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Molecular and cellular microbiology; Mechanisms of microbial pathogenesis and pathogen-host interactions

Research Interests

The main focus in my lab is to study the biology and pathogenicity of the major fungal pathogen of humans, *Candida albicans*, and the interactions of *C. albicans* and its hosts.

As a commensal, *C. albicans* frequently causes irritating and recurrent infections, including oral thrush and vaginal candidiasis. In immunocompromised patients, *C. albicans* can become invasive and causes life-threatening systemic infections. Moreover, *C. albicans* can also gain entry into the bloodstream (candidaemia) during procedures associated with the implantation of medical devices. As such, this organism has emerged as the fourth most common blood-bone infection in the US and candidaemia is a significant nosocomial infection. The projects currently underway include:

(1) Environmental sensing, signal integration and *C. albicans pathogenesis*. During its natural history in the host, *C. albicans* encounters a wide variety of environmental conditions, including changing nutrients, pH, and antimicrobial mediators. One of the features that allow *C. albicans* to transition from a commensal organism to a successful pathogen is its ability to sense these complex environmental signals and respond by controlling cell growth/proliferation, hyphal morphogenesis and expression of associated virulence determinants. Our immediate objective is to characterize a new signaling/regulatory pathway that may play an important role for integrating multiple environmental signals, for cell growth/proliferation and for virulence. The approaches for this project include molecular genetics (deletion of genes, characterization of mutant strains and yeast two-hybrid system), biochemistry (protein purification and biochemical characterization) and animal models.

(2) Regulatory networks affected by iron availability. Iron is important for the microbial pathogen-host interaction. The availability of iron serves as an important signal for the expression of virulence determinants in pathogens, and iron withholding is a defense mechanism of hosts against microbial infections. Using functional genomics and molecular genetics, we have identified genes whose expression is modulated by iron availability and also identified a transcriptional factors, Sfu1, controlling iron gene expression (Lan et al., 2004). To further understand the molecular mechanisms that contribute to the gene regulation mediated by Sfu1 and to characterize functions of iron-regulated genes, we use biochemical, molecular genetics and *in silico* approaches in this study.

(3) Biofilm formation of *C. albicans*. The ability to adhere to surfaces and develop as a

multicellular community is one of the mechanisms used by microorganisms to respond to changing environments. In *C. albicans*, the ability to grow as biofilms is an important virulence trait, facilitating its growth on abiotic surfaces used in medical devices. We are currently studying toward understanding of molecular mechanisms associated with biofilm formation of *C. albicans*. The approaches used in this study include gene deletions, DNA microarrays and DNA-protein interactions.

Recent Publications

1. Tsao, C.-C., Chen, Y-T., and **Lan, C.-Y.*** (2008) A small G protein Rhb1 involved in nitrogen-starvation induced morphogenesis and cell wall integrity of *Candida albicans*. Fungal Genet Biol. In revision. (* Corresponding author)
2. Wang, H.-Y, Ho, P.-C., **Lan, C.-Y.**, and Chang, M. D.-T. (2008) Transcription regulation of human eosinophil RNases by the liver-enriched hepatocyte nuclear factor 4α. J Cell Biochem, In revision..
3. Chen, B.-S., Yang, S.-K., **Lan, C.-Y.**, and Chuang, Y.-J. (2008) A systems biology approach to construct the gene regulatory network of systemic inflammation via microarray and databases mining. BMC Med Genomics, 1, 46.
4. Huang, R.-Y., Chang, H.-T., **Lan, C.-Y.**, Pai, T.-W., Wu, C.-N., Ling, C.-M., and Chang, M.D.-T. (2008). Development and evaluation of a sensitive enzyme-linked oligonucleotide-sorbent assay for detection of polymerase chain reaction-amplified hepatitis C virus of genotypes 1-6. J. Virol. Method. 151, 211-216.
5. Murillo, L. A., **Lan, C.-Y**., N. Agabian, S. Larios, and B. Lomonte (2007) Fungicidal activity of a phospholipase A2-derived synthetic peptide variant against *Candida albicans*. Rev Esp Quimioterap. 20, 330-333.
6. Thesis, S., G. lshdorj, A. Brenot, M. Kretschmar, **Lan, C.-Y.**, T. Nichterlein, J. Hacker, S. Nigam, Agabian, N., and G. A. Kohler (2006). Inactivation of the phospholipase B gene PLB5 in wild-type Candida albicans reduces cell-associated phospholipase A2 activity and attenuates virulence. Int J Med Microbiol. 296(6), 405-420.
7. Murillo, L. A., Newport, G., **Lan, C.-Y.,** Habelitz, S., Dungan, J., and Agabian, N. (2005). Genome-wide transcription profiling of the early stage of biofilm formation by *Candida albicans*. Eukaryot Cell. 4, 1562-1573.
8. **Lan, C.-Y.,** Rodarte, G., Murillo, L. A., Jones, T., Davis, R. W., Dungan, J., Newport, G., and Agabian, N. (2004). Regulatory networks affected by iron availability in *Candida albicans*. Mol. Microbiol. 53, 1451-1469.
9. **Lan, C.-Y.**, Newport, G., Murillo, L. A., Jones, T., Scherer, S., Davis, R. W., and Agabian, N. (2002). Metabolic specialization associated with phenotypic switching in *Candida albicans*. Proc Natl Acad Sci USA 99, 14907-14912.

Selected Conferensce Abstracts/Presentations

1. **Lan, C.-Y.** (2007) Genome-wide study of iron-responsive and other genes in *Candida albicans*. Symposium of Medical Mycology. NHRI, Chunan, Taiwan.
2. **Lan, C.-Y.**, G. Rodarte, L. A. Murillo, T. Jones, R. W. Davis, J. Dungan, G. Newport and N. Agabian. (2006) Toward understanding regulatory networks affected by iron availability in *Candida albicans*. The 16th Congress of the International Society for Human and Animal Mycology, Paris, France. (Invited Oral Presentation and Symposium Abstract)
3. **Lan, C.-Y.** (2006) Genomics approaches to understand *Candida albicans* virulence. International Molecular Mycology Conference, Taipei, Taiwan. (Invited Oral Presentation and Symposium Abstract)
4. **Lan, C.-Y.,** G. Rodarte, L. A. Murillo, T. Jones, R. W. Davis, J. Dungan, G. Newport and N. Agabian. (2004) Regulatory networks affected by iron availability in *Candida albicans*. Functional Genomics of Host-Pathogen Interactions (Joint Cold Spring Harbor Laboratory and Wellcome Trust Conference), Hinxton, UK. (Poster Presentation and Conference Abstract)
5. **Lan, C.-Y.** (2003) Sfu1, a transcriptional factor for iron regulation in *C. albicans*. Research Day Symposium, School of Dentistry, University of California, San Francisco, USA. (Invited Oral Presentation and Symposium Abstract)