THE ROLE OF THE UBIQUITIN SYSTEM DURING LITHIUM STRESS IN *SACCHAROMYCES CEREVISIAE*.

Pacheco-Rosa, T.[1], Azevedo, F.S.[1], Ferreira, C.J.S.[1] and Masuda, C.A.[1]

[1]Instituto de Bioquímica Médica, Universidade Federal do Rio de Janeiro, Brazil.

Ubiquitination is a post-translational modification characterized by the covalent attachment of the small protein ubiquitin to lysine residues of target proteins. Ubiquitination signals many different fates to the target protein such as changes in subcellular localization, modulation of activity and even its degradation. Due to these characteristics, ubiquitination events are frequent and important in many signal transduction pathways such as those involved in cellular responses to abiotic stresses. Lithium is used in the therapy of bipolar disorder but, at higher concentrations, are also very toxic. The molecular mechanisms behind both therapeutic and toxic effects of lithium are still unclear. In order to establish a role for the ubiquitin system during lithium stress in yeast, we screened a series of mutants deleted of ubiquitin-conjugating enzymes. Surprisingly, we observed that the deletion of the *UBC2* gene conferred increased resistance to lithium stress. This resistance is caused by the loss of the ubiquitin-conjugating enzyme activity since we could revert the lithium-resistant phenotype of ubc2Δ strain by expressing the wildtype UBC2 allele, but not with the inactive *ubc2-C88A* allele. These results support a role for *UBC2* as either a negative regulator of a lithium stress response pathway or as part of the toxicity mechanism induced by high lithium concentrations in yeast.

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