FUNCTIONAL CHARACTERIZATION OF THE I91T MUTANT OF SUPEROXIDE DISMUTASE 2 FROM SACCHAROMYCES CEREVISIAE

Carvalho, M. D. C.; Eleutherio, E. C. A.; De Mesquita, J. F.

1Laboratory of Investigation of Stress Factors, UFRJ, Rio de Janeiro, Brasil; 2Bioinformatics and Computational Biology Group, UNIRIO, Rio de Janeiro, Brasil.

Introduction and objectives  The mitochondrial antioxidant enzyme Manganese-Superoxide Dismutase (Sod2) is essential for mammalian survival, hampering the analysis of the effect of polymorphisms to the enzyme function. I82T mutation in human Sod2 has been linked to a wide variety of diseases, including Alzheimer’s and Parkinson’s disease as well as some types of cancer. However, it is not clear if this mutation affects Sod2 performance. Informative data on the activities of mutant Sods have come from the yeast Saccharomyces cerevisiae in which the in vivo activities of the Sod mutants can be easily assessed by their ability to rescue the oxidative stress-sensitive phenotypes of yeast strains deficient in Sod. Using this approach, yeast wild-type (WT) Sod2 and the mutant Sod2 I91T, which correspond to the human mutant Sod2 I82T, were cloned in Δsod1 and Δsod2 yeasts. Methods To assess the functionality of Sod2 I91T under oxidative stress, yeast cells were shifted from glucose (reductive fermentative metabolism) to glycerol growth medium (oxidative respiratory metabolism). Results The overexpression of WT Sod2 or Sod2 I91T increased Sod activity, enhancing, consequently, the tolerance to oxidative stress of both sod1Δ and sod2Δ strains. Furthermore, both WT and mutant Sod2 increased the activity of the mitochondrial enzyme aconitase, suggesting that the I91T mutation does not impair the ability of Sod2 to dismutate superoxide. Aconitase is commonly known as a sensor of superoxide radical production in vivo. Conclusions I91T mutation does not affect the yeast Sod2 activity, indicating that I82T mutation is not detrimental to the functionality of human Sod2.

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