Genetics Day Poster Submission

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Category: Postdoc

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Title: MULTIPLE GENES OF CANDIDA ALBICANS INFLUENCING ECHINOCANDIN SUSCEPTIBILITY IN CASPOFUNGIN-ADAPTED MUTANTS

Abstract: Candida albicans is an opportunistic human fungal pathogen that causes invasive infections in immunocompromised individuals. Despite the high anticandidal activity among the echinocandins (ECNs), a first-line therapy, resistance remains an issue. Furthermore, many clinical isolates display decreased ECN susceptibility, a physiological state which is thought to lead to resistance. Determining the factors that can decrease susceptibility is of high importance. We searched for such factors genome-wide by comparing the transcriptional profiles of five mutants that acquired decreased caspofungin susceptibility in vitro in the absence of canonical FKS1 resistance mutations. The mutants were derived from two genetic backgrounds and arose due to independent mutational events, some with monosomic chromosome 5 (Ch5). We found that the mutants exhibit common transcriptional changes. In particular, all mutants upregulate five genes from Ch2 in concert. Knockout experiments show that all five genes positively influence caspofungin and anidulafungin susceptibility and play a role in regulating the cell wall mannan and glucan contents. The functions of three of these genes, orf19.1766, orf19.6867, and orf19.5833, were previously unknown, and our work expands the known functions of LEU42 and PR26. Importantly, orf19.1766 and LEU42 have no human orthologues. Our results provide important clues as to basic mechanisms of survival in the presence of ECNs while identifying new genes controlling ECN susceptibility and revealing new targets for the development of novel antifungal drugs.