

 FUNGAL BIOLOGY

Fungal shape-shifting

Histoplasma capsulatum is a primary fungal pathogen that can switch between a sporulating hyphal form in the soil and a yeast form in the host. Growth in the yeast form is thought to be essential for pathogenesis. Building on previous work from their laboratory, Webster and Sil

describe two factors that are part of the complex regulatory network that regulates formation of both yeast cells and spores.

The switch from hyphal to yeast forms can be recapitulated by shifting the temperature from room temperature to 37°C, the temperature of the mammalian host. The authors took advantage of the distinct appearance of hyphal- and yeast-form colonies to identify mutants that are unable to grow in the yeast form at 37°C. The deficient genes in these mutants, the hyphae of which grew independently of temperature, were named *RYP2* and *RYP3*. In wild-type cells, both *RYP2* and *RYP3* are more highly expressed at 37°C than at room temperature.

When grown at room temperature, the *ryp2* and *ryp3* mutant hyphae produced spores at a higher frequency than wild-type cells. Many of the mutant spores were not viable and appeared to lyse easily, indicating that Ryp2 and Ryp3 are required for production of viable spores, the most common infectious particle. Those mutant spores that were viable

germinated into hyphae after ingestion by macrophages, unlike wild-type spores, which germinate into yeast forms after phagocytosis.

The Ryp2 and Ryp3 proteins belong to a family that includes the velvet A protein in *Aspergillus nidulans*, a protein that regulates fungal spore formation. Furthermore, the similarity of the phenotypes of the *ryp2* and *ryp3* mutants with the *H. capsulatum ryp1* mutant recently described by the Sil laboratory led the authors to propose that Ryp2 and Ryp3, like Ryp1, could have a role in transcriptional activation. The authors show that Ryp1 binds directly to the upstream region of *RYP2*, but not *RYP3*. The authors speculate that the Ryp proteins function as a complex to regulate the formation of spores at room temperature and to stimulate the switch to the yeast form at 37°C.

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ORIGINAL RESEARCH PAPER Webster, R. H. & Sil, A. Conserved factors Ryp2 and Ryp3 control cell morphology and infectious spore formation in the fungal pathogen *Histoplasma capsulatum*. *Proc. Natl Acad. Sci. USA* **105**, 14573–14578 (2008)

