Identification of novel arsenic resistance genes in yeast

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Abstract

Arsenic is a toxic metalloid that affects human health by causing numerous diseases and by being used in the treatment of acute promyelocytic leukemia. Saccharomyces cerevisiae (budding yeast) has been extensively utilized to elucidate the molecular mechanisms underlying arsenic toxicity and resistance in eukaryotes. In this study, we applied a genomic DNA overexpression strategy to identify yeast genes that provide arsenic resistance in wild-type and arsenic-sensitive S. cerevisiae cells. In addition to known arsenic-related genes, our genetic screen revealed novel genes, including PHO86, VBA3, UGP1, and TUL1, whose overexpression conferred resistance. To gain insights into possible resistance mechanisms, we addressed the contribution of these genes to cell growth, intracellular arsenic, and protein aggregation during arsenate exposure. Overexpression of PHO86 resulted in higher cellular arsenic levels but no additional effect on protein aggregation, indicating that these cells efficiently protect their intracellular environment. VBA3 overexpression caused resistance despite higher intracellular arsenic and protein aggregation levels. Overexpression of UGP1 led to lower intracellular arsenic and protein aggregation levels whilst TUL1 overexpression had no impact on intracellular arsenic or protein aggregation levels. Thus, the identified genes appear to confer arsenic resistance through distinct mechanisms but the molecular details remain to be elucidated.

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