How *Candida albicans* switches phenotype - and back again. The SIR2 silencing gene has a say in Candida's colony type

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Among the many bugs that live in the mouth and digestive tract is the yeast *Candida albicans,* which under normal circumstances lives in 80% of the human population with no harmful effects. However, overgrowth results in thrush, a condition often observed in immunocompromised individuals such as HIV-positive patients. Candidiasis also occurs in the blood and in the genital tract. To infect host tissue, the usual unicellular yeast-like form of *C. albicans* reacts to environmental cues and switches into an invasive, multicellular filamentous form. This switching between two cell types is known as dimorphism.

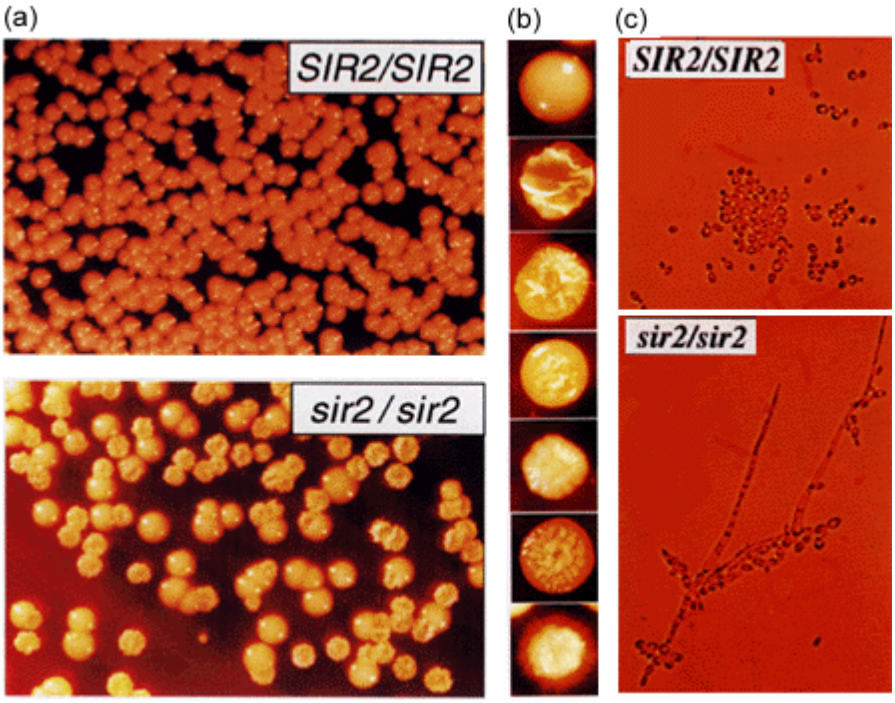
In a process that superficially resembles dimorphism, *C. albicans* undergoes a process called "phenotypic switching", in which different cellular morphologies are generated spontaneously. One of the classically studied strains that undergoes phenotypic switching is WO-1, which consists of two phases, one that grows as smooth white colonies and one that is rod-like and grows as flat gray colonies. The other strain known to undergo switching is 3153A; this strain produces at least seven different colony morphologies. In both the WO-1 and 3153A strains, the different phases convert spontaneously to the other(s) at a low frequency. The switching is reversible, and colony type can be inherited from one generation to another. Although several genes that are expressed differently in different colony morphologies have been identified, some recent efforts have focused on what might be controling these changes. Further, whether there is a potential molecular link between dimorphism and phenotypic switching is a tantalizing question.

In the 3153A strain, a gene called *SIR2* (for silent information regulator) has been found that seems to be important for phenotypic switching. *SIR2* was originally found in *Saccharomyces cerevisiae* (brewer's yeast), where it is involved in chromosomal silencing, a form of transcriptional regulation in which regions of the genome are reversibly inactivated by changes in chromatin structure (chromatin is the complex of DNA and proteins that make chromosomes). In yeast, genes involved in the control of mating type are found in these silent regions, and SIR2 represses their expression by maintaining a silent-competent chromatin structure in this region. The discovery of a *C. albicans SIR2* that is implicated in phenotypic switching suggests that it too has silent regions controlled by *SIR2* in which the phenotype-specific genes may perhaps reside.

Another potential regulatory molecule is Efg1p, a transcription factor found in the WO-1 strain that regulates dimorphism, and more recently has been suggested to help regulate phenotypic switching. Efg1p is expressed only in the white and not in the gray cell type, and overexpression of Efg1p in the gray form causes a rapid conversion to the white form.

Thus far there are few data that dimorphism and phenotypic switching use common molecular components. However, it is not inconceivable that phenotypic switching may occur in response to some change in the environment as well as being a

spontaneous event. How SIR2 itself is regulated in *S. cerevisiae* may yet provide clues as to the switching mechanisms of *C. albicans.*



Phenotypic switching in the yeast *Candida albicans* can be controlled by a *SIR2* gene (a) Yeast colonies that are homozygous positive for the *SIR2* gene *(SIR2/SIR2)* have a uniform colony morphology, while those that lack completely *SIR2* (homozygous negative - *sir2/sir2)* have variant colony morphologies.

(b) Several different colony types are possible for cells of the *sir2/sir2* phenotype. Many of the seven colony types shown here can arise from a single colony of one of the other morphologies, indicating that the phenotypic switching is heritable.

(c) Filamentous growth is enhanced for *sir2/sir2* cells over*SIR2/SIR2,* which suggests that there may be common ground between the mechanisms of phenotypic switching and dimorphism in *Candida albicans.*

Important Links

Live PubMed searches

(1) Dimorphism control in yeast

(2) Phenotypic switching in yeast

(3) SIR2

(4) Efg1p

Additional NCBI resources

OMIM

Taxonomy [http://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=5475&lvl=0]

Box: Search PubMed for gene silencing in humans

Click on the link below to start an html tutorial.

Does gene silencing happen in humans? [http://www.ncbi.nlm.nih.gov/Coffeebreak/CB10_SIR2/PQ.html]

Box: Use BLAST to search for proteins similar to Candida SIR2

Click on the link below to start an html tutorial.

Search for proteins similar to Candida SIR2 [http://www.ncbi.nlm.nih.gov/Coffeebreak/CB10_SIR2/BQ.html]