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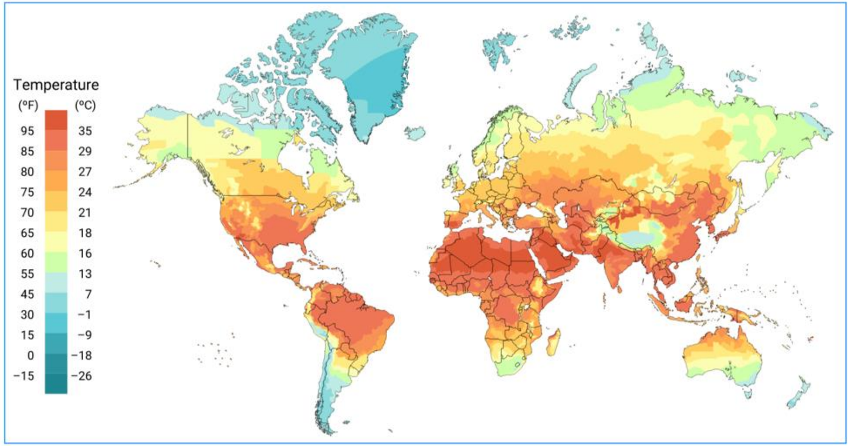
Using fungi to evaluate threats associated with climate change

Aaron Robinson
Scientist II B-GEN

September 18, 2024

Fungi and Climate Change



The future of fungi: threats and opportunities

Nicola T. Case,[1] Judith Berman,[2] David S. Blehert,[3] Robert A. Cramer,[4] Christina Cuomo,[5]
Cameron R. Currie,[6] Iuliana V. Ene,[7] Matthew C. Fisher,[8] Lillian K. Fritz-Laylin,[9] Aleeza C. Gerstein,[10]
N. Louise Glass,[11] Neil A. R. Gow,[12] Sarah J. Gurr,[12] Chris Todd Hittinger,[13] Tobias M. Hohl,[14]
Iliyan D. Iliev,[15] Timothy Y. James,[16] Hailing Jin,[17] Bruce S. Klein,[18,19,20] James W. Kronstad,[21]
Jeffrey M. Lorch,[3] Victoria McGovern,[22] Aaron P. Mitchell,[23] Julia A. Segre,[24] Rebecca S. Shapiro,[25]
Donald C. Sheppard,[26] Anita Sil,[27] Jason E. Stajich,[17] Eva E. Stukenbrock,[28,29] John W. Taylor,[30]
Dawn Thompson,[31] Gerard D. Wright,[32] Joseph Heitman,[33] Leah E. Cowen[1,*]

Global Health

- 1.5 million deaths annually
- ~12 billion annual economic burden
- No vaccines, poor diagnostics, resistance

Global Security

- Agricultural losses -10 to 20% ($100 to $200 billion)
- Expanding geographic range and emerging pathogens
- Antifungal resistance

Ecological Stability

- Species extinction and collapse (land and sea
- Pathogens in the environment

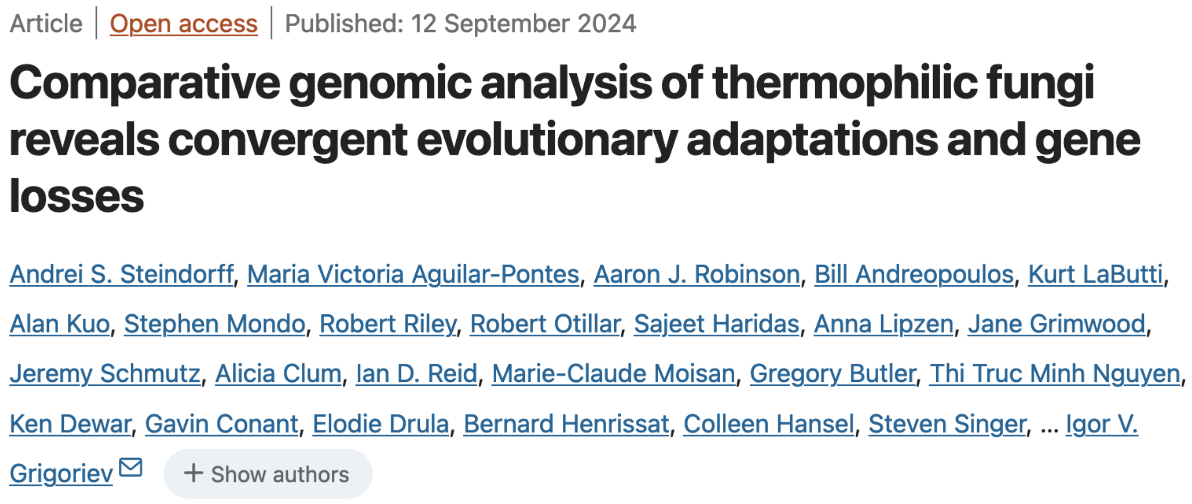
Motivations for studying thermophilic fungi

- Rare unifying trait among fungal pathogens
  - Survive mammalian body temperatures
  - Therapeutic design
  - Agnostic detection of emerging pathogens
- Modeling impacts of climate change
  - Evolutionary trade-offs
  - Effects on metabolism
  - Susceptible populations
- Biotechnology
  - Biomass transformation
  - Protein engineering

Thermophilic: optimal growth above 45°C

Thermotolerant: can grow above 35°C, but not necessarily optimal

Mesophilic: optimal growth at 20 – 34°C



Article | Open access | Published: 12 September 2024

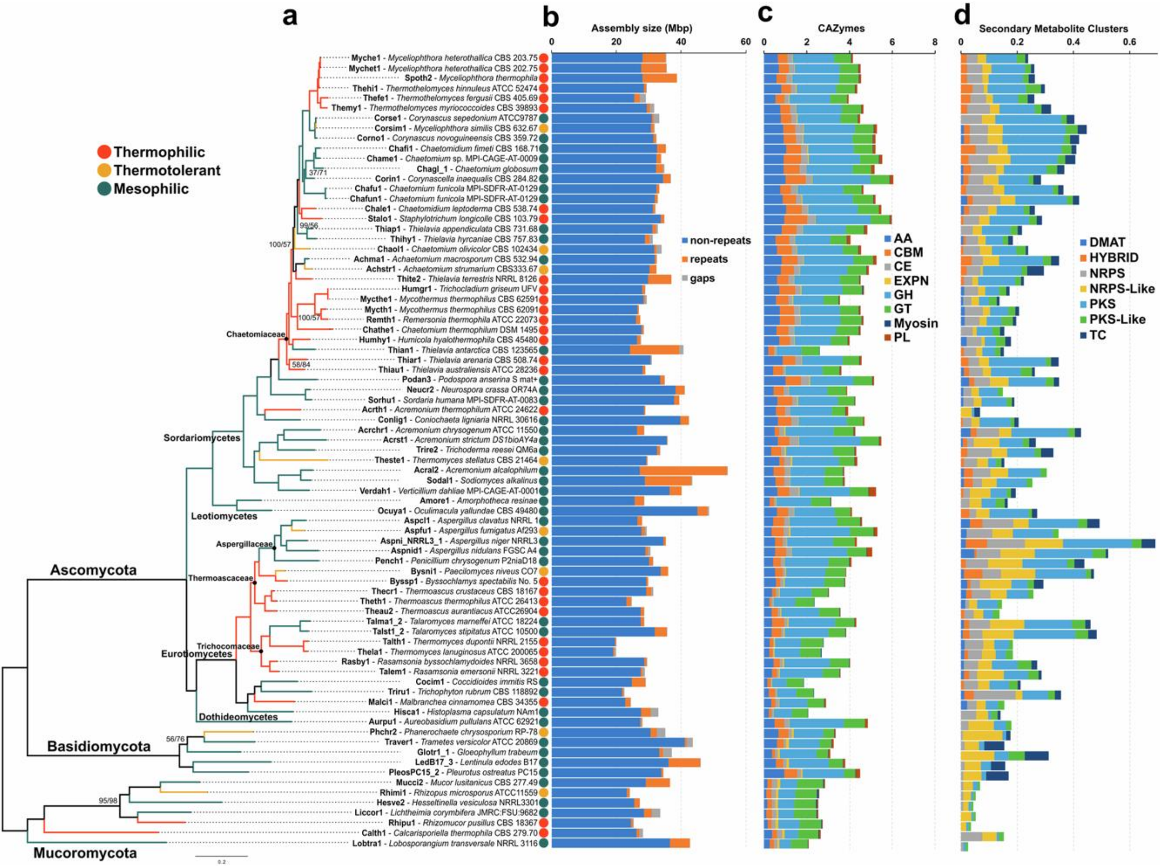
Comparative genomic analysis of thermophilic fungi reveals convergent evolutionary adaptations and gene losses

Andrei S. Steindorff, Maria Victoria Aguilar-Pontes, Aaron J. Robinson, Bill Andreopoulos, Kurt LaButti, Alan Kuo, Stephen Mondo, Robert Riley, Robert Otillar, Sajeet Haridas, Anna Lipzen, Jane Grimwood, Jeremy Schmutz, Alicia Clum, Ian D. Reid, Marie-Claude Moisan, Gregory Butler, Thi Truc Minh Nguyen, Ken Dewar, Gavin Conant, Elodie Drula, Bernard Henrissat, Colleen Hansel, Steven Singer, … Igor V. Grigoriev

JGI MycoCosm

THE FUNGAL GENOMICS RESOURCE

Comparative Genomics



29 thermophiles
8 thermotolerant
42 mesophiles

Ancestral states thermophilic (likelihood reconstruction model)

Thermophilic genomes generally have smaller size (38%)

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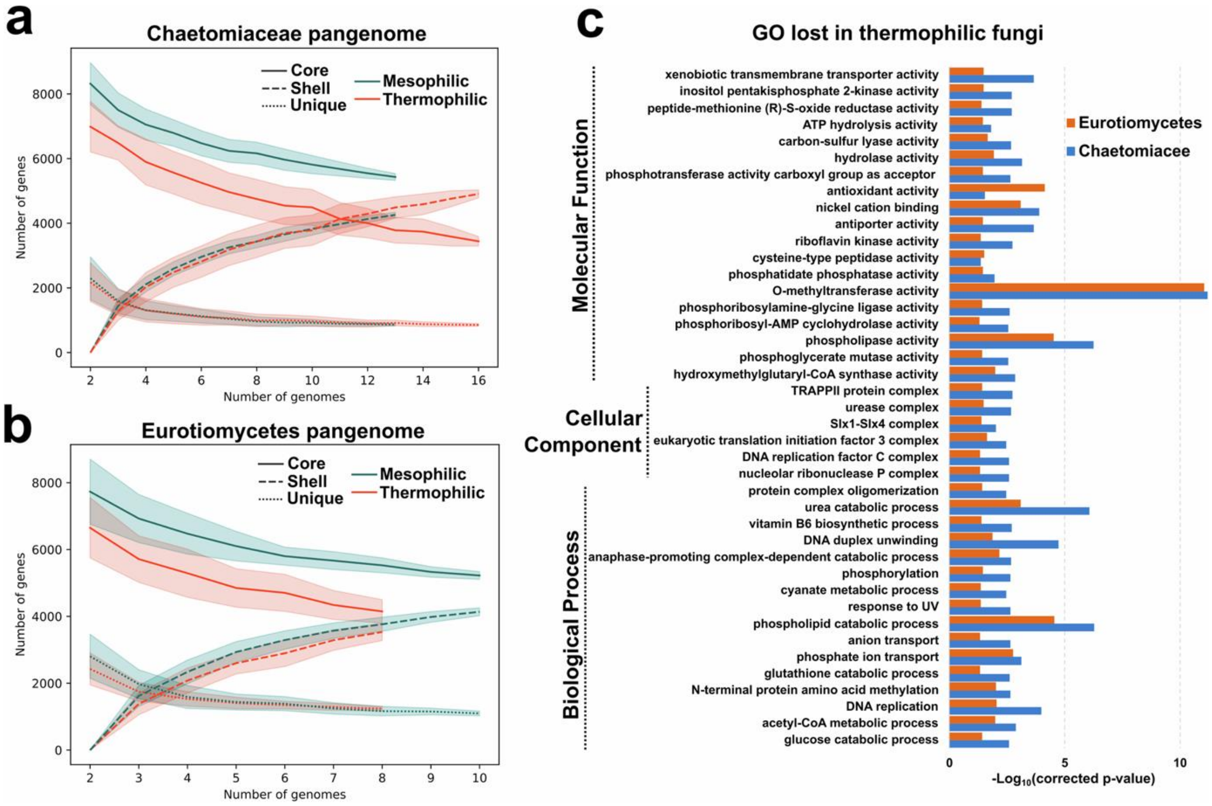
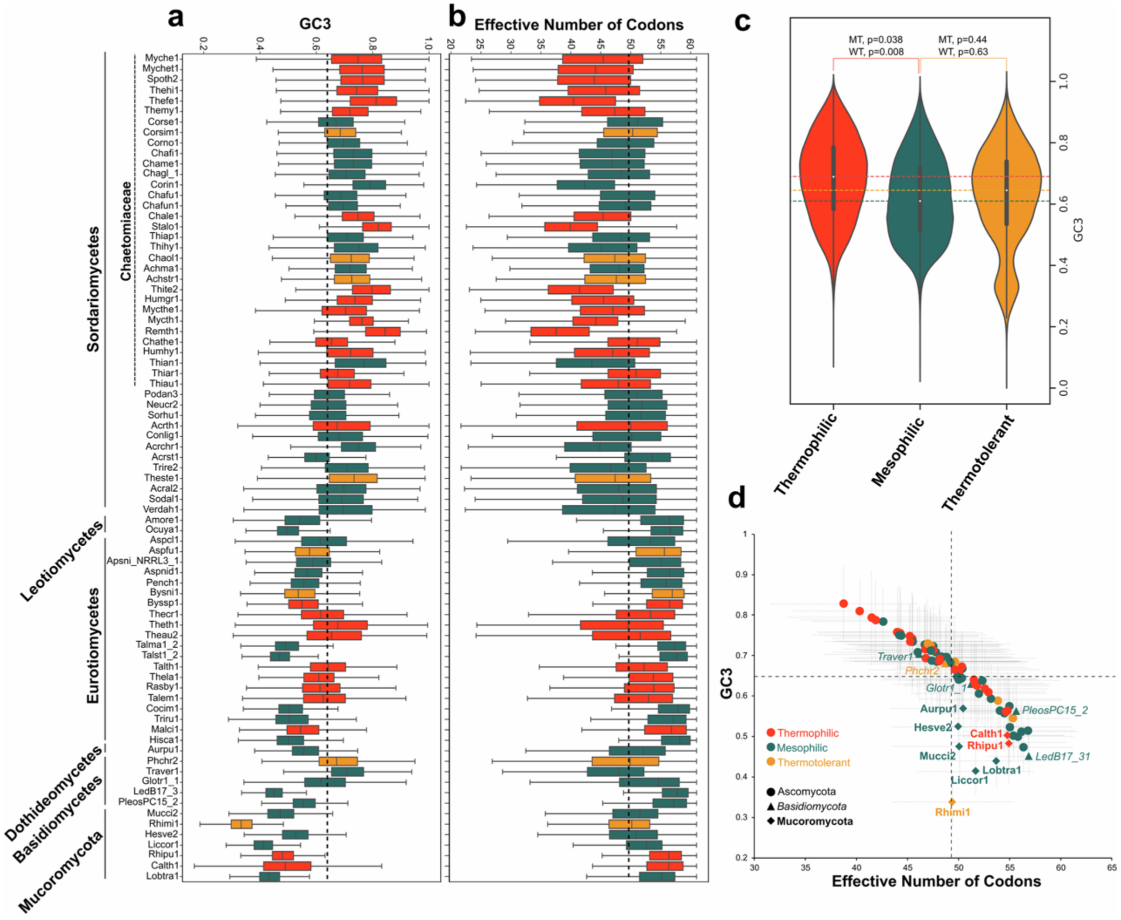
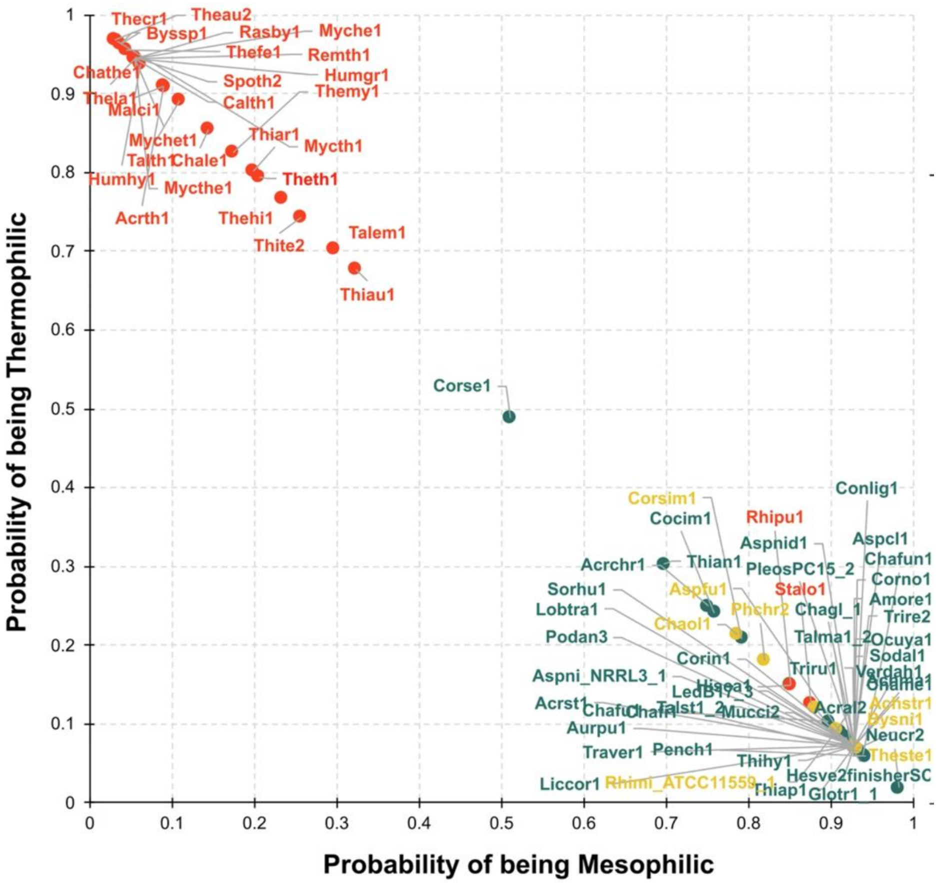


Too many differences…need to constrain the comparisons



Limited examinations showed potential signatures based on GC content of third base of codon (GC3) and ENC….

Again, trends driven by phylogenetic relationships



Support Vector Machine (SVM) to identify correlations between phenotype and gene content

20 thermophilic and 30 mesophilic genomes used for training

100 Orthogroups produced an accuracy of 70%

Identified 8 clusters with 94% accuracy

Thermotolerant consistently classified as mesophilic

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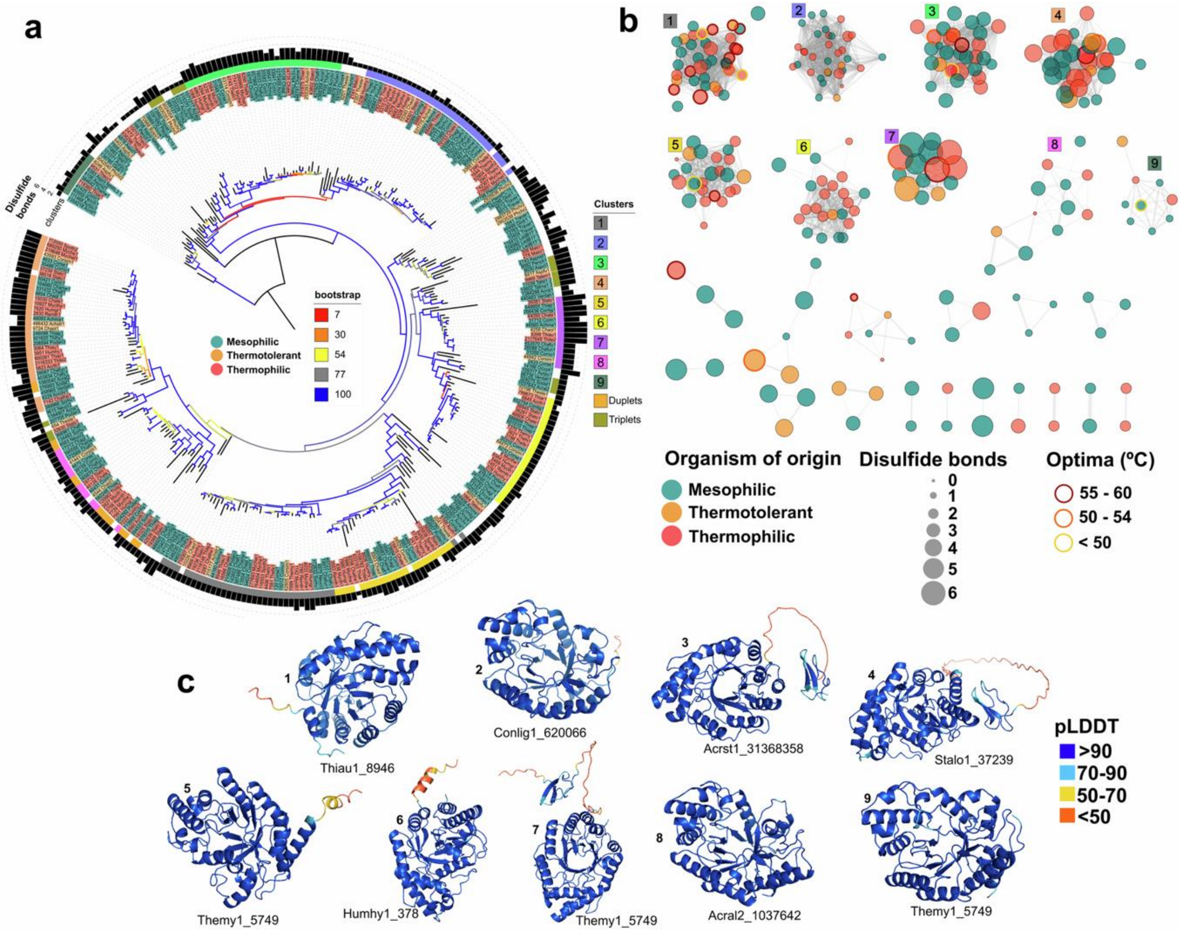


GH10 endoxylanase examined with Foldseek (structural similarity) and Alphafold2

Intermixing of sequences from thermophiles and mesophiles – some long branches (hi evo rate)

Optimal temperature data (heterologous expression) mapped on top

High optima in same cluster

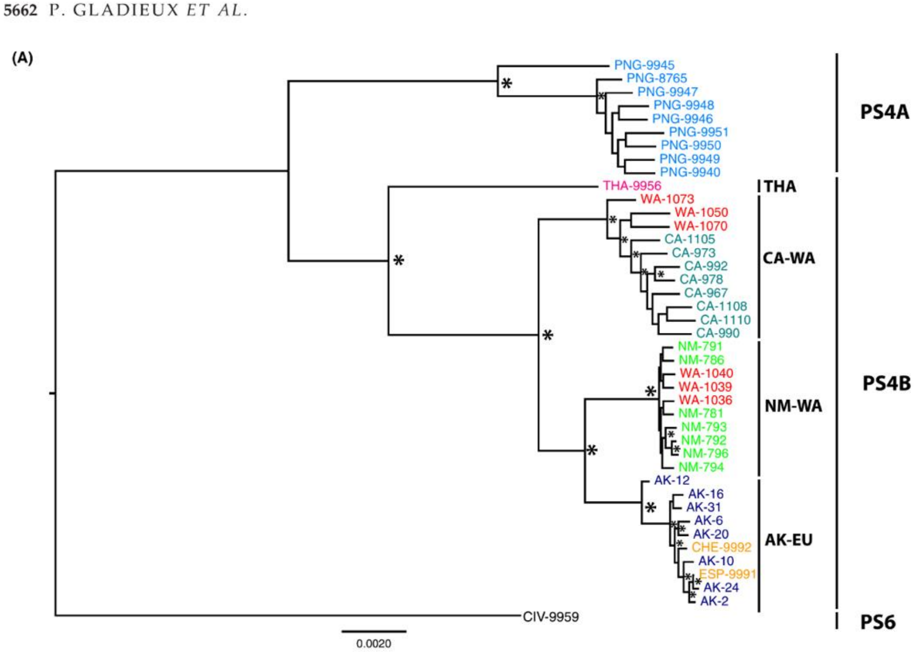
Summary

- Identified some genomic and evolutionary traits of thermophilic fungi
- Unfortunately – identification of things missing from the genome, rather than contributing to thermotolerance
- More detailed examinations and finer scales would be helpful…

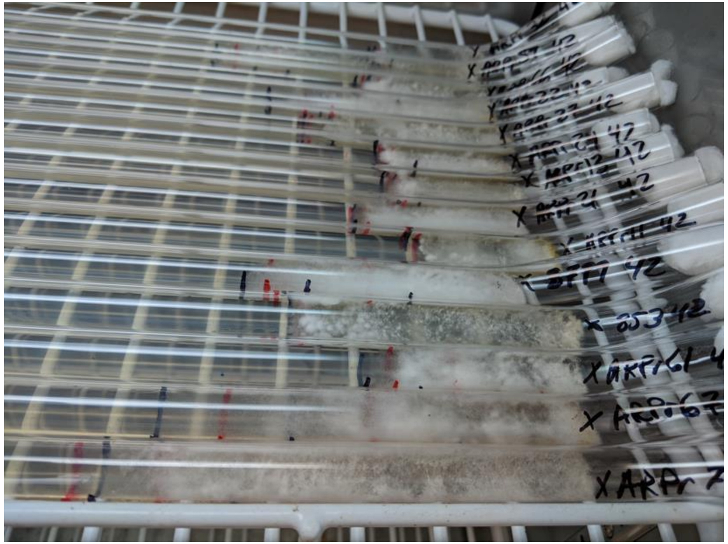
Genetics of thermotolerance in a model fungus

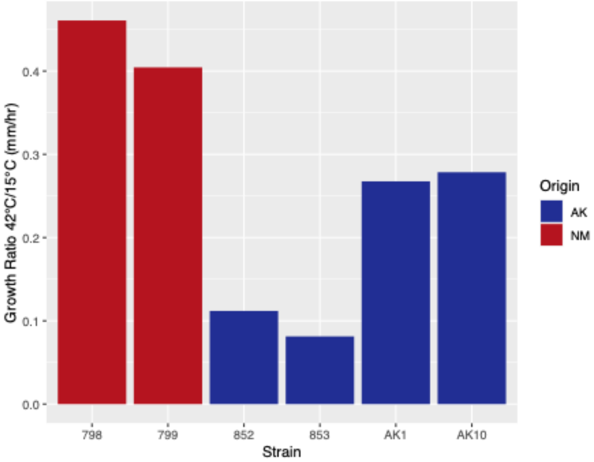
Neurospora discreta

- Found following forest fires
- Phylogenomic studies show evidence of endemic populations
- Lots of genetic resources

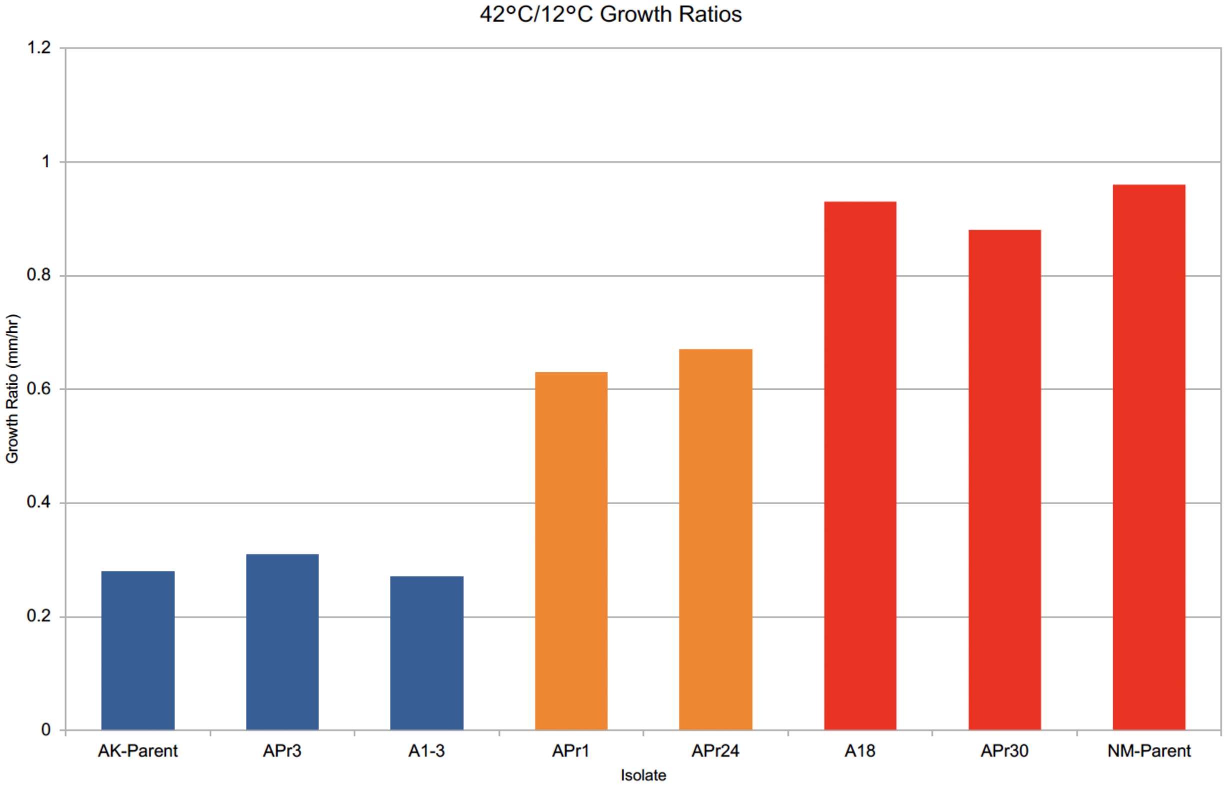


Does isolation location impact thermotolerance?



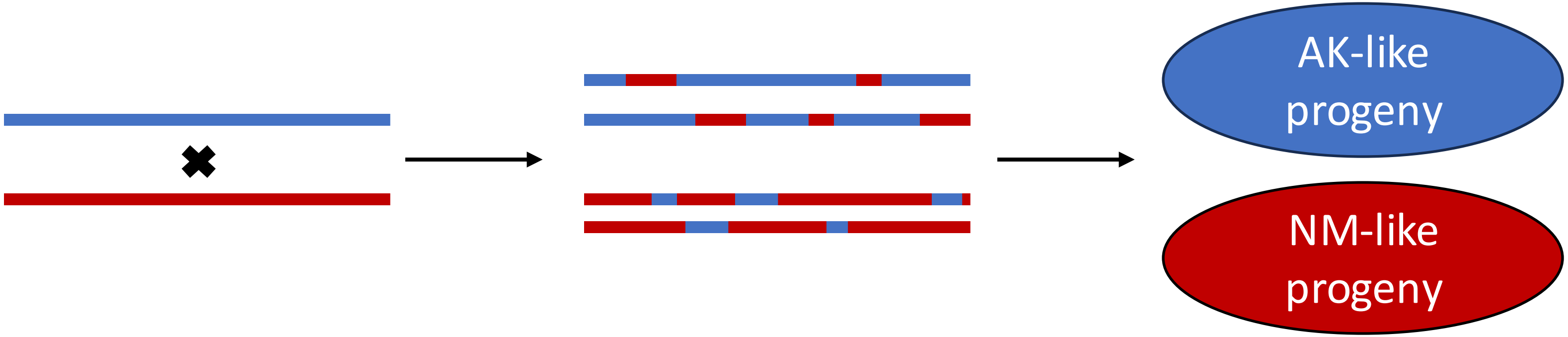


Thermotolerance is heritable and controlled by multiple loci



Identifying genomic regions contributing to thermotolerance

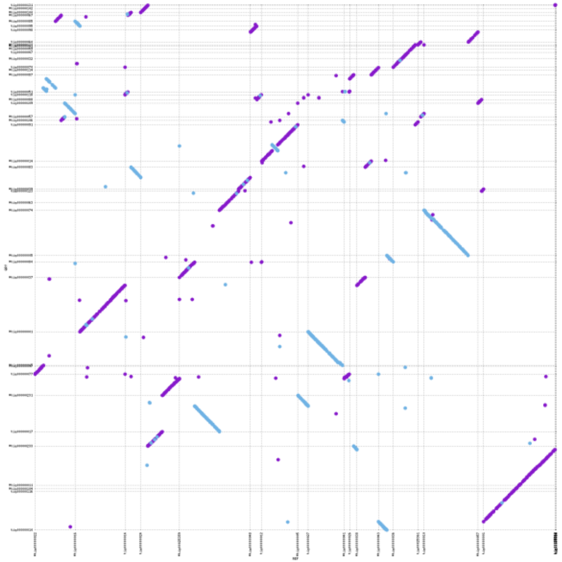
Isolate	Mating genotype
NM - 799	MAT A
NM - 798	MAT a
AK - 852	MAT A
AK - 853	MAT a
AK1	Unknown
AK10	Unknown



Parental Genome Comparison

Isolate	Genome Size	BUSCO
NM – FGSC 10342	37.5 Mb	C:94.9%[S:94.8%,D:0.1%],F:1.4%,M:3.7%,n:3817
AK – FGSC 10343	36.7 Mb	C:96.4%[S:96.2%,D:0.2%],F:1.3%,M:2.3%,n:3817

Oxford NANOPORE Technologies

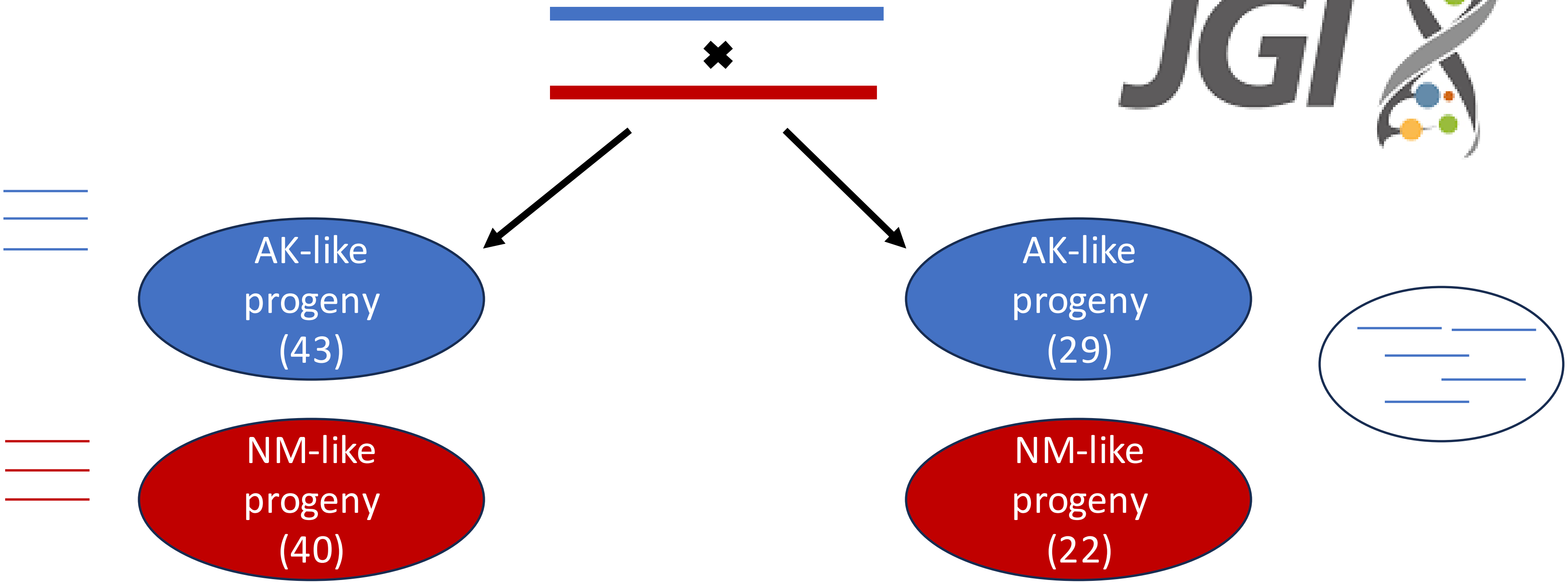


NM Predicted Gene # - 8,397

AK Predicted Gene # - 8,520

Number of genes	Number of genes in orthogroups	Number of unassigned genes
16,917	16,522 (97.7%)	395 (2.3%)

Genome-based approaches



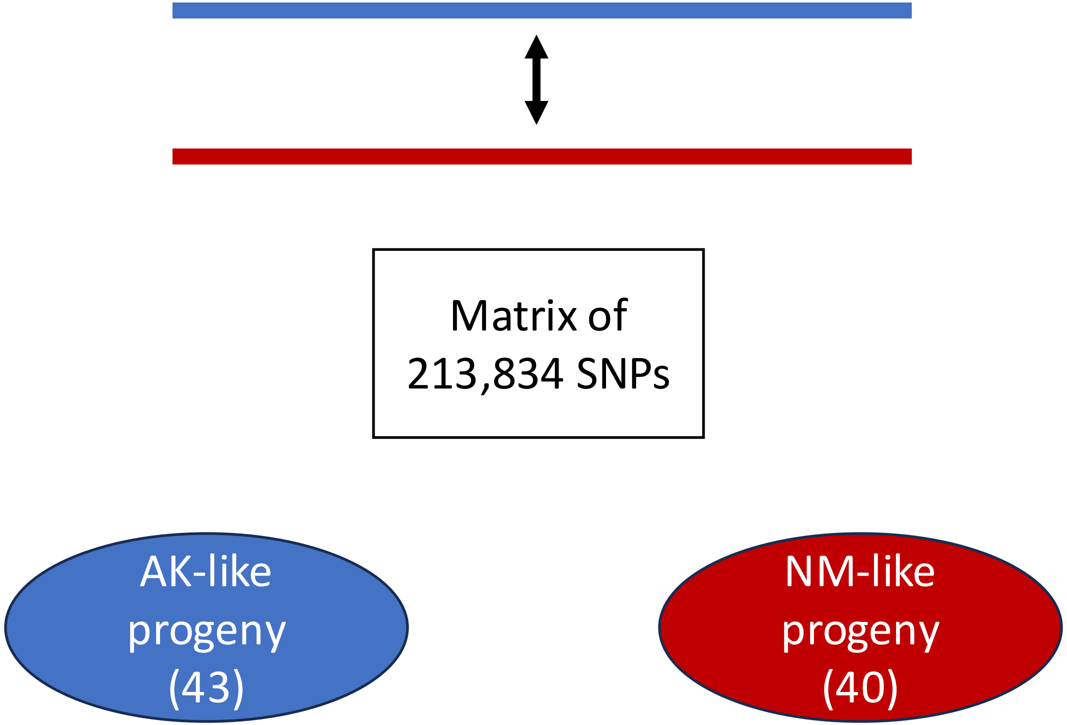
AK-like progeny (43)

NM-like progeny (40)

AK-like progeny (29)

NM-like progeny (22)

Characterizing Genotypes



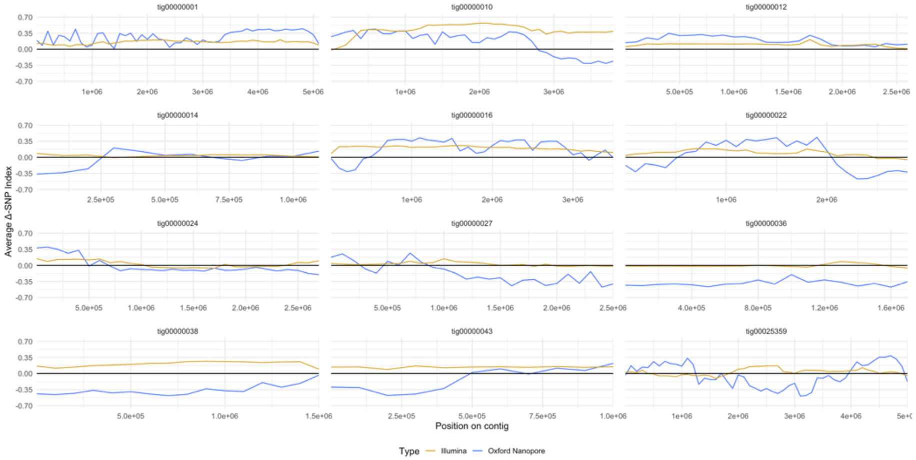
Matrix of
213,834 SNPs

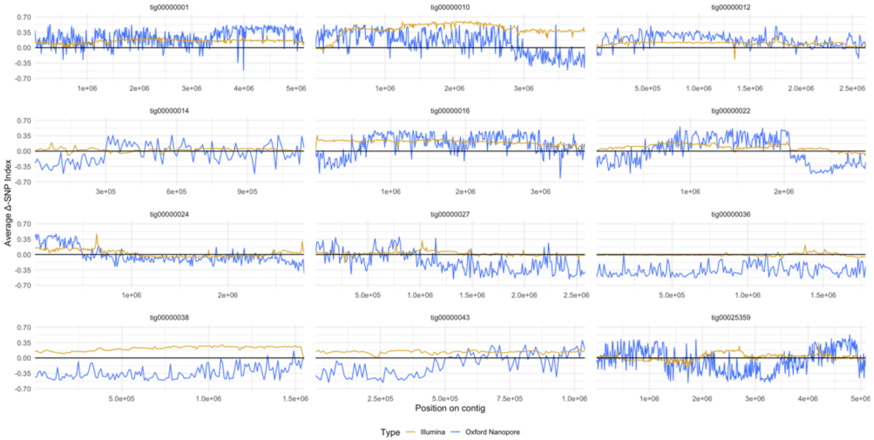
AK-like
progeny
(43)

NM-like
progeny
(40)

Largest difference
between phenotypes

Relationships between genotype and phenotype

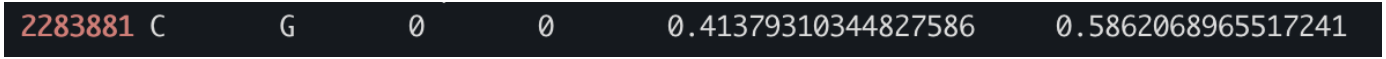




Identification of genes associated with thermotolerance

- 1 Mb region with significant correlations between genotype and phenotype
- 83 putative genes – mix of known and unknown function
- Closest blastp matches to other thermophiles
- Highest significance in NM groups – phenotyping needs improvement in AK groups
- 91 missense mutations, 64 synonymous, 11 other (intron, intergenic, splice)

Lots of intrinsically disordered proteins – next challenge for AlphaFold team!



```
2283881 C        G        0        0        0.41379310344827586        0.5862068965517241
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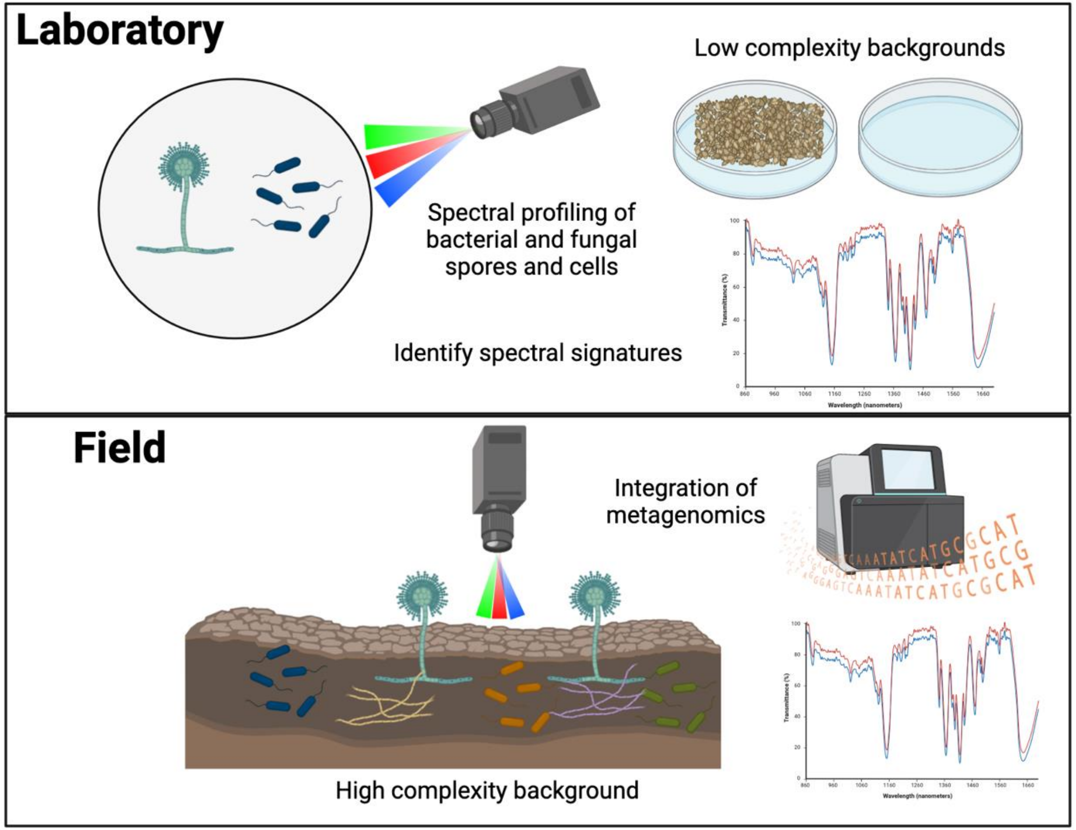
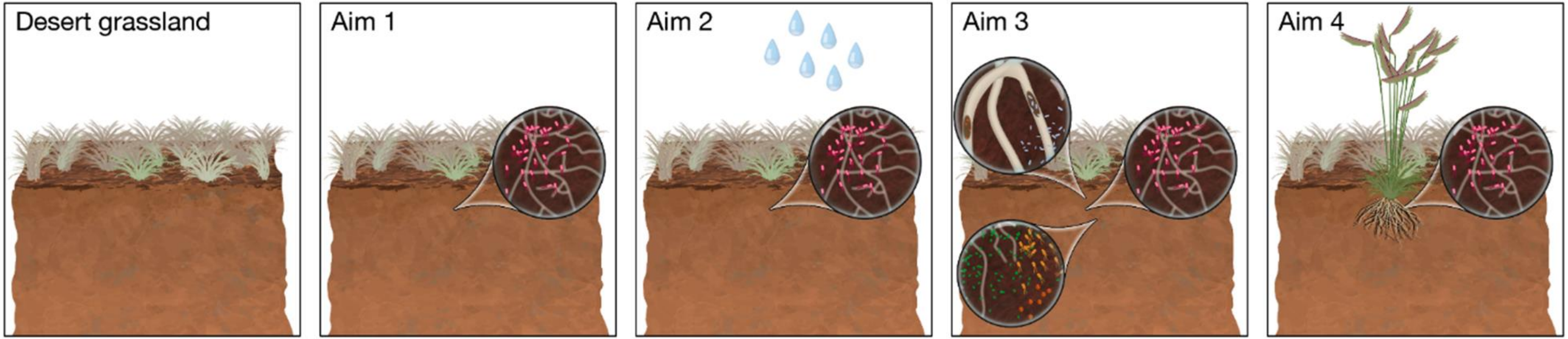
Remote Sensing of Fungi in Complex Environments



In final stages of approval for BSL-2 lab (BLOOM) for working with pathogenic fungi and culturing from soils and wastewater

Integrating other forms of characterization

Fungal Interactions



Bioinformatic Resources for BFI

- Had any interactions been previously described between bacteria and fungi from our system?

- Lack of centralized resources and knowledgebases for BFI research…so we built our own!

BFI Research Portal

https://sfa-bfi.edgebioinformatics.org/

Fungal Biology

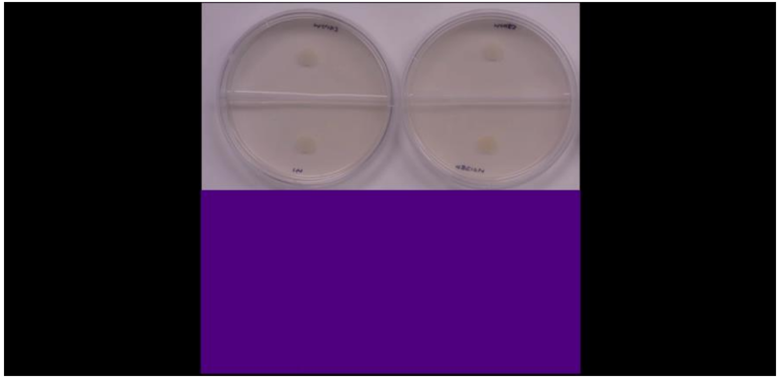
Volume 127, Issue 5, May 2023, Pages 1005-1009

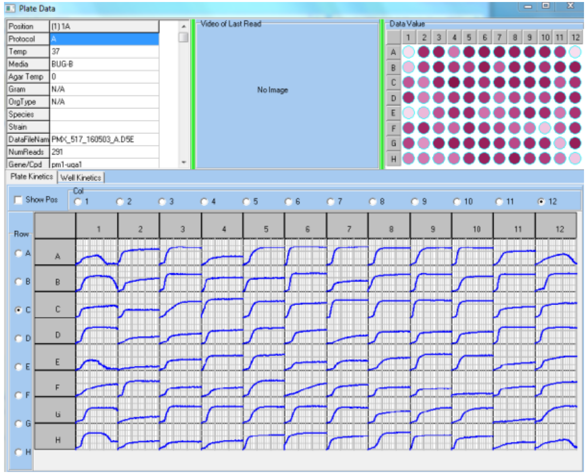
A centralized resource for bacterial–fungal interactions research

Aaron Robinson [1], Michal Babinski [1], Yan Xu, Julia Kelliher, Reid Longley, Patrick Chain

Developing methods to efficiently identify and characterize interactions

- Mix of imaging, metabolic, and omics to characterize how fungi interact with bacteria and other organisms
- **Environmental** – understand community dynamics toward more accurate models (abiotic and biotic)
- **Security** – Signatures of pathogens and potential countermeasures
- Interactions to **enhance** or **deter**





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Agar Temp	0
Gram	N/A
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Species	
Strain	
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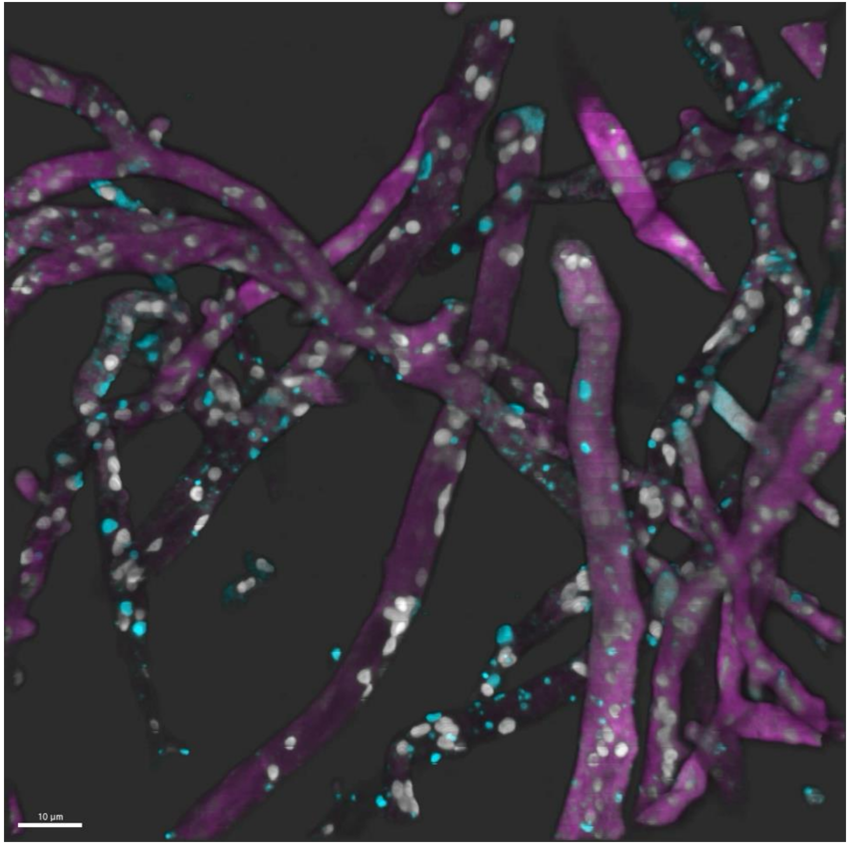
Gene/Cpd	pm1-uga1

Hyphal networks in soil and health



Acknowledgements

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Chain BFI SFA TEAM

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Justine Macalindong
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Remote Sensing DI

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