Simposio Internacional: La Levadura: un organismo modelo para la investigación biomédica
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Cryptococcus neoformans as model to study fungal virulence: Non-conventional morphogenesis and non-conventional hosts

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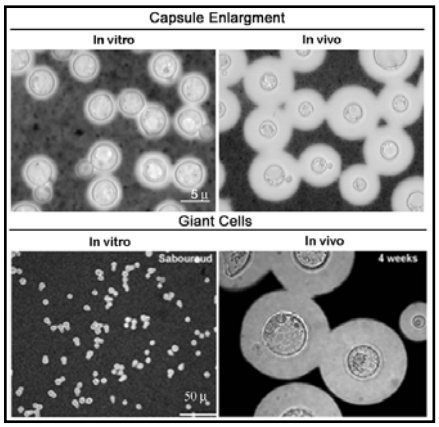
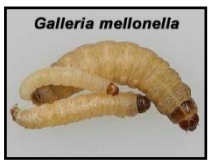
Cryptococcus neoformans is a pathogenic yeast that offers a particular and unique model to study fungal virulence due to the presence of well-defined virulence factors that have deleterious effects on the host. The main one is a polysaccharide capsule that surrounds the cell and that can be observed after suspension of the cells in India Ink. The polysaccharides of the capsule have inmunomodulatory properties that produce immune unresponsiveness.

In addition to the presence of virulence factors, *Cryptococcus neoformans* induces responses that result in adaptation to the host environment. Some of these responses include the induction of morphological changes. In contrast to other pathogenic fungi, filament formation does not play an important role during infection. However, this yeast possesses a non-conventional morphogenetic program that results in the appearance of multiple and different cellular types (see figure at the right). In our group, we are studying two morphological transitions that are typically observed during infection. The first one is caused by a massive increase in the size of the capsule, which happens during the first hours of interaction with the host (see figure at the right, upper panels). Capsule enlargement can be reproduced *in vitro*, and we have been shown that it confers protective properties to the yeast during stress conditions. The second morphological transition involves the formation of “giant/titan” cells, which are cells that have a diameter larger than 30 microns, although cells of 50-80 microns can also be observed (lower panels in the figure, both of them having the same magnification).



To understand the role of these changes in virulence, we are using as a model hosts, not only mice, but also the non-mammalian model *Galleria mellonella*(see picture at the right), which is a Lepidoptera useful to study microbial virulence. This model offers several advantages that have allowed us to understand important aspects of morphogenesis in *C. neoformans*. In addition, it is a valuable tool to screen virulence of mutants affected in morphogenesis.



In my talk I will discuss the importance of morphogenesis in this pathogen, and the approaches that we have followed to identify genes involved in the regulation of these processes.