

Vacancies MBMFS

Pathogenomics and Systems Biology of Fungal Infections - an Integrative Approach

- Vacancies for two four-year PhD projects in the frame-work of an EU-Marie Curie training network

Introduction

The cell wall proteome of the opportunistic fungal pathogen *Candida albicans* consists at any time of at least 20 different covalently linked mannoproteins. Its precise composition can vary widely both qualitatively and quantitatively, depending on the environmental conditions and on whether the fungus grows in the yeast form or in the hyphal form. The functions of the individual cell wall proteins (CWPs) are manifold and include cross-linking of skeletal polysaccharides, formation of a dense, external protein coat that covers and protects the internal skeletal layer, and adhesion to biotic and abiotic surfaces. Other CWPs play a role in post-adhesion steps of biofilm formation, such as the formation of an extracellular matrix, in protein degradation, in coping with oxidative stress and in iron uptake.

EU Framework VII - FINSysB

FINSysB is a EU Marie Curie Consortium of eleven members from various European countries and with complementary expertise. It is set up to train young students in a collaborative study of the pathogenomics of *C. albicans* and the host responses to *Candida* infections, using *in vivo* and *in vitro* models, genomic transcript profiling, advanced mass spectrometric techniques, and modeling of infection-related signaling pathways. An extensive international course program will be part of the training. The Swammerdam Institute for Life Sciences of the University of Amsterdam participates in FINSysB with two four-year PhD projects supervised by Drs Frans Klis and Leo de Koning. Preferred starting date: July - October of 2008. Note that the two projects require close collaboration between both students and other team members for optimal results.

Projects

1. Development of cell wall protein-based vaccines against candidiasis based on quantitative mass spectrometric analysis of the cell wall proteome. Quantitative analysis of the cell wall proteome of *C. albicans* will answer the question, which cell wall proteins are most abundantly expressed under various infection-related conditions and are likely candidates for vaccine development and, possibly, early diagnostics. Cells will be grown as planktonic cells or in biofilms, and in various growth forms (yeast form, the pseudohyphal or the hyphal form) (Yin *et al.*, 2008. Trends Microbiol 16:20-26). Analysis of the cell wall proteins will be performed with a state-of-the-art Fourier transform mass spectrometer and is based on an isotope ratio quantification method with ¹⁵N labeling. We are looking for a candidate with mass spectrometric expertise, who is interested in applying and developing FT-MS techniques for biological research.
2. Dynamics of the cell wall proteome of *C. albicans* occurring during infection-related stress. Cells will be grown either as planktonic cells or in biofilms and subjected to micro-aerobic conditions, iron restriction, and azole drugs. These conditions were selected, because (i) *C. albicans* often encounters these conditions during infection; (ii) we believe that these stress conditions are closely related (micro-aerobic conditions restrict iron uptake; several key sterol-synthesizing enzymes, including the heme protein Erg11, need molecular oxygen and iron to be functional, and azoles inhibit the formation of ergosterol by targeting Erg11); and (iii) earlier research has already shown that the cell wall proteome changes dramatically but similarly when the cells are challenged by micro-aerobic conditions and iron restriction (Sosinska *et al.*, 2008. Microbiol. 154:510-520). We will use a novel *in vitro* model mimicking mucosal infections. The results will also be used for quantifying the output of signaling pathways that control the composition of the cell wall proteome. The candidate should have extensive expertise in fungal molecular biology and be interested in learning quantitative mass spectrometric techniques and in modeling the results where feasible.

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See also website at: www.science.uva.nl/sils/mbmfs.