Copper-ion interaction with the 106-113 domain of the prion protein a solution-equilibria study on model peptides.

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Streszczenie

Prion diseases are characterized by a structural modification of the regular prion protein (PrP^{C}) to its isoform, termed PrP^{Sc} (scrapie). Such a modification involves the secondary and tertiary structure of the protein; the amino acidic sequence remains unchanged. PrP^{Sc} is almost insoluble in non-denaturing solvents, resistant to proteases and it loses its redox activity. PrP^{C} is able to bind copper and other metal ions: these complexes have been suggested to play an important role in the protein refolding leading to PrP^{Sc}. It is well-known that at least one relatively strong copper-binding site is located in the $PrP_{92–126}$ domain, where two His residues (96 and 111) are present. However, in the same domain, other amino acidic residues bear potentially donating atoms, *i.e.* Met, Asn and Lys residues. In order to shed light on the role of the side chains of such potentially tridentate amino acids on copper complexation, the polypeptide Ac–KTNMKHMA–NH_2, corresponding to the $PrP_{106–113}$ fragment, and some synthetic analogues have been investigated as ligands for the copper ion, by means of both thermodynamic and spectroscopic techniques. The pivotal role of imidazolic side chain of His in “anchoring” the metal ion has been confirmed. On the other hand, no clue was found on the participation of sulfur atom of Met or side amino-group of Lys residues to copper complex-formation.

Adres publiczny

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