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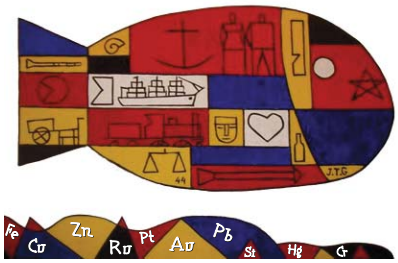

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Interaction of divalent cations with protein PARK9

Zoroddu, M.A.[1]; Peana, M.[1]; Medici, S.[1]; Solinas, C.[1]; Juliano, C.[1]; Remelli, M.[2]

[1]*Chemistry and Pharmacy, University of Sassari, Sassari, Italy*
[2]*Chemical and Pharmaceutical Sciences, University of Ferrara, Ferrara, Italy*
zoroddu@uniss.it

Metals have been shown to play a role in the genesis and development of many neurodegenerative diseases. Park9 encoded protein can protect cells from manganese poisoning, an environmental risk factor for a Parkinson's disease- like syndrome[1,2]. Park9 belongs to a family of ATP-ases involved in metal coordination and transportation; familial mutations of this gene may result in early development of PD. We tested two peptide sequences from Park9, -$P_1D_2E_3K_4H_5E_6L_7$- (1) and -$F_1C_2G_3D_4G_5A_6N_7D_8C_9G_{10}$- (2), for Mn(II), Zn(II) and Cu(II) binding. These fragments are located from 1165 to 1171 and from 1184 to 1193 residues in Park9 sequence, and are highly conserved in a number of organisms, from yeasts to humans. Experiments have been carried out at different pH values and ligand/metal molar ratios with both potentiometric and spectroscopic (NMR, UV-vis) techniques, showing that the three metals are able to effectively bind the examined peptides. Mn(II) and Zn(II) coordination with peptide (1) involves imidazol of His5 and carboxyl γ-O of Asp_2, Glu_3 and Glu_6 residues, in a distorted octahedral geometry, possibly involving bidentate interaction of carboxyl groups; four donor atoms participate in Zn(II) binding, resulting in a tetracoordinated geometry. Mn(II) and Zn(II) coordination involves the two cysteines in peptide (2); Mn(II) accepts additional ligand bonds from D4 and D8 to complete the coordination sphere, together with some water molecules. Details of Cu(II) coordination are under study.

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