Structure Determination and Analysis of Yeast Cytosolic Thioredoxin Peroxidase I

Tairum-Jr, C.A.[1], Oliveira, M.A.[1], Genu, V[2] ,Discola, K. F.[2], Bathagin, F.[1], Alves, S.V.[2] Guimarães B. G.[3], & Netto, L.E.S.[2]
[1]Universidade Estadual Paulista, Campus São Vicente, SP, Brazil.
[2]Universidade de São Paulo, São Paulo, SP, Brazil
[3]Laboratório Nacional de Luz Síncrotron, Campinas, SP, Brazil

Saccharomyces. cerevisiae cTPxI and cTPxII are cytosolic enzymes that present a high primary structure homology (86% identity and 96% similarity), exhibit peroxidatic activity and were characterized as homodimers of ~43 kDa. Nonetheless, exposure of yeast cells to heat shock or oxidative stress triggers an intense oligomerization resulting in the formation of [(α2)5] and high-molecular-weight complexes. This structural change is correlated with a transition of the protein function from peroxidase to molecular chaperone. Despite their similarities, a recent study showed that the pKa of the peroxidatic cysteines differ considerably between the two TPx. The difference in the reactivity probably relies on slight differences between the two protein structures, which may have consequences for their intrinsic peroxidatic and chaperone activities. Accordingly, human representatives TPx cytosolic isoforms Prx1 and Prx2 which share a very high degree of sequence homology (78% identity and 91% similarity), present differences in their chaperone and peroxidase activities. Prx1 is more efficient as a chaperone, while Prx2 is a better peroxidase. A cysteine residue in Prx1 (Cys83) which is not found in Prx2 plays a critical role in these differences. Sequence analysis shows that the yeast proteins do not possess an equivalent cysteine. Here, we report structure resolution and refinement at 2.8Å of yeast cTPxI carrying the Cys47Ser substitution. The comparison of cTPxI structure with its human counterparts reveals slight differences between the proteins. The accurate analysis may help in comprehending the differences underlying their peroxidase and chaperone functions.

Financial Support: FAPESP & CNPq.