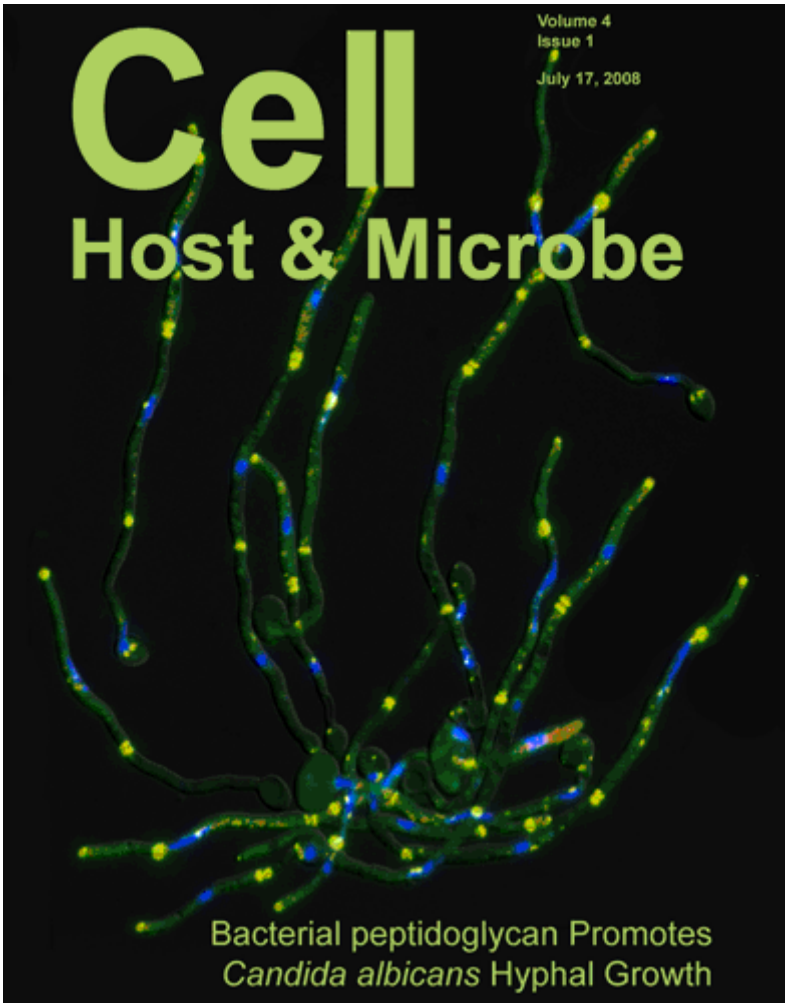
Research

Candida albicans Molecular & Cellular Biology

Infectious diseases are the leading cause of human death worldwide. Previously controllable pathogens are returning with higher virulence and unknown pathogens are emerging to cause new diseases. Drug-resistant 'bugs' have rendered many of our best antibiotics obsolete. The great challenge to medical science is to invent new ammunition with which to fight back.

Since the beginning of the AIDS pandemic about 25 years ago, the fungus *Candida albicans*, once an almost harmless commensal of human body, has rapidly become the most prevalent fungal pathogen. It often causes life-threatening systemic infections in immuno-compromised patients. This fungus is polymorphic and can switch between yeast, pseudohyphal and hyphal forms of growth in response to environmental cues. This property has strong links with its ability of infection. Dr. Yue Wang's laboratory investigates the molecular mechanisms that control the growth transition, particularly how cells establish and maintain the highly polarized hyphal morphogenesis. In 2004, this laboratory found a key regulator, named Hgc1, of the yeast-hypha growth transition. The HGC1 deletion mutant grows constitutively in the yeast form and exhibits markedly reduced virulence. Hgc1 is a G1 cyclin-related protein and directly interacts with the master cell-cycle regulatory kinase Cdc28. In the past few years, this lab has identified a number of central components of the polarity machinery as direct substrates of the Hgc1-Cdc28 kinase, providing new insights into the molecular mechanisms that control polarized morphogensis in *C. albicans*.

C. albicans hyphal growth starts with the formation of a thin cell surface protrusion called germ tube. Similar structures are found in many cell types in diverse organisms, such as dendritic protrusions of neurons, root hairs and pollen tubes. Recent discoveries by Dr. Wang's lab suggest that many aspects of the underlying mechanisms for polarized cell growth are evolutionarily conserved. This renders *C. albicans* a relevant model for addressing the fundamental biological issue of how cells establish and maintain polarity.



Major Discoveries In The Lab

- Discovery of the Cdc42 GAP Rga2 as a direct substrate of CDK/Hgc1. Upon hyphal induction CDK/Hgc1 phosphorylates Rga2 and prevents this negative regulator of polarized growth from localizing to hyphal tips. This finding establishs a direct link between CDK and the central polarity regulator of the cell.
  Published in ***EMBO J*** 26:3760-3769 (2007)

- Identification of the septin Cdc11 as a regulatory target of two G1-cyclin/CDKs important for both yeast bud morphogenesis and hyphal morphogenesis. This study establishes a direct molecular link between CDK and the septin cytoskeleton.
  Published in ***Dev Cell*** 13:421 (2007)

- Identification of a key regulator of hyphal development, Hgc1. This study reveals the first and so far the only hypha-specific gene required for hyphal development. Published in ***EMBO J.*** 23:1845-1855 (2004)

- Discovery of a high-affinity iron permease, Ftr1, essential for *Candida albicans* virulence. The permease is activated in iron-limiting conditions both in vitro and in the tissues of the host, allowing the pathogen to acquire the growth-essential nutrient iron.
  Published in ***Science*** 288:1062-1064 (2000)