Protective Mechanisms of Diphenyl Diselenide Against Methylmercury Toxicity in *Saccharomyces Cerevisiae*

Lovato, F.L.[1]; Rocha, J.B.T.[1]; Dalla Corte, C.L.[1,2]

[1]Programa de Pós-graduação em Ciências Biológicas: Bioquímica Toxicológica, Dep. de Bioquímica e Biologia Molecular, UFSM, Santa Maria, RS; [2]UNIPAMPA, Caçapava do Sul, RS, Brazil

Introduction: Methylmercury (MeHg) is a highly toxic pollutant ubiquitously found in the environment. Several studies demonstrated organic and inorganic selenium can influence deposition of MeHg in the body and protect against its toxicity. Diphenyl diselenide [$(PhSe)_2$], an organoseleno-compound, has been investigated due to its protective effects against MeHg toxicity, although the exact mechanism of this protection was not completely elucidated. **Objectives:** Single gene deletions were employed to investigate the role of the antioxidant system in the protective effects of $(PhSe)_2$ agaisnt MeHg toxicity in *Saccharomyces cerevisiae*. **Materials and Methods:** Yeast cells (wild type and knockout strains) were cultured in YPD liquid medium, treated with $(PhSe)_2$ and/ or MeHg up to 24h. Cell growth was analyzed spectrophotometrically measuring the optical density at 600 nm (OD600). Intracellular ROS levels were detected by flow cytometry using the fluorescent probe H_2-DCFH-DA. Cell membrane integrity was estimated by staining with the vital dye propidium iodide using flow cytometer. Thiol content was determined by flow cytometry using the fluorescent probe CMFDA. **Results and Discussion:** In the wild type strain, $(PhSe)_2$ protected against the growth inhibition, ROS production and decrease in membrane integrity induced by MeHg, and restored the levels of thiol to values similar to control. Single deletions of YAP1, SOD1, SOD2, GSH1, GSH2, GPX1, GPX2, TRX1, TRX2 and TRX3 decreased the capacity of $(PhSe)_2$ in prevent MeHg toxicity in yeast. The genes regulated by the transcription factor Yap1p include antioxidant genes such as TRX2, GSH1, SOD1, SOD2 and GPX2 suggesting that these and other components of the antioxidant system are required for the protective effects of $(PhSe)_2$. **Conclusion:** Together these results sheds light on the mechanisms involved in $(PhSe)_2$ protection against MeHg toxicity indicating a role of $(PhSe)_2$ in activating the transcription factor YAP1 leading to the expression of important antioxidant defenses in *S. cerevisiae*.

Keywords: Methylmercury; Selenium; Antioxidant defenses

Supported by: FAPERGS, CNPq and CAPES