Simposio Internacional: Biología y Comunicaciones
***International Symposium**: Biology and Communications*
Madrid, 26 y 27 de marzo de 2012
Madrid, March 26-27, 2012

The Pir proteins of the Candida albicans cell wall, a potential target of new antifungal drugs?

Eulogio Valentín-Gomez

Candida albicans is a polymorphic fungus that colonizes the human gastrointestinal tracts as a commensal in healthy humans. However, it is able to produce deep-rooted infections in patients suffering cancer, organ-transplantation and other immunocompromising conditions. During these interactions *C. albicans* establishes contact with host cells through its cell wall, which is the outermost fungal structure.

The fungal cell wall determines the shape of the fungal cell and protects the protoplast against physical, osmotic and oxidative damage. The *C. albicans* cell wall is mainly composed of β-glucans (β- 1,3 and β-1,6-glucan), chitin and mannoproteins. These three components are dispersed throughout the cell wall, although mannoproteins are mostly concentrated on the outer surface. Mannoproteins represent 30-40% of the total cell wall and determine the surface properties, enabling *C. albicans* cells to interact with and adhere to host tissues. Mannoproteins can be bound to the cell wall components by different kind of linkages: (I) Hydrogen bonds and/or hydrophobic interactions; (II) Disulphide-bridges and (III) covalently bound mannoproteins; amongst these proteins two types have been detected: Glycosylphosphatidylinositol proteins (GPI-dependent wall proteins) and Pir proteins (proteins with internal repeats) The proteins of the first group are linked to 1,3-β-glucan through a 1,6-β-glucan connector whereas the proteins of the second group are attached to the 1,3-β-glucan in the cell wall by alkali-labile bonds.

Pir proteins were firstly described in *Saccharomyces cerevisiae.* The S. *cerevisiae* Pir family consists of four members which present some characteristic features: (i) these proteins are synthesized as pre-proteins, and processed by the serine proteinase Kex2 in the Golgi, (ii) contain a variable number of intemal repeats matching the consensus pattern Q[IVJXDGQ[IVPJQ, and (iii) have a conserved C-terminal domain containing four cysteine residues. In the C. *albicans* strain SC5314 two Pir proteins have been identified, named Pir1 and Pir32. The two alleles of C. *albicans PIR1* gene encode for two different-size cell wall mannoproteins with 9 and 7 internal repeats (-Q-I-(SfT/GIN)-D-G-Q-(IIV)-Q-H-Q-T-) respectively in their amino acid sequences. A search for *PIR* genes in a collection of several *Candida albicans* clinical isolates strains showed six different patterns as combination of the four *PIR1* length variants found, only differing in the amount of internal repeats. Mutants in *PIRl* gene present abnormal phenotypes. The *pir1/pir1 C. albicans* strains are markedly attenuated in a mouse model of systemic infection. While Pir1 is not essential for viability *in vitro*, its presence is required for full virulence of *C. albicans*. This fact make that Pir1 was a good candidate as target for designing new antifungal drugs.

.

*Todos los derechos de propiedad intelectual son del autor. Queda prohibida la reproducción total o parcial de la obra sin autorización expresa del autor.
© FUNDACIÓN RAMÓN ARECES. Todos los derechos reservados.

**All intellectual property rights belong to the author. Total or partial reproduction of the work without express permission of the author is forbidden.*
© FUNDACIÓN RAMÓN ARECES. All rights reserved.