Genetics Day Poster Submission

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Title: AT LEAST 10 GENES ON CHROMOSOME 5 OF CANDIDA ALBICANS ARE DOWNREGULATED IN CONCERT TO CONTROL CELL WALL AND TO CONFER ADAPTATION TO CASPOFUNGIN

Abstract: Candida albicans is part of normal microbiota, however, can cause superficial and life threatening infection in immune-compromised individuals. Drugs from echinocandin (ECN) class that disrupt cell wall synthesis, are being used as a major treatment strategy against candidiasis. As the use of ECNs for the treatment of candidiasis is increasing, resistance against ECNs is also emerging. Previously, we reported involvement of 5 chromosome 2 (Ch2) genes in adaptation to ECN drugs. Here, we explored 22 candidate-genes on Ch5 that are consistently downregulated in independent mutants adapted to caspofungin (CAS), for their role in ECN adaptation. We also compared cell wall remodelling in CAS-adapted mutants and in 10 knockouts (KOs) from Ch5. Independent KO experiments as combined with broth microdilution assay, demonstrated that, as expected, 10 out of 22 Ch5 genes decrease ECN susceptibility by controlling the levels of three major components of the cell wall, glucan, mannan, and chitin. Some KOs decreased glucan or increased chitin or both. Similar cell wall remodelling, decreased glucan and increased chitin, was found in CAS-adapted mutants with no ploidy change. Some other KOs had no glucan change, but increased the level of either mannan or chitin. Our results identify the function of two uncharacterized genes, orf19.970 and orf19.4149.1, and expand the functions of DUS4, RPS25B, UAP1, URA7, RPO26, HAS1 , and CKS1 . The function of CHT2 , as negative regulator of ECN susceptibility, has been previously established. Importantly, half of the above genes are essential indicating that essential processes are involved in cell wall remodelling for adaptation to ECNs. Also important, orf19.970 and orf19.4149.1 have no human orthologues. Finally, our work shows that multiple mechanisms are used by C. albicans cells to remodel cell wall in order to adapt to CAS. This work continues to identify common pathways that are involved in drug adaptation, as well as new genes controlling ECN susceptibility and reveals new targets for development of novel antifungal drugs.