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Glyoxylate cycle as drug target?

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The fungus *Candida albicans* is part of the normal intestinal flora of mammals but is responsible for most of the fungal infections seen in immunocompromized patients. *Candida* cells are normally phagocytosed by macrophages and neutrophils, and patients deficient in these immune cells are highly susceptible to systemic candidiasis.

In the 5 July issue of Nature, Michael Lorenz and Gerald Fink at the Whitehead Institute for Biomedical Research, Cambridge, Massachusetts, demonstrate that the glyoxylate cycle is required for fungal virulence, and suggest that this may provide a novel target for chemotherapy.

They demonstrated that phagocytosis leads to the upregulation of the glyoxalate cycle in *C. albicans*, as marked by the upregulation of the principal enzymes isocitrate lyase (ICL1) and malate synthase (MLS1). When mice were infected with either wild-type fungus or a strain lacking *ICL1*, those injected with wild-type fungus rapidly developed candidiasis and died after an average of 3 days; those infected with the *ICL1*-deficient strain survived much longer (at day 28, 7 of 10 mice were still alive).

Glyoxylate cycle genes have now been identified in two organisms capable of surviving in macrophages: a bacterium, *Mycobacterium tuberculosis*, and a fungus, *C. albicans*. The enzymes of the glyoxylate cycle are not present in humans and so may present an ideal target for novel antibiotics.

References

1. Lorenz MC, Fink GR: The glyoxylate cycle is required for fungal virulence. *Nature* 2001, 412:83-86., [http://www.nature.com/nature]

2. Whitehead Institute for Biomedical Research, [http://www-genome.wi.mit.edu]