RESEARCH ADVANCES

Host Signals Can Trigger Virulence in Candida albicans

Shannon Weiman

The virulence of Candida albicans changes in response to signals within and from the host, according to several researchers who spoke during the 28th Fungal Genetics Conference, held in Pacific Grove, Calif., last March. In some cases those host signals render this yeast innocuous. In other circumstances, however, C. albicans upregulates virulence factors in response to host signals, becoming an outright pathogen. A recent thrust of research is to reveal those signals that trigger such responses as well as the fungal regulatory pathways that respond to them, with a longer-term goal of combating infections not by killing this yeast, but by blocking virulence.

“C. albicans is the dominant [fungal] commensal of the human gastrointestinal tract, as well as the most common invasive fungal pathogen,” says Suzanne Noble of the University of California, San Francisco. In its commensal state, gastrointestinal induced transition (GUT) cells of C. albicans are attenuated for mutualism. However, in its pathogenic invasive “white” form, metabolic and other adaptive changes enable these changed yeast cells to invade the host. This switch of C. albicans is triggered by gut environmental signals and mediated by the Wor1 transcription factor, she says. “The resulting GUT cells differ morphologically and functionally from previously defined cell types, and express a transcriptome that is optimized for the digestive tract ... exhibiting a striking reorientation of cellular metabolism towards nutrients available in the distal mammalian GI tract.”

Carbon dioxide and N-acetylglucosamine are candidate signals from the host controlling this Wor1-induced transcription, Noble continues. “Our results indicate that the ability of a commensal organism to produce disease is not merely a consequence of impaired host immunity. The identification of specialized states for C. albicans commensalism and virulence offers opportunities for prevention as well as treatment of clinical diseases produced by this important human pathogen.”

Meanwhile, temperature changes unambiguously can increase the virulence of C. albicans, according to Michelle Leach of the University of Aberdeen in the United Kingdom. When exposed to relatively higher tempera-
C. albicans host develops a fever, features such as those encountered when a host makes called virulence factors involved in adhesion, biofilm formation, and filamentation. This takeover can be followed in vitro by growing these two bacterial species together on a plastic substrate or on airway epithelial cells from individuals with CF, according to O’Toole. Identifying and determining the mechanisms underlying the takeover “are the initial steps to understanding how CF microbial lung communities develop and affect patient health,” he says.

When P. aeruginosa steals iron from other bacteria, levels of the molecule it makes called Pseudomonas quinolone signal (PQS) also rise, according to Oglesby-Sherrouse’s graduate student Angela Nguyen. During coculture in anaerobic metabolism, slowing the latter’s growth while appropriating lactate and iron to accelerate its own growth, according to O’Toole. This process depends on the quorum sensing molecule 4-hydroxy-2-heptylquinolone-N-oxide (HQNO) and two iron-binding molecules, pyoverdine and pyochelin, boosting expression of fermentation pathway genes in S. aureus, he says.