

Lead toxicity in *Saccharomyces cerevisiae*: The role of glutathione

Rita R. Perez,¹ Thomas Vankeersbilck,^{1,2} and Eduardo V. Soares,^{1,3}

1. Bioengineering Laboratory, Chemical Engineering Department, Superior Institute of Engineering of Porto Polytechnic Institute, Rua Dr António Bernardino de Almeida, 431, 4200-072 Porto, Portugal;
2. KaHo St.-Lieven, Department Industrial Engineering, Gebroeders Desmetstraat 1, 9000 Ghent, Belgium; and
3. IBB-Institute for Biotechnology and Bioengineering, Centre for Biological Engineering, Universidade do Minho, Campus de Gualtar, 4710-057 Braga, Portugal

evs@isep.ipp.pt

Lead is a non-essential metal for biological functions and is classified by the International Agency for Research on Cancer (IARC) as a probable human carcinogen. *S. cerevisiae* is a suitable model for studying Pb toxic effects since it is an eukaryote cell that can be easily manipulated and has a completely sequenced genome.

In the present work, the role of reduced glutathione (GSH) as a defense mechanism against Pb-induced toxicity in *S. cerevisiae* was investigated. Yeast cells exposed to Pb (3h) lost cell viability (quantified by a clonogenic assay), accumulated intracellular reactive oxygen species (ROS) (evaluated by 2',7'-dichlorodihydrofluorescein diacetate, H₂DCFDA) and decreased GSH level (assessed by monochlorobimane, mBCl). Yeast cells lacking the *GSH1* (*Dgsh1*) or *GSH2* (*Dgsh2*) genes were compared with wild type (WT) cells for loss of cell viability and Pb-induced ROS accumulation. We verified that *Dgsh1* and *Dgsh2* cells did not exhibit an increased loss of viability and did not experience ROS accumulation compared with WT cells. However, the treatment of WT cells with iodoacetamide (an alkylating agent which binds covalently to thiol groups) enhanced sensitivity to Pb. Incubation of WT cells with an amino acid mixture constituting GSH (L-glutamic acid, L-cysteine and glycine) reduced oxidative stress and loss of Pb-induced proliferation capacity. Together, the results suggest that intracellular GSH is involved in the defense against Pb-induced toxicity; however, it seems insufficient to sustain the oxidative stress and Pb-induced loss of cell viability.