Involvement of Grx Proteins in Resistance/Sensitivity To Cisplatin in *Saccharomyces cerevisiae.*

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Cisplatin is an antitumor drug capable to induce indirectly, by mobilizing glutathione, an increase of reactive oxygen species generation in the cell. Grx proteins are involved in glutathione system as well as in DNA synthesis and enzymatic regulation. Thus, we aimed to study in this work the role of Grx during cisplatin stress. For this study we used the yeast, *Saccharomyces cerevisiae*, as a eukaryotic model system for cisplatin sensitivity and resistance. The first step was to analyze the structural similarities between the human and yeast Grx proteins using the workbench and ExPASYy proteomic service. The score found and others analysis showed an absence of structural homology between proteins from these models. However, probably these proteins might share functional homology. Strains of *S. cerevisiae,* wild type and mutants *grx1?, grx2?* and *grx5?,* growing on fermentative metabolism, characteristic to cancerous cells, or on respiratory metabolism (Calorie Restriction-CR), characteristic of healthy cells were submitted to 0.45mM of cisplatin. Cells were collected at 1, 2, 3 and 4 h of cisplatin stress for viability and lipid oxidation analysis. All strains in respiratory metabolism showed to be more resistant than cells in fermentative metabolism. However, the *grx2?* was more resistant than wild type wit minor difference between the two metabolisms. Results from lipid peroxidation showed that all strains presented an increasing oxidative damage after cisplatin exposure in fermentative metabolism, being the *grx2?* more oxidized. Our results indicate a relation to oxidative stress and GRX proteins with cellular response to cisplatin evidencing the protection of CR during cisplatin stress.

Key word: Cisplatin, *S.cerevisiae*, GRX, Calorie Restriction.