

Cu^{II} binding sites located at His-96 and His-111 of the human prion protein: thermodynamic and spectroscopic studies on model peptides.

Autorzy

Ewa K. Gralka
Daniela Valensin
Elena Porciatti
C. Gajda
Elena Gaggelli
Gianni Valensin
Wojciech Kamysz

R. Nadolny

Remo Guerrini

D. Bacco

Maurizio Remelli

Henryk Kozłowski

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Streszczenie

The prion protein (PrP) is a Cu²⁺-binding cell-surface glycoprotein. Using PrP peptide fragments, by means of potentiometric, spectroscopic and thermodynamic techniques, we have shown that Cu²⁺ ions bind to the region comprising His-96, His-111 and the octarepeat domain within residues 60–91. Cu²⁺ may bind in different modes, which strongly depend both on His position within the peptide sequence and on the adjacent residues. We have used a series of protected oligopeptides having His at the C- or the N-terminus, inducing different binding modes to amide nitrogens around the His residue, either towards the N- or C-terminus. His imidazole acts as an anchoring site for Cu²⁺ and then binding to ionized amide nitrogens follows. When it is directed towards the C-terminus the formation of a less stable seven-membered chelate ring with a {N_{im}, N⁻} binding mode occurs. When coordination goes towards the N-terminus the thermodynamically more stable six-membered chelate ring is formed. NMR data suggest that both the coordination modes are possible for the model peptides; however, the thermodynamic measurements show that they only slightly differ in energy and the influence of the adjacent amino acid residues can address the coordination toward the C- or the N-terminus.

Adres publiczny

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