
legans-NP_872069.1 Creinhardtii-XP_001699095.2 Cre  
-XP_042918154.1 Dmelanogaster-NP_001015121.3 Dmela  
r-NP_001104348.2 Dmelanogaster-NP_001104349.1 Dmel  
er-NP_001287635.1 Dmelanogaster-NP_477163.1 Dmelan  
5.1 Drerio-NP_001013469.2 Drerio-NP_001018581.2 Dr  
rerio-NP_571482.1 Drerio-NP_571797.1 Drerio-NP_878  
9.1 Drerio-XP_005167118.1 Drerio-XP_009292731.1 Dr  
rerio-XP_021330663.1 Gprolifera-XP_137976 Gprolife  
P_057415130.1 Ljaponicus-XP_057415360.1 Ljaponicus  
3.1 Ljaponicus-XP_057415909.1 Ljaponicus-XP_057415  
cus-XP_057416889.1 Ljaponicus-XP_057416890.1 Ljapo  
19311.1 Ljaponicus-XP_057420998.1 Ljaponicus-XP_05  
ponicus-XP_057449077.1 Ljaponicus-XP_057450000.1 L  
1161980.1 Mmusculus-NP_001161985.1 Mmusculus-NP_00
```



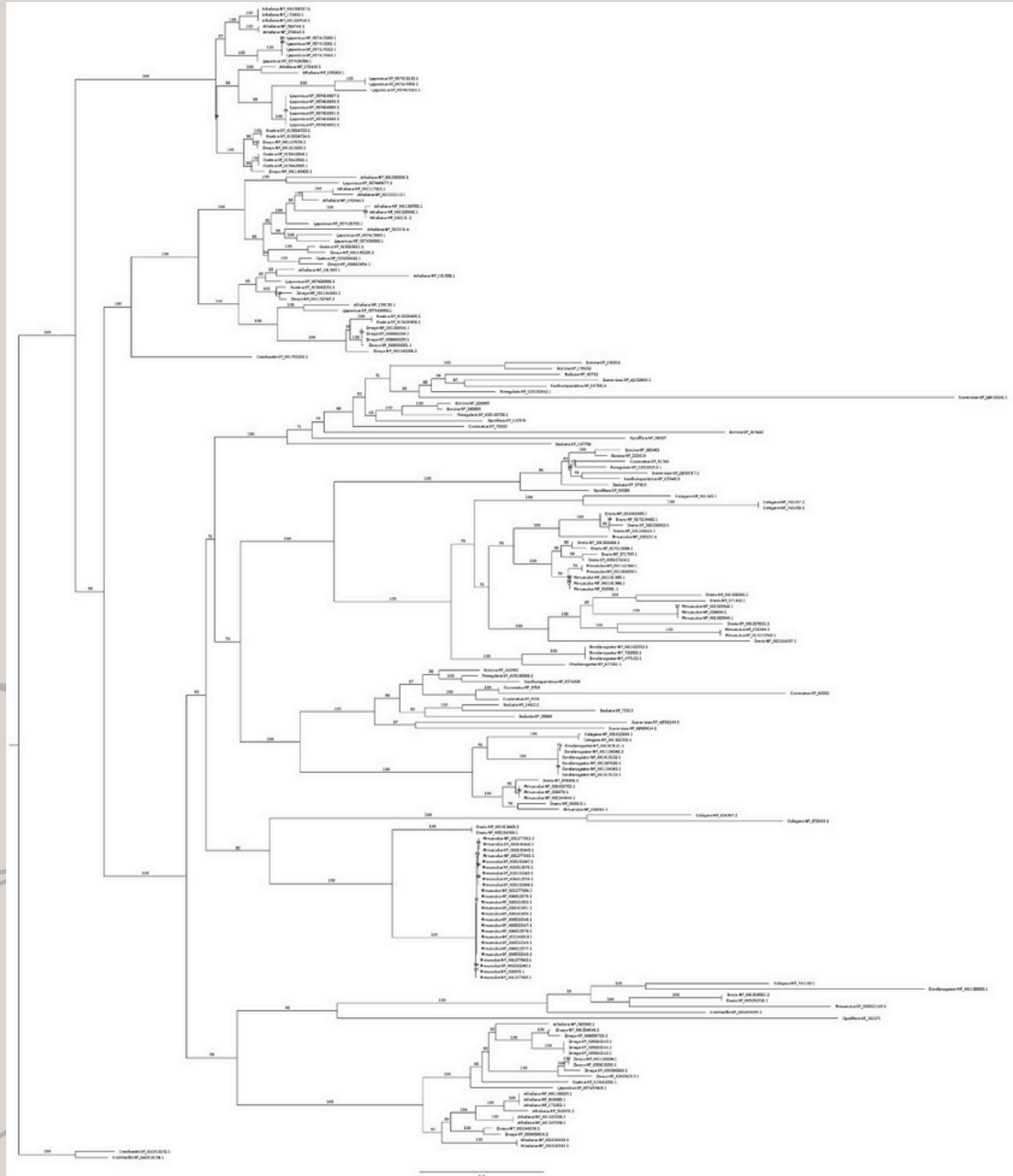
# MAFFT Multiple Sequence Alignment Result



- MAFFT result of OG00000053 MAPK orthogroup
- High degree of conservation across positions 248 to 718 of the MAPK orthogroup sequences

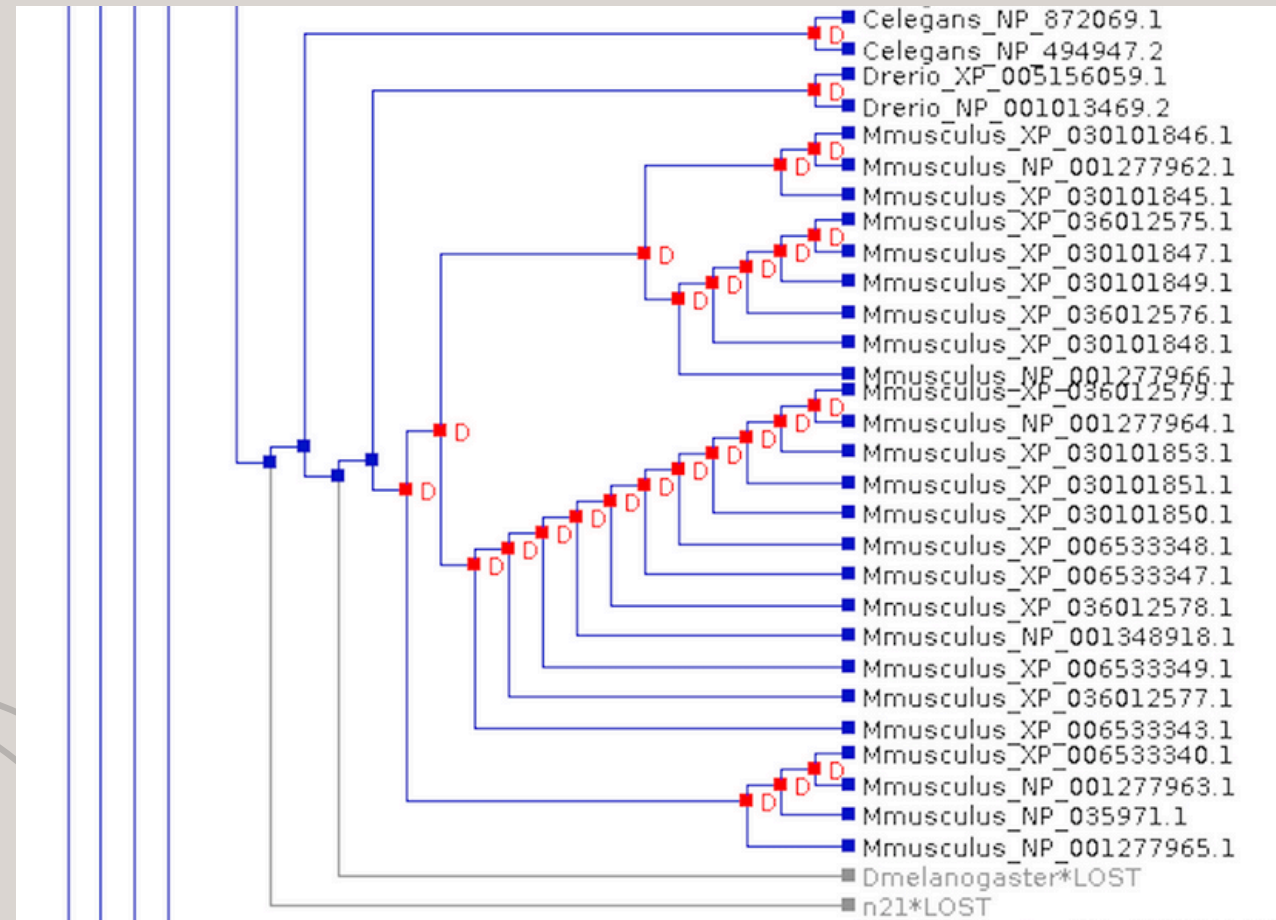
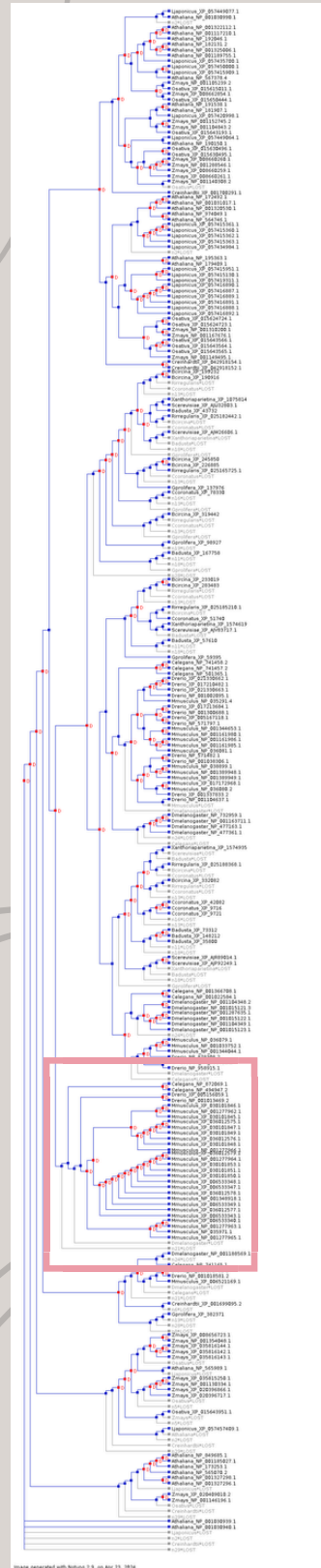


# IQ-TREE maximum likelihood phylogenetic tree



- Creinhardtii-XP\_042918152.1 and Creinhardtii-XP\_042918154.1, were used to reroot the tree.
- Support values are generally greater than or equal to 95

# Notung gene tree-species tree reconciliation



- Reconciliation Information
  - **Duplications: 151**
  - Co-Divergences: 0
  - Transfers: 0
  - Losses: 83
  - Number of Temporally Feasible Optimal Solutions: 1
- Gaining new function or a subfunction of the original function of the gene



# Conclusions

- Comparative analysis of gene trees and species trees does show that fungal MAPKs are more similar to animal MAPKs than plant MAPKs
- This aligns with the known evolutionary relationship between animals and fungi
- Potential developing targeted antifungal drugs with minimal side effects toward animals and humans

# Reference

Gladieux, Pierre & Ropars, Jeanne & Badouin, H  l  ne & Branca, Antoine & Aguilera, Gabriela & de Vienne, Damien & Rodr  guez de la Vega, Ricardo & Branco, Sara & Giraud, Tatiana. (2013). Fungal evolutionary genomics provides insight into the mechanisms of adaptive divergence in eukaryotes. *Molecular ecology*. 23. 10.1111/mec.12631.

Mohanta, Tapan Kumar, et al. "Genome-Wide Identification of Mitogen-Activated Protein Kinase Gene Family across Fungal Lineage Shows Presence of Novel and Diverse Activation Loop Motifs." PLOS ONE, Public Library of Science, 26 Feb. 2016, journals.plos.org/plosone/article?id=10.1371%2Fjournal.pone.0149861#pone-0149861-t001.

Cargnello, M., & Roux, P. P. (2011). Activation and function of the MAPKs and their substrates, the MAPK-activated protein kinases. Microbiology and molecular biology reviews : MMBR, 75(1), 50–83.

Lawrence MC, Jivan A, Shao C, Duan L, Goad D, Zaganjor E, Osborne J, McGlynn K, Stippec S, Earnest S, Chen W, Cobb MH. The roles of MAPKs in disease. *Cell Res.* 2008 Apr;18(4):436-42. doi: 10.1038/cr.2008.37. PMID: 18347614.

Sinkala, M., Nkhoma, P., Mulder, N., & Martin, D. P. (2021). Integrated molecular characterisation of the MAPK pathways in human cancers reveals pharmacologically vulnerable mutations and gene dependencies. *Communications biology*, 4(1), 9.

Hamel LP, Nicole MC, Sritubtim S, Morency MJ, Ellis M, Ehling J, et al. (2006) Ancient signals: comparative genomics of plant MAPK and MAPKK gene families. *Trends Plant Sci* 11: 192–198.

Baldauf, S. L., & Palmer, J. D. (1993). Animals and fungi are each other's closest relatives: congruent evidence from multiple proteins. *Proceedings of the National Academy of Sciences of the United States of America*, 90(24), 11558–11562.

Mohanta, T. K., Mohanta, N., Parida, P., Panda, S. K., Ponpandian, L. N., & Bae, H. (2016). Genome-Wide Identification of Mitogen-Activated Protein Kinase Gene Family across Fungal Lineage Shows Presence of Novel and Diverse Activation Loop Motifs. *PloS one*, 11(2), e0149861.

Emms, D.M., Kelly, S. OrthoFinder: phylogenetic orthology inference for comparative genomics. *Genome Biol* 20, 238 (2019). <https://doi.org/10.1186/s13059-019-1832-y>

Katoh K, Asimenos G, Toh H. Multiple alignment of DNA sequences with MAFFT. *Methods Mol Biol.* 2009;537:39-64. doi: 10.1007/978-1-59745-251-9\_3. PMID: 19378139.

Minh BQ, Schmidt HA, Chernomor O, Schrempf D, Woodhams MD, von Haeseler A, Lanfear R. IQ-TREE 2: New Models and Efficient Methods for Phylogenetic Inference in the Genomic Era. *Mol Biol Evol.* 2020 May 1;37(5):1530-1534. doi: 10.1093/molbev/msaa015. Erratum in: *Mol Biol Evol.* 2020 Aug 1;37(8):2461. PMID: 32011700; PMCID: PMC7182206

BCHM521 Final Project

# Thank You

Presented by Julie Li