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0841 Fluconazole Exposure Induces Genotypic and Phenotypic Changes in Candida glabrata

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Candida glabrata is recognized as a leading fungal pathogen of mucosal and systemic infections in compromised individuals, second only to *C. albicans*. One reason for this is the widespread use of fluconazole which leads to emergence of fluconazole resistant strains in *C. glabrata*. Objectives: To obtain a fluconazole resistant *C. glabrata* strain with sequential, repeat exposure to fluconazole *in vitro* and determine its genotypic and phenotypic attributes. Methods: *C. glabrata* ATCC 2001 was cultured in Sabourauds dextrose agar and exposed repeatedly to RPMI medium laced with fluconazole (×2MIC) for a continuous period of 43 days. Molecular data of the drug exposed *Candida* strain was compared with the control yeast, using randomly amplified polymorphc DNA (RAPD) and, pulsed-field gel electrophoresis (PFGE) of chromosomal DNA treated with restriction endonuclease SfiI. Fluconazole MIC changes were evaluated using the E-test (AB Biodisk; Kalvagen, Solna, Sweden), cell viability monitored using both the ATP bioluminescence and conventional colony forming unit assays and phenotypic switching monitored in RPMI/16µg/ml fluconazole. Results: After drug exposure for 11 days, there was an increase in the MIC from 8µg/ml to 64µg/ml, with fluctuating cell viability and a reduction in total cell yield (from 1.0 - 0.6 × 10^4 cells/ml). A strong positive correlation between the ATP and CFU counts ($r = 0.8556$; $p<0.001$) was also noted. Phenotypic switching of *C. glabrata* was observed after 36 days at a frequency of 1.6% and significant changes in the chromosomal DNA profile was observed after 43 days of drug exposure. Conclusion: Chromosomal DNA changes as well as phenotypic changes in *C. glabrata* may occur due to sequential exposure of this yeast to fluconazole. (Supported by the Research Grants Council and the Committee of Research and Conference grants (a/c 10205959) of the University of Hong Kong, Hong Kong SAR.

Seq #72 - *Candida*
11:00 AM-12:00 PM, Thursday, 29 June 2006 Brisbane Convention & Exhibition Centre Exhibit Hall 1

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