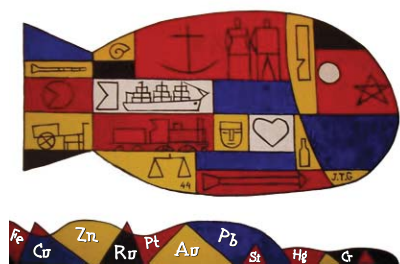


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Interaction of divalent cations with protein PARK9Zoroddu, M.A.¹; Peana, M.¹; Medici, S.¹; Solinas, C.¹; Juliano, C.¹; Remelli, M.²¹*Chemistry and Pharmacy, University of Sassari, Sassari, Italy*²*Chemical and Pharmaceutical Sciences, University of Ferrara, Ferrara, Italy*
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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, -P₁D₂E₃K₄H₅E₆L₇- (1) and -F₁C₂G₃D₄G₅A₆N₇D₈C₉G₁₀- (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 Asp₂, Glu₃ and Glu₆ 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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