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Molecular fingerprints of anti- *Candida* antibodies in serum: A mine for clinical biomarker development invasive candidiasis

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Statement of the Problem: Despite great advances in antifungal therapy, invasive candidiasis (IC) remains a significant public health problem worldwide. This opportunistic fungal infection caused by *Candida* spp. (commonly *Candida albicans*) often results in delayed initiation of appropriate antifungal therapy and poor clinical outcomes. We investigated whether molecular profiling of the serum IgG- antibody responses to the *C. albicans* immunome could reveal diagnostic and prognostic signatures that may serve to devise diagnostic and clinical-outcome prediction models for IC and contribute to known clinical factors.

Methodology & Theoretical Orientation: We combined serological proteome analyses (two-dimensional gel electrophoresis followed by Western blot analysis and mass spectrometry) with data mining procedures to explore the serum IgG- antibody responses to *C. albicans* protein species in IC and non-IC patients.

Findings: Unsupervised two-way hierarchical clustering and principal-component analyses of these IgG antibody-reactivity patterns accurately discriminated IC patients from non-IC patients as well as IC survivors from IC non-survivors. Supervised discriminant analyses identified two-IgG and five-IgG antibody-reactivity signatures as the most simplified and accurate IC diagnostic and prognostic predictors, respectively. Multivariate logistic-regression analyses revealed a positive association between these predictors and IC risk or two-month death risk. Receiver-operating characteristic curve analyses indicated that these diagnostic and clinical-outcome predictors for IC outperformed known clinical factors. Further validation of molecular fingerprints of these anti-*Candida* IgG antibodies in serum on multiplexed immunoassays substantiated the serological proteome analysis results (Figure 1).

Conclusion & Significance: We conclude that these prediction models may be useful to reliably diagnose IC and predict patient clinical-outcome for individualized therapy of IC. Our study shed new light on the anti-*Candida* IgG antibody response development in IC, and further highlights the importance of defining pathogen-specific antigens at the chemical and molecular level for their potential use as diagnostic or prognostic reagents or vaccine candidates for infectious diseases.

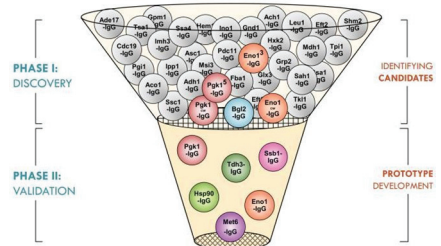


Figure 1. Diagnostic and prognostic biomarkers for IC discovered and validated in this study by serological proteome analysis and multiplexed prototype immunoassays, respectively

Biography

Aida Pitarch Velasco has her expertise in the clinical biomarker development for infectious diseases and in translational research. She has identified a large panel of novel clinical biomarkers and therapeutic candidates for invasive candidiasis. She has built diagnostic and clinical-outcome prediction models for these life-threatening fungal infections based on molecular fingerprints of the serologic responses to the *Candida* immunome. She has also developed new prototype immunological assays for the diagnosis and prognosis of invasive candidiasis. Her studies have further contributed to unraveling the great diversity and complexity associated with the pathogen-encoded immunome.

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