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Sensitivity of *ITT1Δ* and *RPS1AΔ* Yeast Strains to Arsenite Reveals their Role in Translation of *URE2*, a Key Gene Involved in Metal Detoxification

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Heavy metal and metalloid contaminations are among the most concerning pollutions in the world. Many parts of the world are polluted with toxic heavy metals and metalloids. Consequently, investigating the molecular mechanisms that drive the detoxification pathways in living organisms is of importance. A variety of genes have known functions in detoxification. The expression of these genes is controlled at both transcriptional and translational levels. When under heavy-metal stress, 5' cap-dependent translation is often down-regulated or even completely inhibited. In baker's yeast, *Saccharomyces cerevisiae*, resistance to a wide range of toxic metals is regulated by glutathione S-transferase products. Yeast URE2 protein has glutathione peroxidase activity and is homologous to mammalian glutathione S-transferases. In addition to 5' cap-dependent translation, yeast *URE2* mRNA is also translated through an internal structure, free of 5' cap and eIF4E. It possesses a unique Internal Ribosome Entry Site (IRES) element between nucleotides 205 and 309 in its coding region. *URE2* deletion mutants are hypersensitive to toxic metals such as arsenic, nickel and cadmium. Here, we report on the finding of two genes, *ITT1*, inhibitor of translation termination, and *RPS1A*, ribosomal protein 10 whose deletion strains exhibit similar drug sensitivity phenotype as *URE2* mutant. Neither of these genes was previously linked to metal toxicity. Our gene expression analysis illustrates that these two genes affect *URE2* mRNA expression at the translational level. Subsequent investigations suggest that the deletion of *ITT1* or *RPS1A* may negatively regulate the translation of *URE2* mRNA through its IRES element. Polysome profile analysis suggest a strong tie between candidate genes and protein synthesis mainly at the initiation step. Our genetic interaction analysis also showed strong communication between our two candidate genes and the genes involved in the regulation of translational and translation initiation.

Biography:

Houman Moteshareie completed his Bachelor's degree in Cambridge, UK in Medical Genetics. He continued his education with obtaining a Master's degree from University of Wales, UK in Biotechnology and Molecular Genetics. He is now in the final year of his PhD at Carleton University, Canada in Molecular Genetics and Systems Biology. Houman is currently a lecturerat Carleton University and Algonquin College. His research focuses on identification and investigation ofnovel genes that are involved in protein biosynthesis. In particular, he is working on Internal Ribosome Entry Sites (IRES) utilizing baker's yeast, *Saccharomyces cerevisiae* as a model organism. During his graduate education, Houman has been involved in many research and collaborated with excellent scientists, which resulted in many scientific publications.