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Adhesins in Candida parapsilosis: Understudied players in virulence

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Candida species are the leading cause of fungal bloodstream infections that are associated with a very high mortality, especially in immunocompromised patients. The first step of Candida infection involves a tight adherence to human cells in the skin, epithelium or endothelium. The ability to stick these host tissues and/or abiotic surfaces such as catheters or prosthetic devices is enabled by genes coding for different families of fungal cell wall adhesins. One of the most extensively studied group of proteins involved in this process belong to the Als (agglutinin-like sequence) family (reviewed in). Despite their broadly acknowledged importance as virulence factors in C. albicans, we lack detailed information concerning the biological role of the Als proteins in other Candida species such as C. parapsilosis.

Over the past 2 decades, C. parapsilosis has become an increasingly important human pathogen as it is now the second most commonly isolated Candida species from blood cultures worldwide, and even outranks C. albicans in some hospitals. C. parapsilosis typically is a commensal of human skin and is considered to be of low pathogenicity in the setting of intact integument. The species is notorious for its frequent cause of disease in low birth weight newborns, Falgier et al found that C. parapsilosis showed little capacity to adhere to primary immature human enterocytes compared with C. albicans. Bertini and coworkers previously showed that C. parapsilosis and C. orthopsilosis have similar adhesion capacities to human buccal epithelial cells, in contrast the third member of the C. parapsilosis sensu lato species complex, C. metapsilosis, which displayed a significantly lower adhesive affinity. One of the important roles of fungal adhesins is to bind extracellular matrix (ECM) proteins such as fibronectin, vitronectin and laminin, and a recent study identified Als-like proteins on the surface of C. parapsilosis pseudohyphae that can bind to ECM components and thus can serve as the first step to cross mechanical barriers.

In this issue Bertini and colleagues demonstrate the role of a yet uncharacterized C. parapsilosis gene in adhesion to host surfaces and its contribution to the virulence of this species. The authors identified and disrupted a hypothetical, adhesion effecting gene “CPAR2_R04800,” (ortholog of C. albicans ALS genes), using a previously described gene deletion method. After testing the heterozygous and null mutants, the results suggested that CPAR2_R04800 does not influence the growth, morphologic potential, or cell wall stressor resisting abilities of C. parapsilosis; however, it does play a role in cell adhesion and pathogenicity. Significantly, reduced cell adhesion was observed on human buccal epithelial cells, and a remarkable reduction in virulence was detected in vivo using a murine urinary candidiasis model. Hence, the authors provide the first evidence for a direct role of C. parapsilosis adhesins in pathogenesis and virulence.

The work by Bertini et al highlights the need for more detailed investigations of one of the most important features of the pathogenesis program by fungi—the adhesion to host tissues and cells—not only in C. albicans but in other emerging Candida pathogens. There are several reports about the different adhesion capacities for individual Candida species, including C. parapsilosis. In general C. albicans has a greater capacity to adhere to host tissues, such as epithelial cells and vascular epithelium. This difference could be explained due to the presence of more α-L-fucose residues in the C. albicans cell wall relative to other species. Interestingly, despite the fact that C. parapsilosis is known to be more a more

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Recently an analysis of the presence and distribution of ALS genes in clinical and environmental isolates of C. parapsilosis has been performed revealing that different strains code a variable number of ALS genes, ranging from a single member (GA1, CBS1954), to 3 (CBS6318) and 5 (CDC317) members.22 Phylogenetic analysis reveals a rather complex and highly dynamic genetic process—including gene conversation—shaping the ALS gene family within pathogenic Candida species.22 It is still unclear how this high variability in ALS gene family of C. parapsilosis affects host-pathogen interactions.

While growing evidence in various disease models, including mouse and reconstituted human tissues, has demonstrated that C. albicans adhesins are key virulence factors as they play an essential role in pathogenesis.26-28 We have very little information about the role of adhesion in C. parapsilosis virulence and pathogenesis. Only a few studies have investigated the virulence properties of C. parapsilosis with different adhesion capacity in vitro and in vivo systems. The same group that presented the work detailed in this review has previously shown in an experimental vaginitis model in estrogen-treated mice that there are slight differences in disease as demonstrated by fungal burdens between C. parapsilosis and C. metapsilosis, which correlates with the latter’s lower adhesion capacity.23 This finding is supported by results in a study using a Galleria mellonella larvae infection model that found a significantly reduced mortality rate in the larvae infected with C. metapsilosis isolates compared to larvae infected with C. parapsilosis sensu stricto or C. orthopsilosis strains.29 In contrast, a disseminated candidiasis model showed no significant differences among the C. parapsilosis sensu lato species.30

Taken together, there is still a substantial gap in our knowledge regarding the detailed genetic determinants of adhesion properties of C. parapsilosis, and how these affect the interaction with the human host, including the tendency to disproportionally affect specific groups of patients. In sum, it is incontrovertible that we need a clearer understanding of the role of C. parapsilosis cell wall adhesins in the establishment of candidiasis in order to better understand host-pathogen dynamics as well as to develop new strategies to combat this emerging fungal pathogen.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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