# Application of the whole-genome approach for the development of novel diagnostic and molecular typing techniques of pathogenic fungi and special pathogens

Abstract:

Invasive Candida infections continue to cause high morbidity and mortality in a diverse range of debilitated and immunocompromised hosts and constitute an important public health problem. Rapid species identification and molecular epidemiology studies is important in elucidating transmission characteristics of pathogens. Further analysis of differences of virulence, antifungal resistance profiles and epidemiological behaviour will help to eluciadate the underlying mechanisms of such phenotypic and geographic differences. All of these can help to fine tuning the control strategy.

Through our previous efforts, we have laid a sound foundation in applying molecular typing to the study of molecular epidemiology. The research in this year will further develop rapid species identification method, standardize typing methods, systematically collect more domestic and international isolates, and integrate clinical, epidemiological data with typing data to establish a database. Identify significant clonal clusters and explore the specific differences at molecular levels. Our major findings can be summarized into five points: Firstly, we have developed a novel multiplex beads array system to identify 9 clinically important yeasts, including *Candida albican*s, *C. guilliermondi*i, *C. lusitaniae*, *C. glabrata*, *C. tropicalis*, *C. glabrata*, *C. parapsilosis*, *C. krusei* and *Cryptococcus neoformans*. Secondly, one or more closely related fluconazole resistant *C. tropicalis* clones seemed to have evoleved in 1999 and subsequently vanished in 2002. It is worthwhile to further investigate the molecular mechanisms of their evolution. Thirdly, the Taiwanese isolates thus far analysed showed no identical MLST genotypes with the vast western isolates. However, with the only 19 Japanese isolates analyzed we already identify 2 MLST genotypes identical to Taiwanese isolates. More studies will be conducted to find out their epidemiological links and the underlying mechanisms of geographical preferences. Fourthly, some *C. glabrata* isolates from AIDS patients phylogenetically form distinct clusters. The possibility of horizontal transmission among HIV infected patients deserves further investigation. Fifthly, *Nae* I is superior to *Rsr* II and *Bss* HII as the best restriction enzyme for PFGE typing of *C. tropicalis*. Sixthly, we use RAPD typing to identify specific bands and subject them to cloning and sequencing. PCR primers for these specific bands will be designed to further testing the discriminatory power of these specific fragments.

At least 10 SCI papers have been generated: 3 papers are already published, 1 paper has been revised, 3 have been submitted, and 3 articles are finished will be submit to SCI journals soon, 4 manuscripts are in preparation and will be submitted to SCI journals. Further publications derived from collaboration are also underway. Furthermore, we will feedback the subtyping data to clinicians and collaborate to establish databases integrating typing results with clinical and epidemiological data. Such continuous efforts will help to understand the epidemiology as well as the evolution mechanisms of some high resistant/virulent clones, which can potentially help to identify specific diagnostic, vaccine, and epidemiological marker molecules.

Keywords：*Candida spp.*, whole genomic typing, resistance