Expression of hSOD1 in porin1-less yeast strain restores mitochondrial functionality modulating the protein composition of mitochondrial membranes

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The Superoxide Dismutase I (SOD1) is the most important enzymatic defense against ROS, catalyzing the dismutation reaction of superoxide anion in hydrogen peroxide and water [1]. For this reason, SOD1 plays a key role in controlling the ROS steady-state levels and in modulating ROS-mEDIATE signaling. Recent studies have suggested that SOD1 is also involved in metabolism regulation. In yeast S. cerevisiae, SOD1 controls the repression of respiration in presence of glucose, through the direct regulation of specific casein kinase proteins: indeed, strains devoid of endogenous SOD1 (Δsod1) are not able to totally repress the respiration [2]. Moreover, Δsod1 strain shows altered levels of outer mitochondrial membrane (OMM) proteins, suggesting that SOD1 might also influence mitochondrial respiration. The Voltage-Dependent Anion Channel (VDAC) represents a family of OMM mitochondrial porins, directly involved in ATP/ADP, ions and metabolites exchanges across OMM [3]. In S. cerevisiae two different VDAC isoforms are expressed: por1, the most abundant and characterized, and por2, an uncharacterized sequence homologous. It was shown that absence of SOD1 strongly decreases the expression levels of por1, as well as the component of traslocase complex of OMM, Tom40 and Tom55. Also, in this condition, por1 conductance results compromised [4]. To unravel the effect of SOD1 on VDAC-mediated metabolism, in our work we expressed human SOD1 in a yeast strain devoid of endogenous por1 (Δpor1). Δpor1 strain cannot grow in the presence of a not fermentable carbon source as glycerol, possibly due to altered mitochondrial functionality. Our results clearly indicate that in Δpor1 yeast hSOD1 expression, in addition to the endogenous SOD1, relieves the growth defect and restores the mitochondrial membrane potential, compromised in Δpor1 strain. These overall data suggest that hSOD1 has a strong effect in Δpor1 mitochondria functionality. In addition, our preliminary analysis of gene expression profiles shows that hSOD1 increases por2 expression levels, usually very low. These results indicate that SOD1 may take part in the regulation of transcription. It was indeed recently shown that SOD1 can translocate in nucleus under oxidative stress conditions, acting as transcription factor for genes involved in oxidative stress response [5], with a well conserved mechanism from yeast to mammals.

References

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