INTEGRATED PROTEOMIC AND GENOMIC STRATEGIES BRING NEW INSIGHT INTO C*ANDIDA ALBICANS* RESPONSE UPON MACROPHAGE INTERACTION.

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The interaction of *C. albicans* with macrophages is considered a crucial step in the development of an adequate immune response in systemic candidiasis. The single utility of proteomic and genomic approaches to study host -pathogen interaction has been previously described in the literature (1, 2, 3). An *in vitro* model of phagocytosis that includes a differential staining procedure to discriminate between internalized and non-internalized yeast was developed. Upon optimization of a protocol to obtain an enriched population of ingested yeasts, a thorough genomic and proteomic analysis was carried out on these cells. Both proteins and mRNA were obtained from the same sample and analyzed in parallel. The combination of 2D-PAGE with MS revealed a total of 132 differentially expressed yeast protein species upon macrophage interaction. Among these species, 67 unique proteins were identified. This is the first time that a proteomic approach has been used to study *C. albicans*-macrophage interaction. We provide evidence of a rapid protein response of the fungus to adapt to the new environment inside the phagosome by changing the expression of proteins belonging to different pathways. The clear down-regulation of the C-compound metabolism, plus the up-regulation of lipid, fatty acid, glyoxylate and tricarboxylic acid cycles, indicates that yeast shifts to a starvation mode. There is an important activation of the degradation and detoxification protein machinery. The complementary genomic approach led us to detect specific pathways related to *Candida's* virulence. Network analyses allowed us generate a hypothetical model of *Candida* cell death after macrophage interaction, highlighting the interconnection between actin cytoskeleton, mitochondria and autophagy in the regulation of apoptosis (4). In conclusion, the combination of genomic, proteomic and network analyses is a powerful strategy to better understand the complex host-pathogen interactions.

References:

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