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ABSTRACT BOOK

THE ROLE OF Y-PARK9 PROTEIN IN PREVENTING MANGANESE-INDUCED PARKINSON'S DISEASE

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A variety of metals are essential trace elements but can reach localized toxic concentrations through various disease processes or environmental exposures and have been implicated as having a role in neurodegeneration. In particular, chronic inorganic manganese exposure causes selective toxicity to the nigrostriatal dopaminergic system, resulting in a Parkinsonian-like neurological condition known as Manganism. YPK9 gene (Yeast PARK9; also known as YOR291W) encodes a transmembrane P-type transport ATPase presumably involved in metal coordination and transportation, though its substrate specificity still remains unknown. Mutations in the human homolog of YPK9, PARK9 (ATP13A2), have been linked to genetic forms of early onset parkinsonism. Recently a strong genetic interaction between YPK9 and another Parkinson's disease protein, α-synuclein, has been evidenced in multiple model systems, indicating a crucial role for YPK9 in manganese detoxification in yeast and a specific protecting effect against manganese poisoning [1,3].

With the purpose to shed light on the protective property of YPK9 in Manganese-induced Parkinsonism, we tested the binding ability of Mn(II) and other divalent cations (Cu(II), Zn(II)) towards several peptide sequences from YPK9, with a particular focus on highly conserved sequences from yeast to human. The work was carried out at different pH values and ligand/metal molar ratios by means of potentiometric and spectroscopic techniques (multidimensional and heteronuclear NMR and UV-visible), in order to evaluate and compare the coordination propensity of such fragments with Mn(II) and the other metal probes selected [4,5].

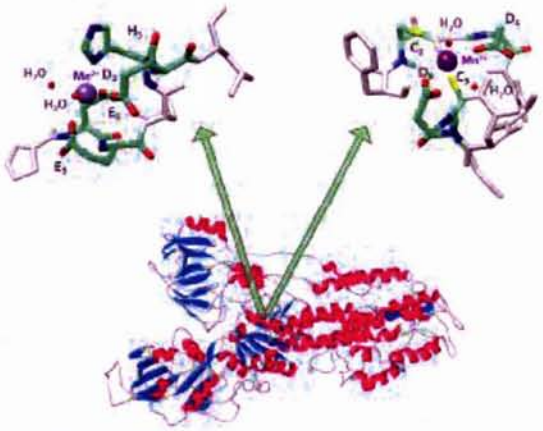

Figure 1. The model of the YPK9 protein built with ESyPred3D using the 3D crystal structure of the sodium-potassium pump (PDB 3B8E chain A) as the template, and the 3D structural models proposed for the Mn(II) ion complexed with selected fragments of YPK9 protein sequence.

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