Molecular mechanisms of *Candida albicans*-host interactions

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I. Introduction

Candida albicans is a major fungal pathogen of humans. As a commensal, it frequently inhabits on the cutaneous and mucosal surface of oral, gastrointestinal, urinary and vaginal tracts of healthy individuals. However, *C. albicans* is also an opportunistic pathogen and can cause infections ranging from superficial mucosal infections to hematogenously disseminated candidiasis. In immunocompromised patients, *C. albicans* is responsible for a number of life-threatening infections. Moreover, *C. albicans* is the leading cause of nosocomial bloodstream infections and has a mortality rate of approximately 40%. Several virulence factors contributed to *C. albicans* infection have been reported, including adhesins, yeast-hyphae morphogenesis and secreted aspartyl proteinases and phospholipases. The main focus of our laboratory is to study *C. albicans*-host interactions. Recent studies related to different aspects of these interactions are presented here.

II. Regulation of virulence factors expression by *C. albicans* Rhb1-TOR signaling pathway

(1) Tsao *et al*. (2009) *Fungal Genet Biol*, 46:126
(2) Chen *et al*. (2011) *Eukaryot Cell*, 11:168
(3) Chen *et al*. (2014) in submission

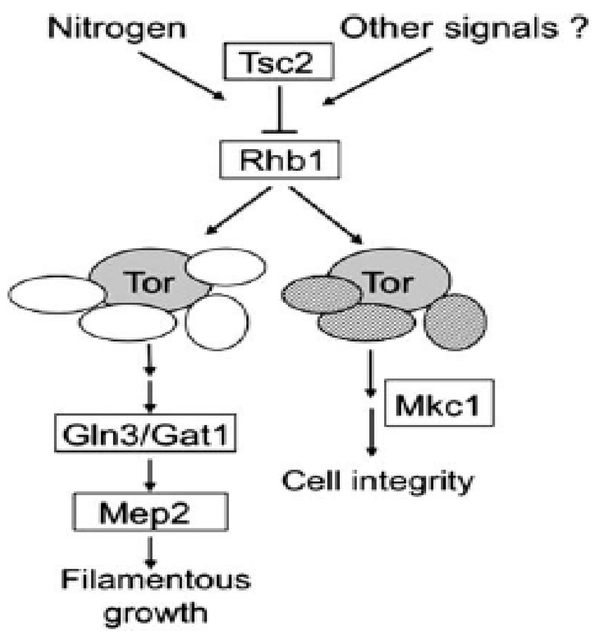

Fig. 1. *C. albicans* Rhb1 controls nitrogen starvation-induced morphogenesis andcell wall integrity via TOR pathway. Rhb1 is a small GTPase and Tsc2 is a GTPase-activating protein. Rhb1 regulates the TOR kinase along with different sets of protein in response to nitrogen starvation. In turn, TOR activates *MEP2* expression possibly via transcriptional factors Gln3 & Gat1, and leading to morphological transition. Alternatively, Rhb1 activates TOR kinase along with another set of proteins. This TOR complex affects Mkc1 kinase cascade that maintains cell wall integrity.

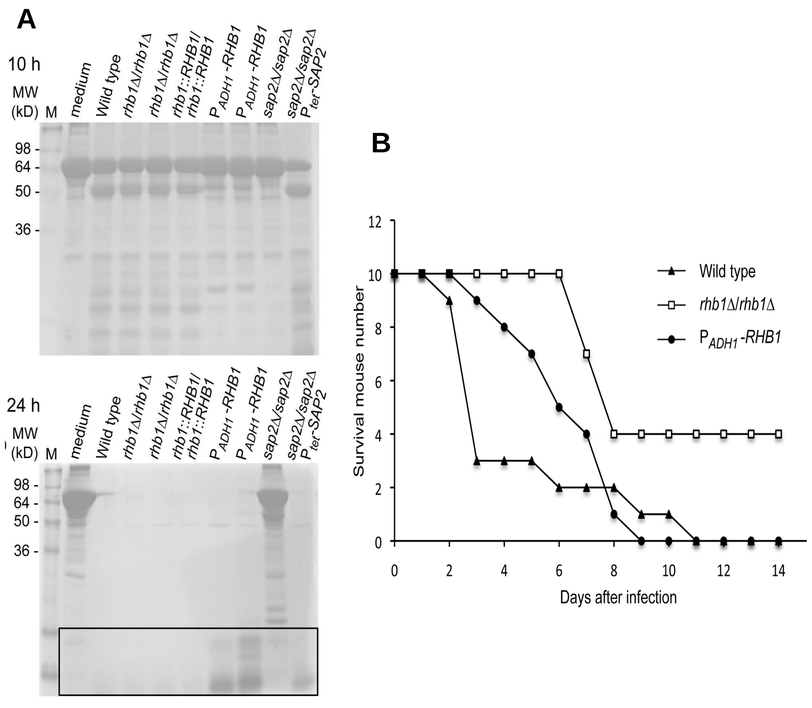

Fig. 2. *C. albicans* Rhb1 also controls expression of secreted aspartyl protease (A) and involves in virulence from a mouse model of systemic infection (B).

III. Modes of action for human antimicrobial peptide to against *C. albicans*

(1) Tsai *et al*. (2011) *PLoS One*, 6:e17755
(2) Tsai *et al*. (2011) *PLoS One*, 6:e21394
(3) Chang *et al*. (2011) *Biochem J*, 441:963
(4) Tsai *et al*. (2014) *J Microbiol*, 52:581

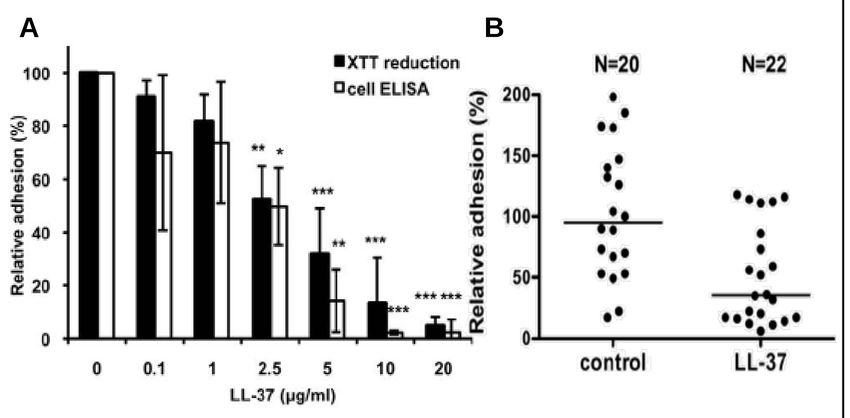

Fig. 3. LL-37 inhibits *C. albicans* adhesion to polystyrene surface (A), and mouse bladder mucosa (B).

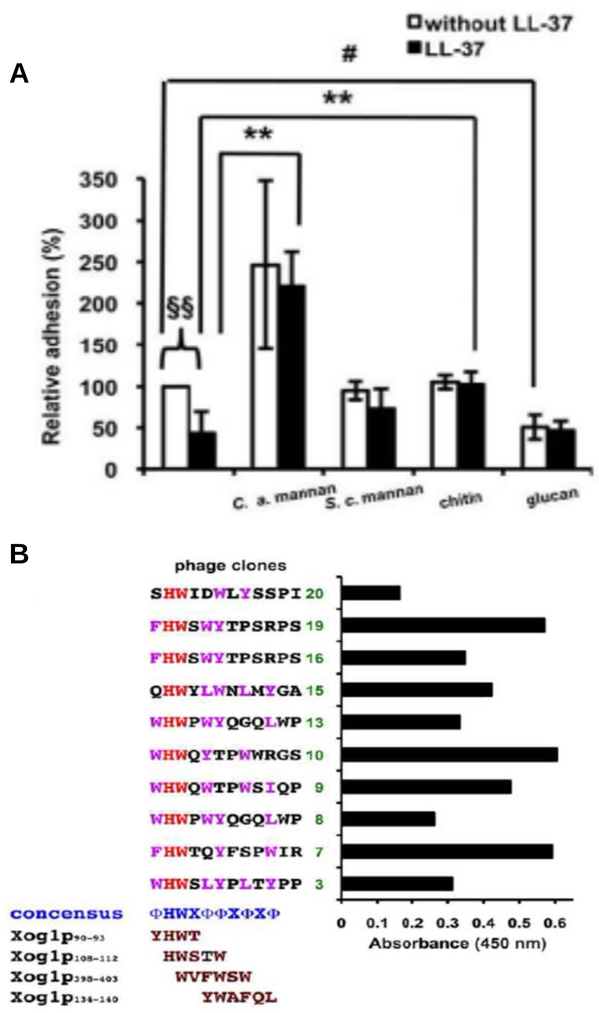

Fig. 4. LL-37 inhibits *C. albicans* adhesion via its interaction and modulation of cell wall carbohrdrates and beta-1,3-exoglucanase Xog1p. (A) LL-37 binding to cell wall polysaccharides reduces *C. albicans* adhesion. (B) Identification of Xog1p is a potential LL-37-binding target by phage display.

III. The roles of Hap43 and a CCTTA-binding complex in iron-responsive transcriptional regulation and *C. albicans* virulence

(1) Lan *et al*. (2004) *Mol Microbiol*, 53:1461
(2) Hsu *et al*. (2011) *Eukaryot Cell*, 10: 207
(3) Hsu *et al*. (2013) *Eukaryot Cell*, 12: 804
(4) Hsu *et al*. (2014) in preparation

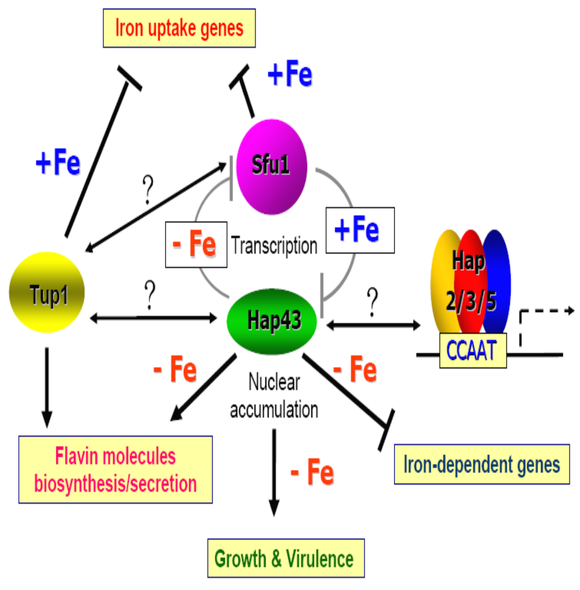

Fig. 5. A simple model for the functions of Hap43 and a CCAAT-binding complex in transcriptional regulation of *C. albicans*.

IV. Study of *C. albicans* biofilm formation & pathogen-host interactions

(1) Wang *et al*. (2010) *BMC Bioinformatics*, 11:53
(2) Wang et al. (2012) *PLoS One*, 7:e35339
(3) Kuo *et al*. (2013) *J Innate Immun*, 5:137
(4) Wang *et al*. (2013) *BMC Syst Biol*, 7:79
(5) Chen *et al*. (2013) *PLoS One*, 8:e72483
(6) Wang *et al*. (2014) *Biomed Res Int*, 2014:136130
(7) Tsai *et al*. (2014) *Mol Genet Genomics*, 289:807
(8) Lin *et al*. (2014) *BMC Syst Biol*, 8:116
(9) Chen *et al.* (2014) In preparation

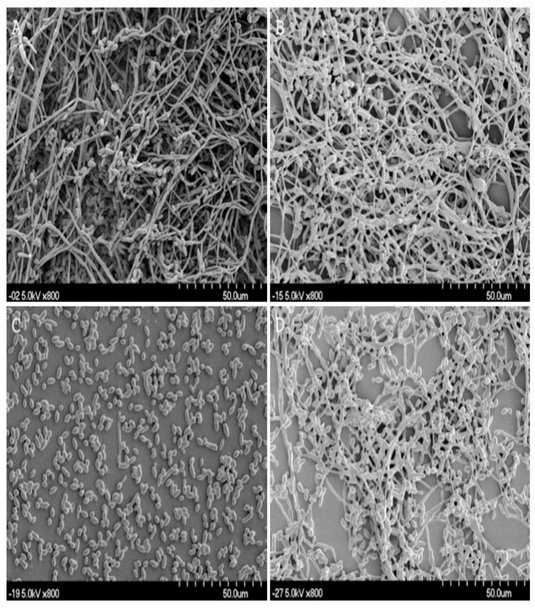

Fig. 6. Mss11 and *C. albicans* biofilm formation examined by SEM. The strains used: (A) wild type, (B) *mss11*-deletion (heterozygous), (C) (homozygous) *mss11*-deletion and (D) *MSS11*-reconstituted.

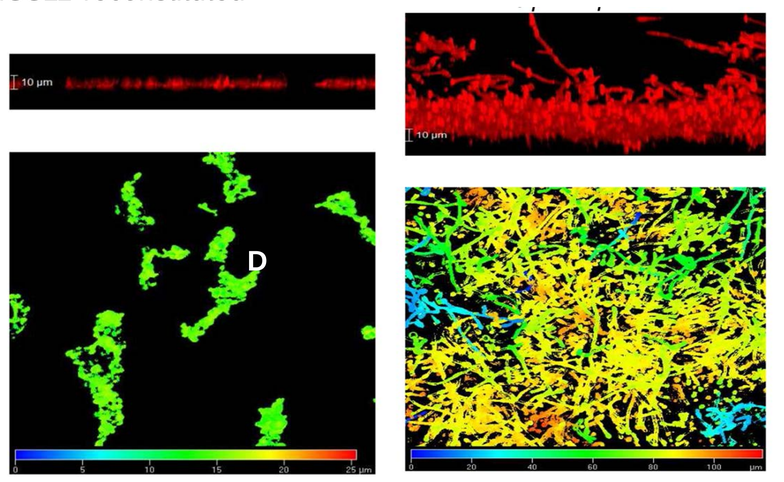

Fig. 7. *C. albicans* biofilm formation examined by confocal electron microscope. Biofilm of wild type and a mutant strains is compared.

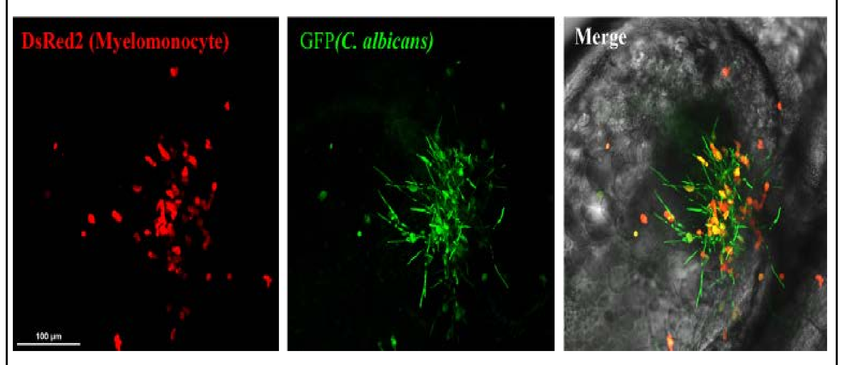

Fig. 8. Zebrafish as a model host for *C. albicans* infection.

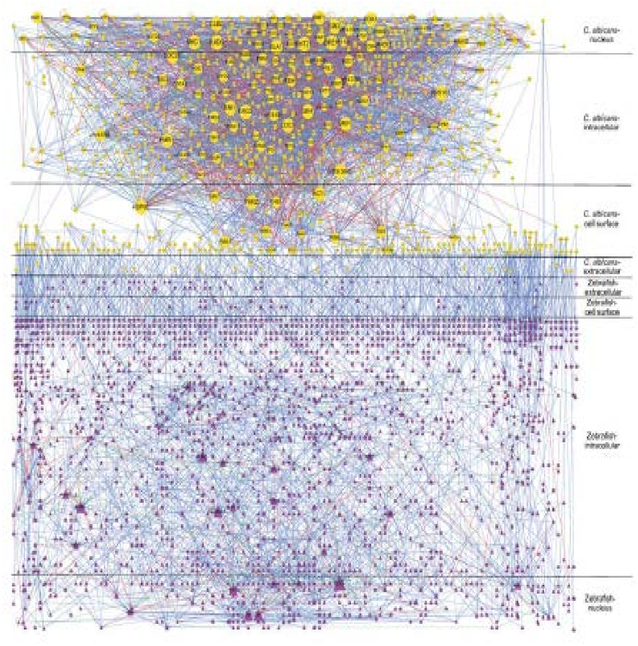

Fig. 9. Integrated intercellular dynamic protein-protein interaction network during *C. albicans* infection of zebrafish.