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The Unfolded Protein Response is Required for Antifungal Drug Resistance in Yeast

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Malisa Fernando and Patrick Lajoie

Antifungal drug resistance is increasingly becoming a larger cause for mortality, especially in immunocompromised individuals. In yeast, the Unfolded Protein Response (UPR) functions to restore proteostasis of secretory proteins in the Endoplasmic Reticulum (ER) through the activation of the ER stress sensor Ire1. The Ire1 can be activated both by accumulation of misfolded proteins in the ER lumen, and ER lipid bilayer stress. This triggers a transcription response to restore the ER folding environment, lipid homeostasis and cell wall integrity. However, the mechanisms of UPR activation and genes responsible for yeast resistance from exposure to common antifungals, like caspofungin remains unknown. Interestingly, we found deletion of the Ire1 luminal domain, which senses misfolded protein accumulation sensitizes cells to caspofungin treatment. Using genetic screens and genome-wide transcriptome analysis, we are now seeking to identify UPR target genes required for the antifungal response in both *Saccharomyces cerevisiae* and the pathogen *Candida albicans*.