Genetics Day Poster Submission

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Title: CANDIDA ALBICANS STRAINS ADAPTED TO CASPOFUNGIN DUE TO ANEUPLOIDY BECOME HIGHLY TOLERANT UNDER CONTINUED DRUG PRESSURE

Abstract: Candida albicans is a prevalent fungal pathogen in humans. Understanding the development of decreased susceptibility to ECN drugs of this microbe is of substantial interest, as it is viewed as an intermediate step allowing the formation of FKS1 resistance mutations. We used six previously characterized mutants that decreased caspofungin susceptibility either by acquiring aneuploidy of chromosome 5 (Ch5) or by aneuploidy-independent mechanisms. When we exposed these caspofungin-adapted mutants to caspofungin again, we obtained 60 evolved mutants with further decreases in caspofungin susceptibility, as determined with the CLSI method. We show that the initial adaptation to caspofungin is coupled with the adaptation to other ECNs, such as micafungin and anidulafungin, in mutants with no ploidy change, but not in aneuploid mutants, which become more susceptible to micafungin and anidulafungin. Furthermore, we find that the initial mechanism of caspofungin adaptation determines the pattern of further adaptation as parentals with no ploidy change further adapt to all ECNs by relatively small decreases in susceptibility, whereas aneuploid parentals adapt to all ECNs, primarily by a large decrease in susceptibilities. Our data suggest that either distinct or common mechanisms can govern adaptation to different ECNs.