Report: Travel Grant for Training in a Foreign Institution

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Elucidating molecular mechanisms underlie azole resistance of *C. parapsilosis*

The aim of the project was to elucidate the molecular mechanisms responsible for azole resistance in *C. parapsilosis*, an important infection agent in Portuguese hospitals. Analysis of the global pattern of gene expression of resistant species was performed using microarray tool in a foreign institution with expertise in the field.

One susceptible and three induced resistant *C. parapsilosis* strains were studied. Resistant strains were obtained by *in vitro* incubation with different azoles: fluconazole, voriconazole and posaconazole, fluconazole being the fastest inducer and posaconazole the slowest.

Different gene expression profiles were obtained after comparasion between susceptible and three resistant strains. Moreover, several genes were identified as involved in azole resistance mechanisms adopted by *C. parapsilosis*. In *C. parapsilosis* strains incubated with fluconazole and voriconazole, the transcription factor MRR1 was up-regulated. This transcription factor is responsible for overexpression of major facilitator transporters, like MDR1p, an efflux pump that expel antifungal drugs from intracellular environment. In *C. parapsilosis* strain incubated with posaconazole, two other

transcription factors were up-regulated, *UPC2* and *NDT80*, which trigger the expression of *ERG* genes linked to ergosterol biosynthesis pathway. In this last case, it is likely that ABC transporters also play an important role in resistance mechanism.

Other genes involved in diverse cell functions, as structural molecule activity, transferase and hydrolase activity, were affected by treatment with these three azoles, which may be implicated directly or indirectly in azole resistance. These assumptions need to be confirmed.

Performing this project gave Ms Ana Silva a great opportunity to learn and practice a new technology in an expert laboratory, which afterwards can be implemented in a Portuguese laboratory.