Evolution & adaptation in pathogenicity

“Nothing in biology makes sense except in the light of evolution” (T.Dobzhansky)

The host-pathogen interaction is no exception from this rule: while the pathogens adapt to the specific stresses and requirements inside their hosts, the hosts themselves are selected for best defense against damage done by these microorganisms. This evolutionary battle led to many astonishingly specific adaptations, from optimized nutrient uptake systems to our adaptive immunity.

We are interested in the mechanisms responsible for the adaptation of *Candida albicans* and *C. glabrata*, the two most important opportunistic pathogens among the *Candida* species, during the infection process. It is known for both species that they exhibit phenotypic and genotypic plasticity and can therefore react to changing environments by generating new phenotypes. For example, microevolution has clearly been demonstrated for the acquisition of high levels of antifungal drug resistance. In our laboratory, we used serial passage experiments to monitor the in vitro adaptation of fungi to macrophages, the “big eaters” of the immune system. We used two models: a wild type strain of *C. glabrata* and a hyphal-deficient *C. albicans* strain, which cannot escape from macrophages (as *C. albicans* normally does). In both cases we observed a striking change in the morphology of the strains after a series of co-culture passages. Usually, both strains grow as single cells, but during the microevolution experiment this growth form switched to a more filamentous form. Interestingly, the ability to form filaments is a well characterized virulence trait in wild type *C. albicans*, which was recreated here. We characterized the evolved strains in more detail using *in vitro* and *in vivo* experiments to investigate the impact of this phenotypic alteration on the pathogenicity of the strains. To determine the underlying genetic mechanisms, which cause the phenotypic alterations, we used different molecular techniques like microarrays, DNA and RNA sequencing. An in vivo adaptation experiment of *C. albicans* to the specific environment in the kidney complements our investigations into the adaptability of pathogenic yeasts in the host.

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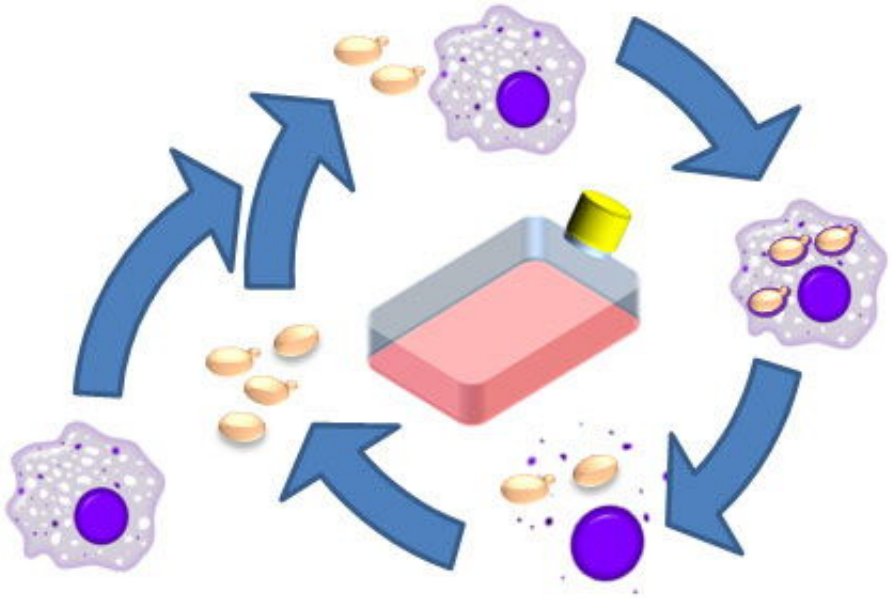
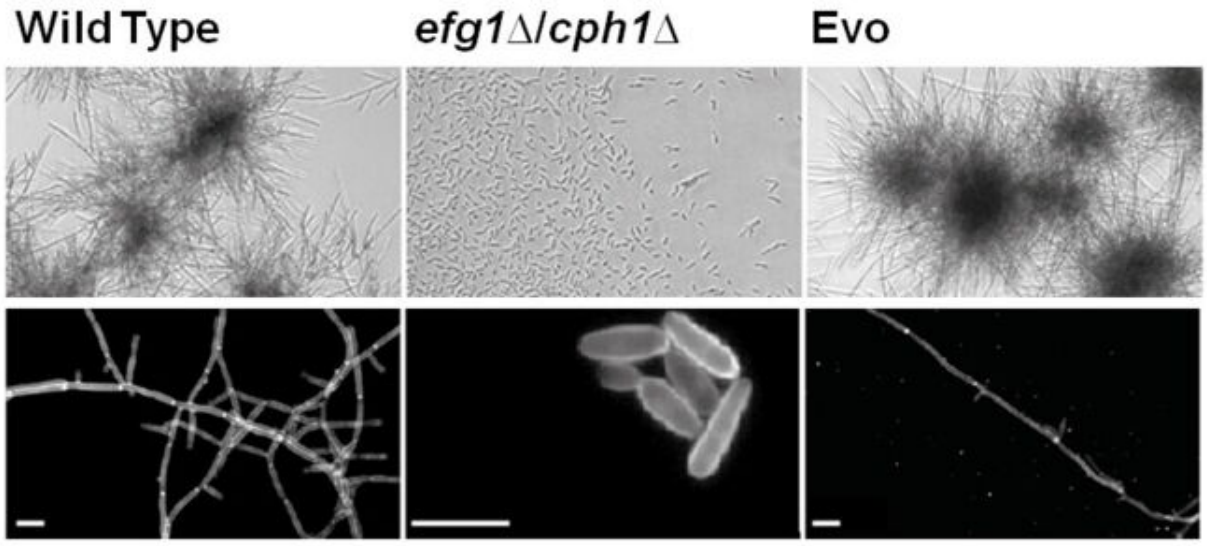


_ Basic laboratory evolution scheme -- the fungus is exposed to immune cells for 24 h, then re-isolated and confronted with fresh immune cells. This cycle is continued for months until the *Candida* species adapts to the immune cells.

- 

_ Result of an evolution experiment -- the mutant *efg1*Δ/*cph1*Δ cannot form hyphae any more and is stuck in macrophages. After continuous co-incubation, hyphae formation re-appears and allows the mutant to kill the host cell like the non-mutated strain. Top, overall morphology of microcolonies; bottom, single cell morphologies.