Nature Reviews Microbiology | AOP, published online 18 February 2013; doi:10.1038/nrmicro2991

FUNGAL GENETICS

Candida gets a better half

> haploids arose through concerted chromosome loss

The opportunistic fungal pathogen *Candida albicans* has been considered an 'obligate diploid' with a diploid–tetraploid parasexual mating cycle that has made classical genetics difficult. Now, a new study by Hickman *et al.* demonstrates that *C. albicans* can in fact form viable, mating-competent haploids.

Although early genetic studies had indicated that *C. albicans* had a haploid state and putative haploid clinical isolates had been identified, later work, as well as the complete genome sequence, indicated that *C. albicans* is an obligate diploid. Hickman *et al.* established a genetic screen for loss of heterozygosity in a derivative of the *C. albicans* laboratory strain SC5314, selecting for loss of heterozygosity at the gene encoding galactokinase. In one galactokinase-negative strain, all the gene loci they examined were homozygous, including multiple SNPs on each chromosome. Flow cytometric DNA measurements revealed that the DNA content of this strain was half that of a diploid control, confirming that the strain was in fact haploid. Ten more haploid strains were isolated *in vitro* and from mouse models of *C. albicans* infection. As the genomes of these strains showed little evidence of crossover, the authors proposed that the haploids arose through concerted chromosome loss rather than through meiosis, although the exact mechanism involved remains unclear.

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In culture, haploid strains could spontaneously revert to a homozygous diploid state (auto-diploids). Furthermore, haploid strains of opposite mating types could mate, thereby producing heterozygous diploids. In addition, haploid strains underwent morphogenetic changes typical of diploids, including the yeast–hypha transition and white–opaque switching. Both haploid and auto-diploid strains showed reduced fitness *in vitro* and *in vivo*. Such a fitness defect was absent in heterozygous diploids produced by haploid mating, indicating the complementation of detrimental recessive alleles. This, combined with the fact that certain alleles were absent from the haploids, perhaps because they were lethal, led the authors to suggest that the formation of haploids increases the genetic diversity of *C. albicans* and serves to eliminate lethal recessive alleles from the population.

The reduced fitness of haploid strains and the low frequency with which they occur might explain why they have not been detected previously. This new study not only contributes to our fundamental understanding of *C. albicans*, but also paves the way for the creation of a new suite of tools for the genetic analysis of this important opportunistic pathogen.

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ORIGINAL RESEARCH PAPER Hickman, M. A. *et al.* The 'obligate diploid' *Candida albicans* forms mating-competent diploids. *Nature* **494**, 55–59 (2013)