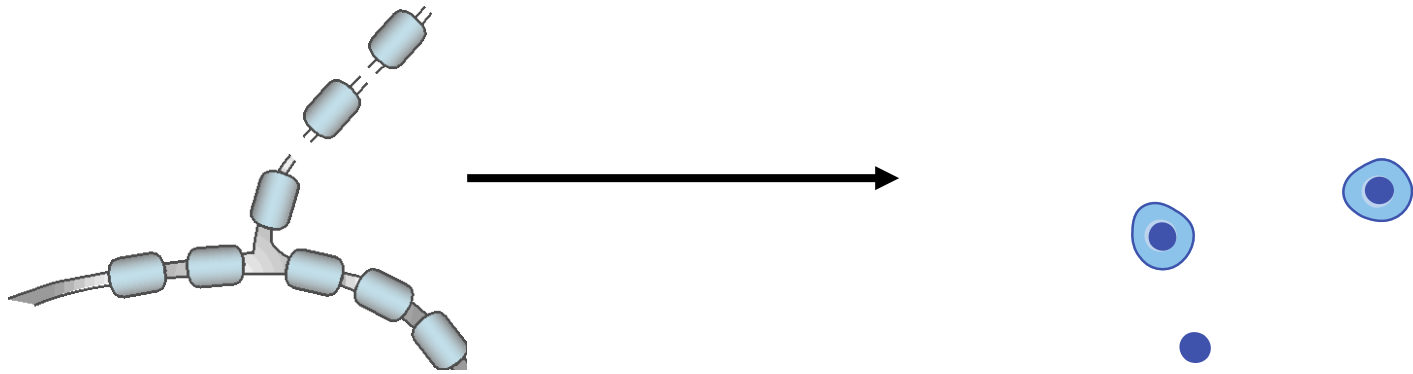


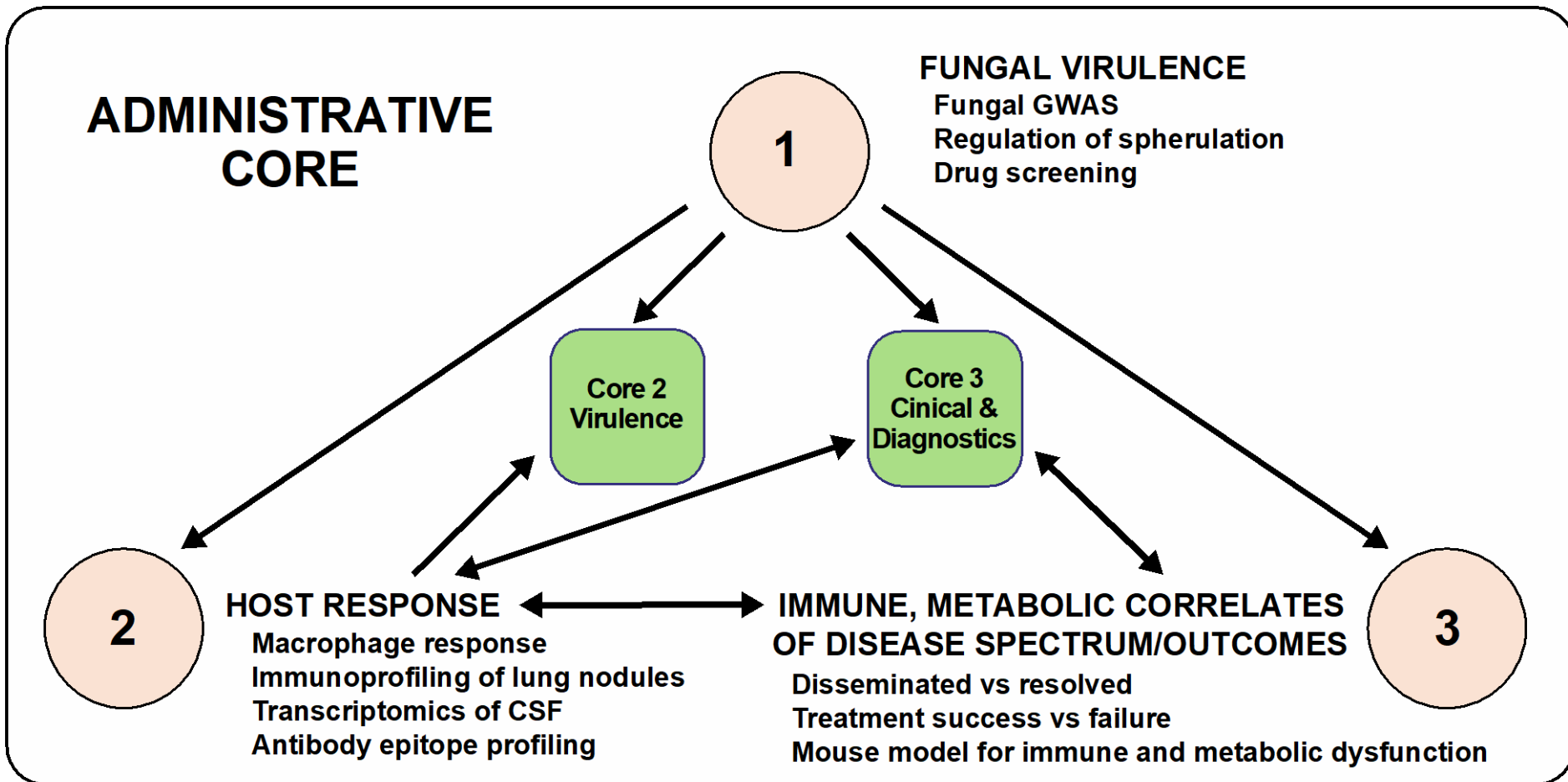
Virulence Gene Discovery in *Coccidioides*



Anita Sil

Dept. of Microbiology & Immunology, UCSF

***Coccidioides* Collaborative Research Center Grant**

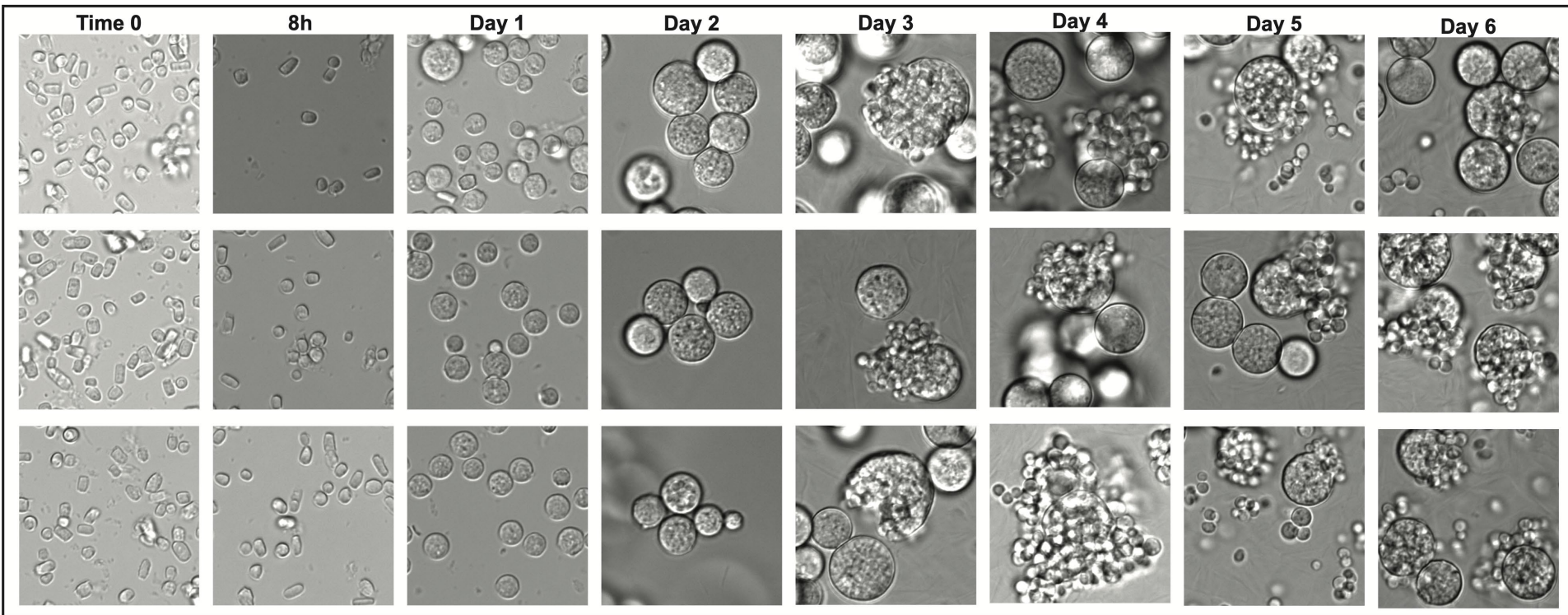


PIs: Anita Sil (UCSF) and Satya Dandekar (UCD)

Rachel Brem, Michael Wilson, Michael Peterson, GR Thompson, Bridget Barker

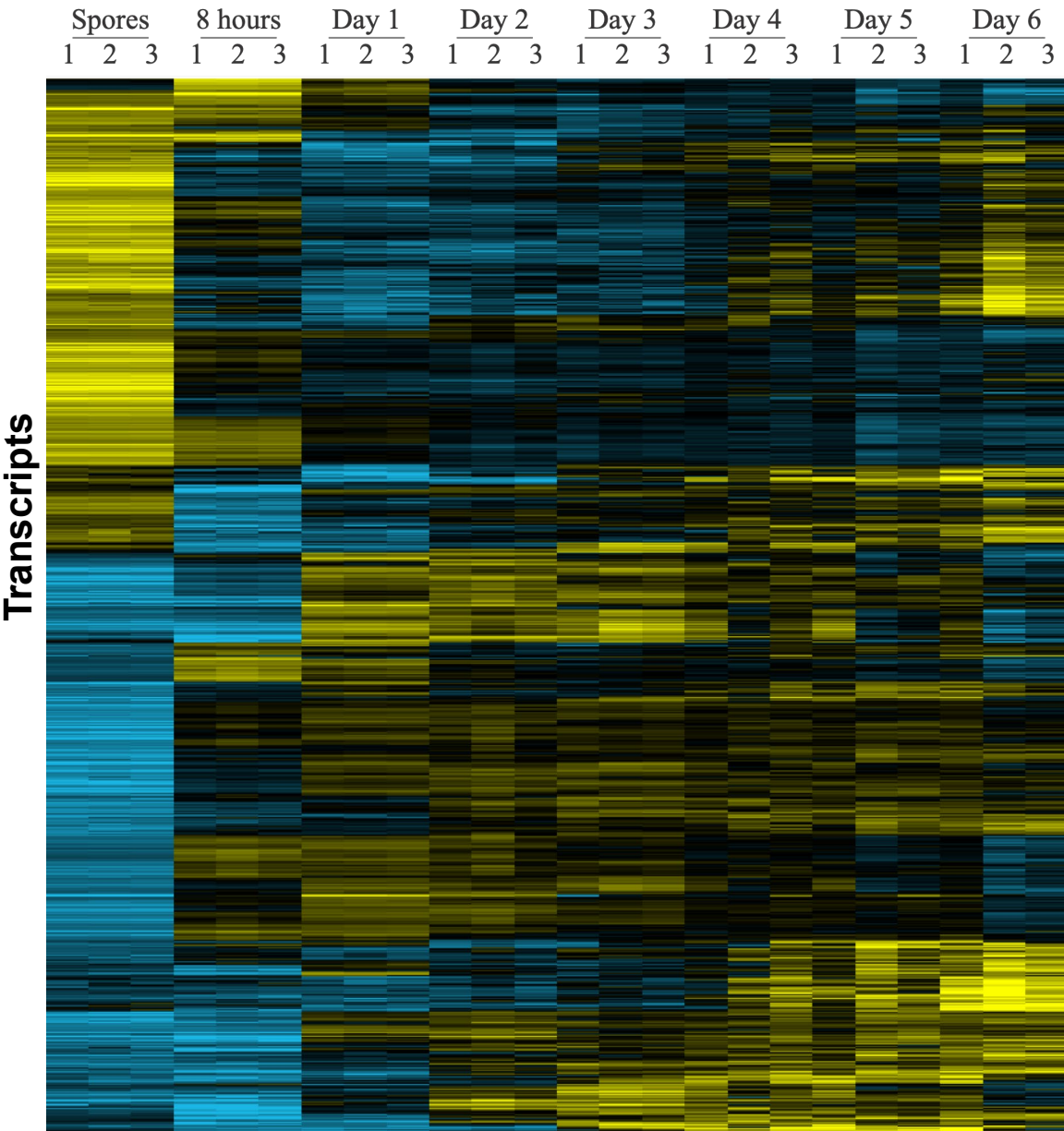
Investigating the transcriptional program of *Coccidioides* development

Robust and reproducible production of endosporulating spherules



DIC 40x, 1.6x eyepiece
Converse + 0.5% Tamol, 39°C, 10% CO₂

Massive transcriptional remodeling during spherulation

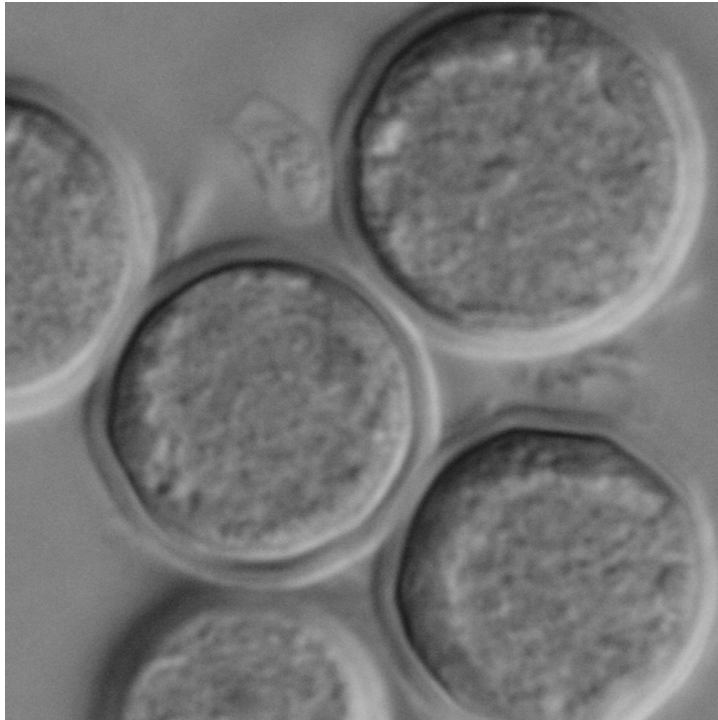


3345 genes

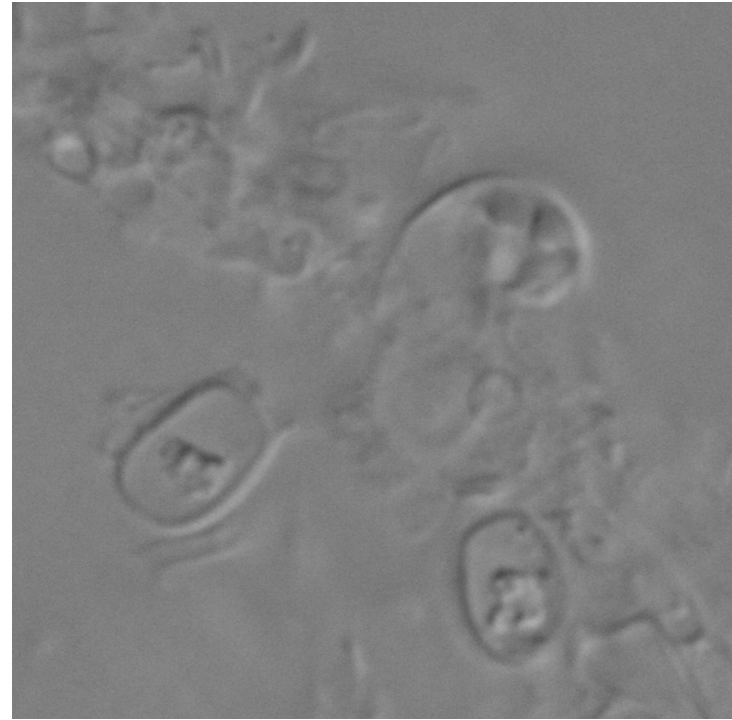
4X change, FDR 1

Ryp1 is required for spherulation in *Coccidioides*

Wild-type

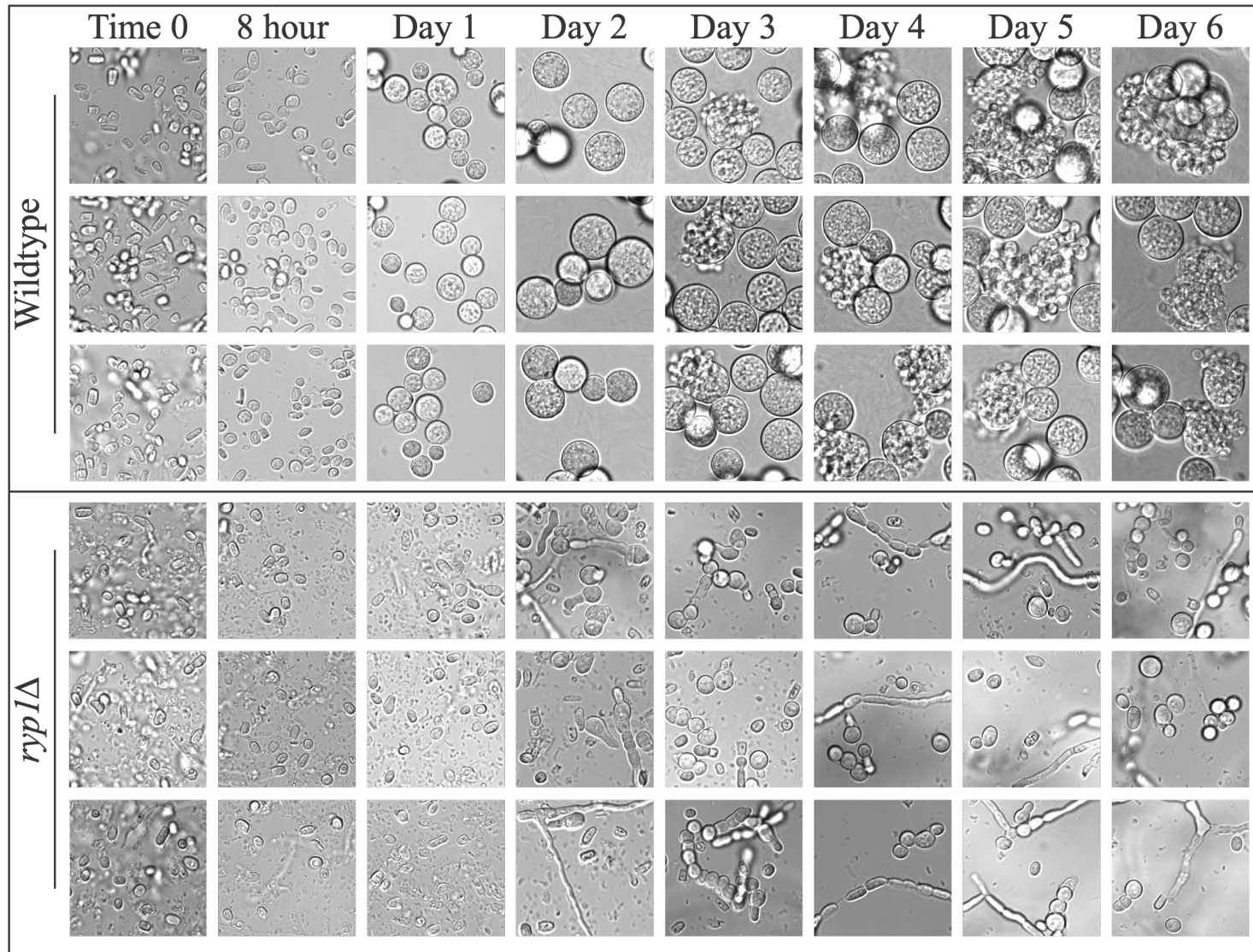


$\Delta ryp1$



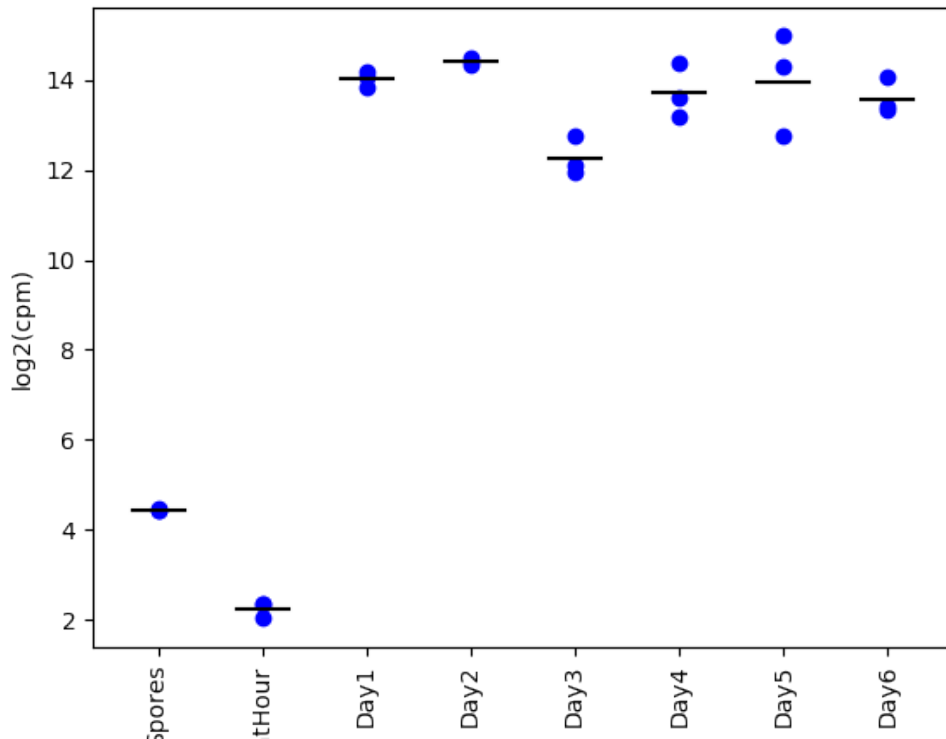
$\Delta ryp1$ mutants are avirulent in the mouse model of infection

ryp1 mutant undergoes aberrant development



DIC II 40x, 1.6x eyepiece

SOWgp is a spherule outer wall protein specific to *Coccidioides*



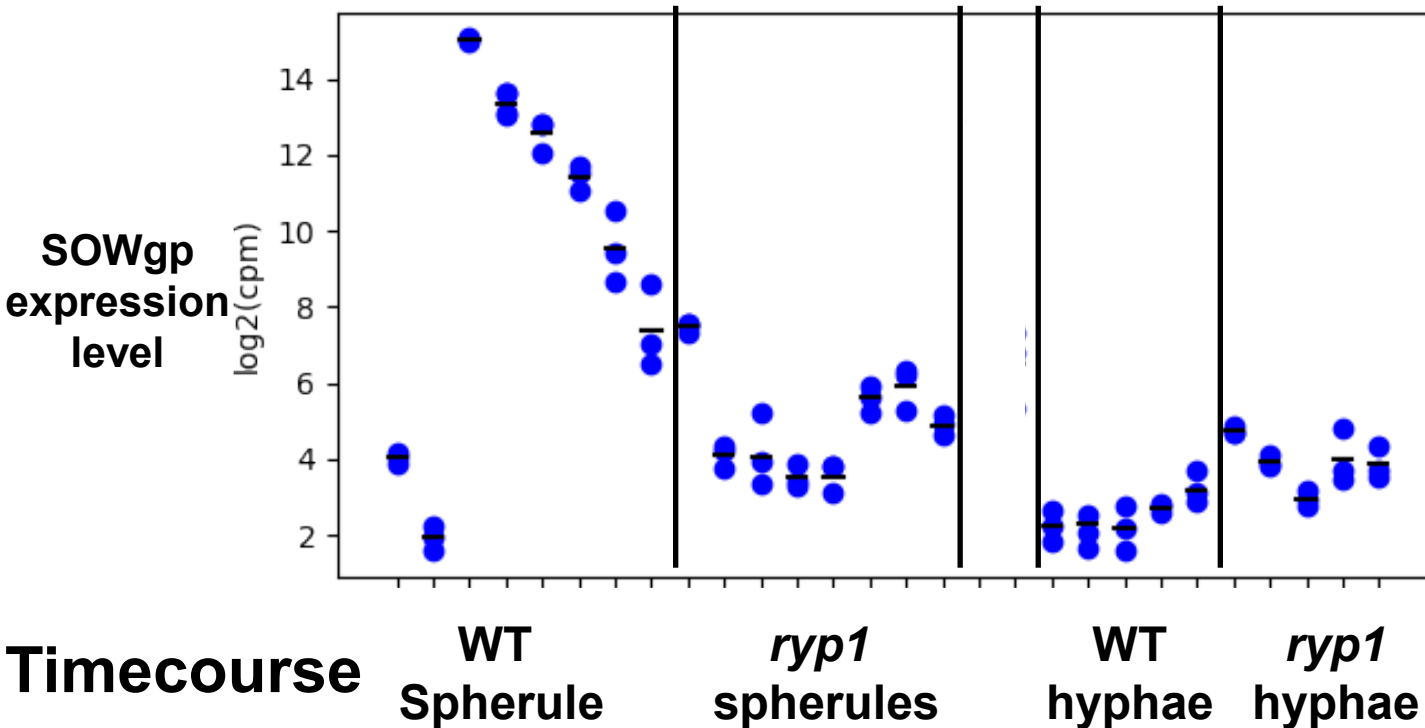
Identified by Chiung-Yu Hung and Garry Cole

Immunodominant cell-surface proline-rich antigen

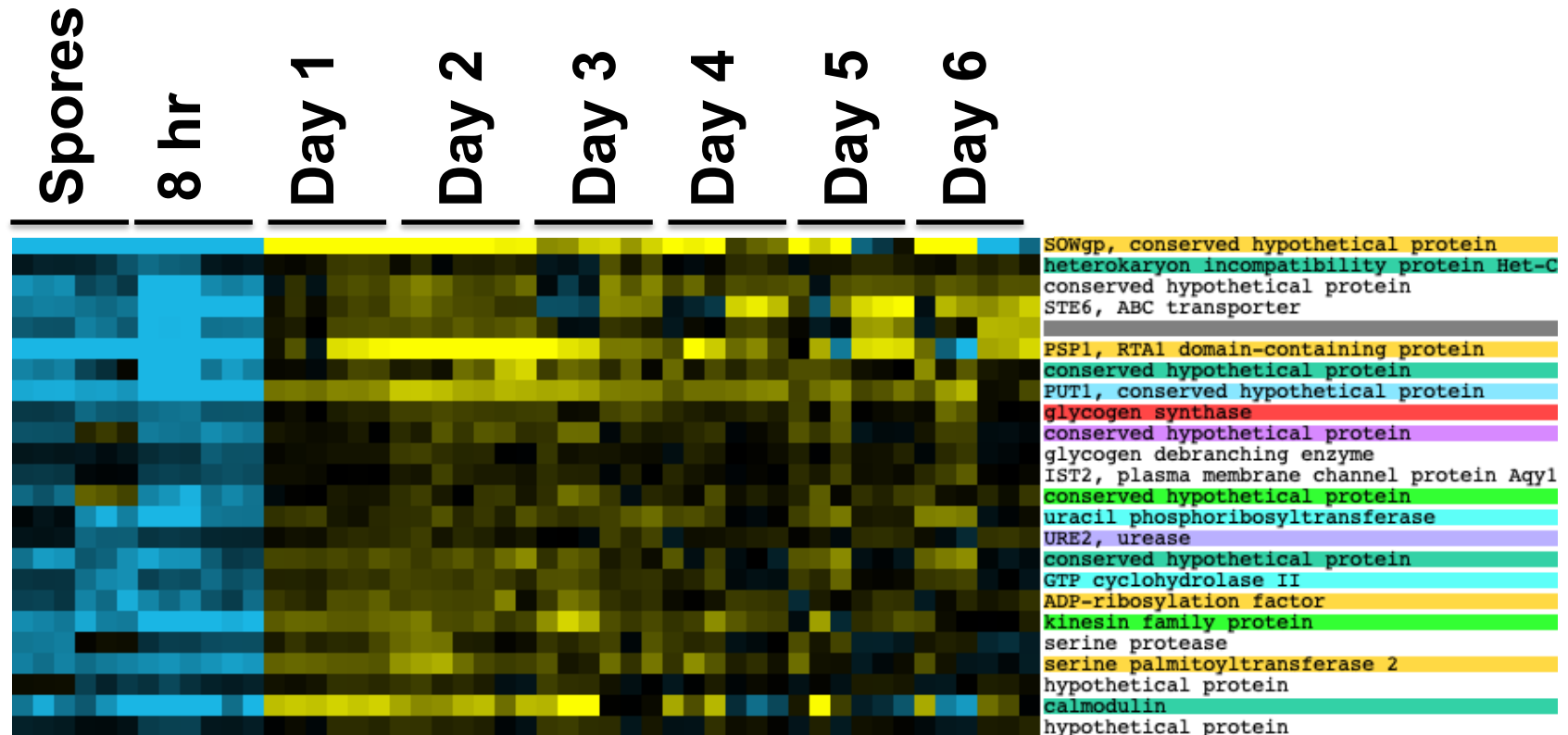
Expressed only in spherules

Mutants have reduced virulence in mouse model

SOWgp expression in spherules is Ryp1-dependent

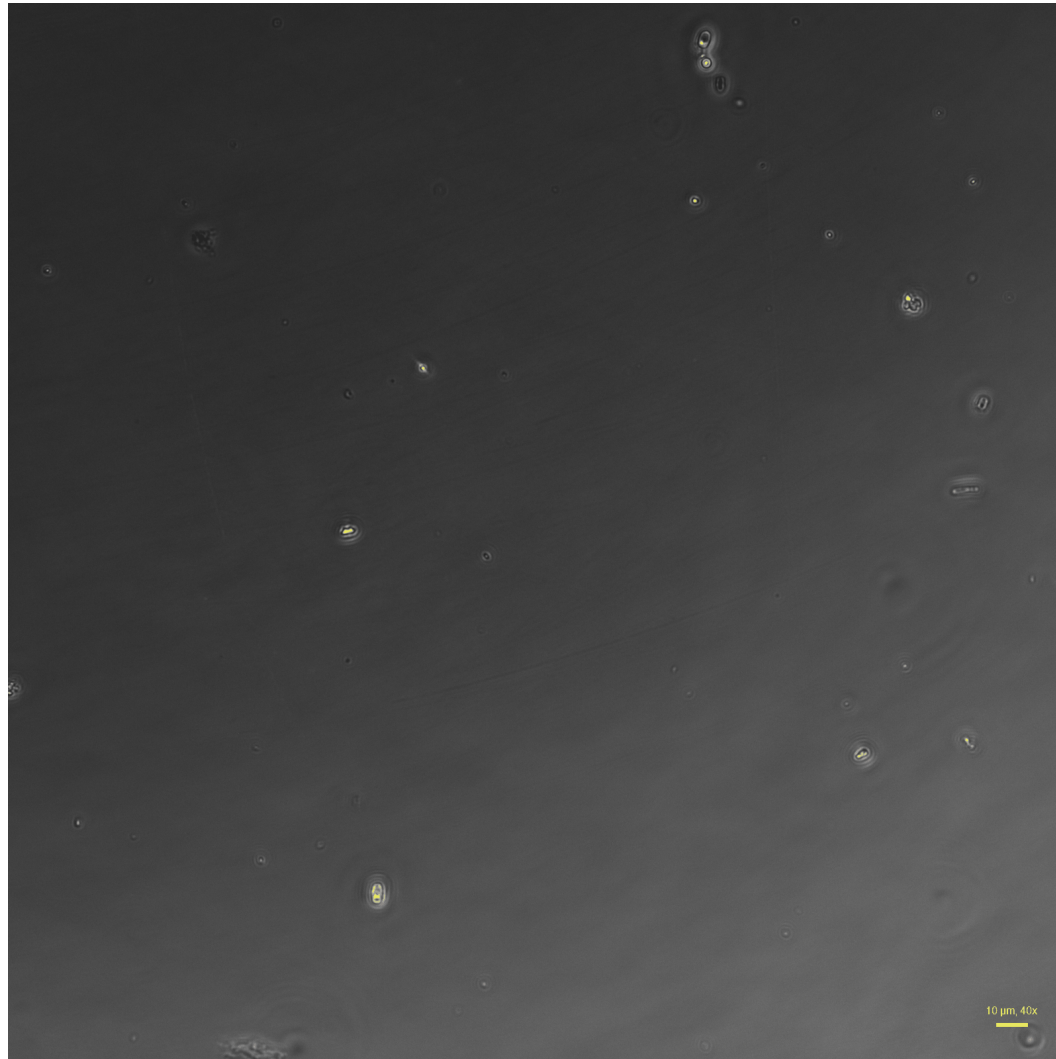


Ryp1-dependent genes that cluster with SOWgp will be interrogated for roles in virulence

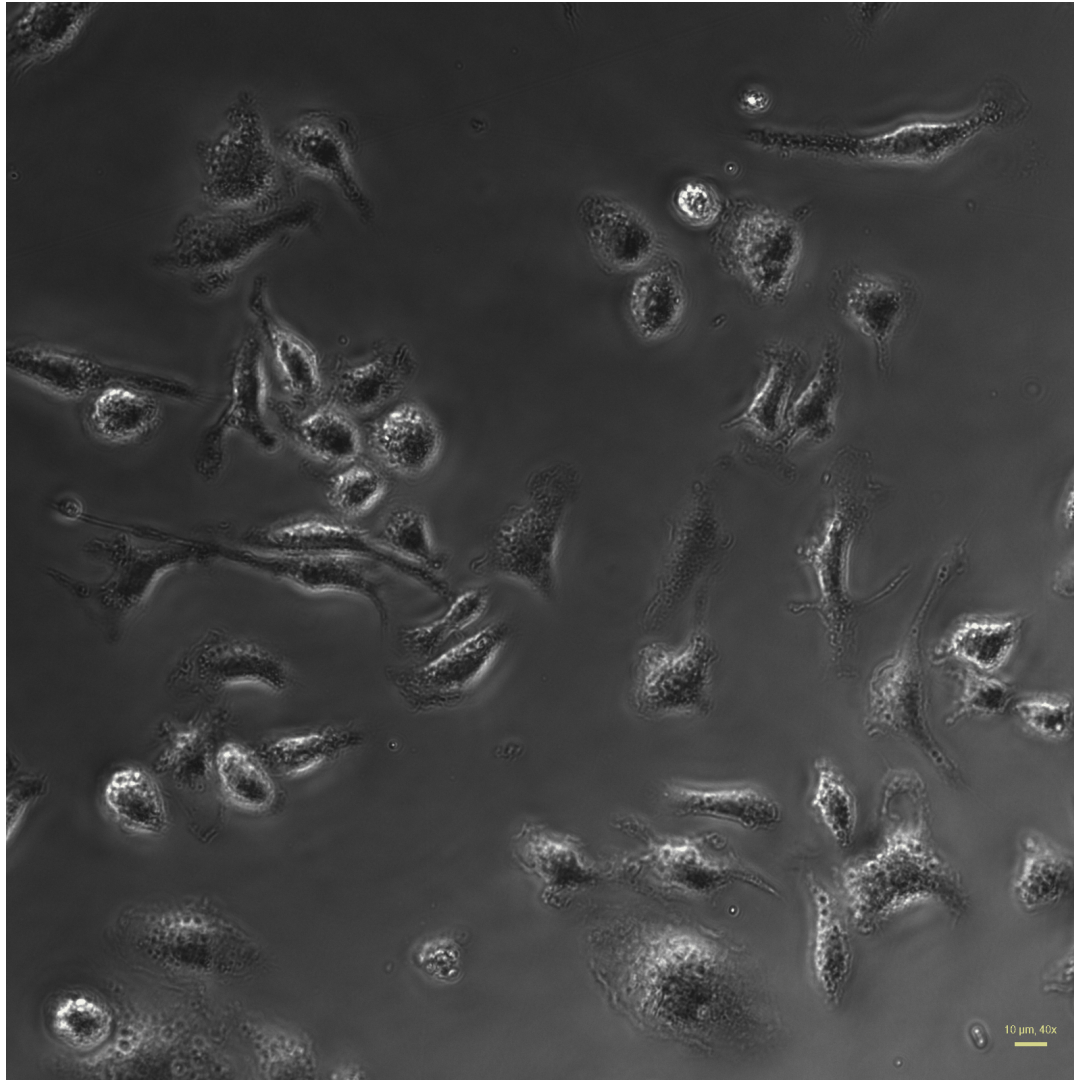


**What is the conversation
between *Coccidioides* and
innate immune cells?**

***Coccidioides* arthroconidia germinate to give rise to hyphae under “macrophage” conditions**



Macrophages stimulate development of spherules



Conclusions

- **Dramatic transcriptional shifts occur during spherulation**
- **The transcriptional programs of *Coccidioides* spherules and hyphae are partially dependent on the transcription factor Ryp1**
- **Spherule-specific genes will be interrogated for roles in virulence**
- **Macrophages stimulate spherulation**

Acknowledgements

Current Lab Members

Nebat Ali
Dror Assa
Bevin English
Anyce Godoy
Sarah Heater
Noé Madrueno Hernandez
Christina Homer
Murat Can Kalem
Anna Morrison
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Mark Roxas
Jane Symington
Mark Voorhies

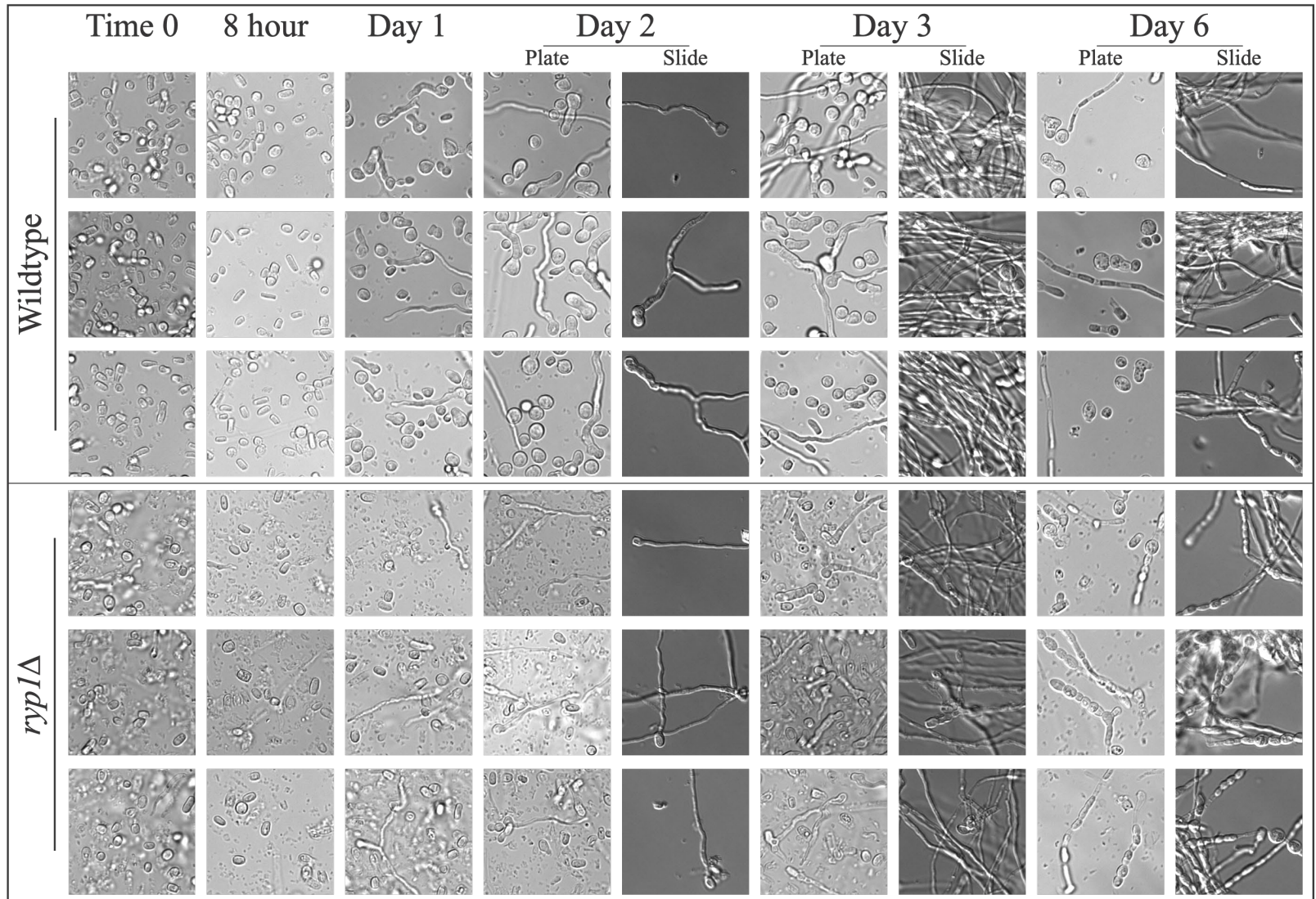
Coccidioides collaborators

Bridget Barker, NAU
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Aaron Hernday, UCM
Katrina Hoyer, UCM
Jason Stajich, UCR
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Michael Peterson, UCSF Fresno
Marc Orbach and Ale Mandel, UAZ
Satya Dandekar and GR Thompson, UCD
Michael Wilson, UCSF

Former Lab Members who started *Coccidioides* work

Sinem Beyhan (JCVI, UCSD)
Jessie Uehling (now at Oregon State University)
Bastian Joehnk (now at Formo, Germany)
Keith Walcott (first-year Tetrad student UCSF)

Hyphal formation by WT and *ryp1* mutant



DIC II 40x, 1.6x eyepiece