

Copper-induced structural propensities of the amyloidogenic region of human prion protein.

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Streszczenie

Transmissible spongiform encephalopathies are associated with the misfolding of the cellular Prion Protein (PrP^C) to an abnormal protein isoform, called scrapie prion protein (PrP^{Sc}). The structural rearrangement of the fragment of N-terminal domain of the protein spanning residues 91–127 is critical for the observed structural transition. The amyloidogenic domain of the protein encloses two copper-binding sites corresponding to His-96 and His-111 residues that act as anchors for metal ion binding. Previous studies have shown that Cu(II) sequestration by both sites may modulate the peptide's tendency to aggregation as it inflicts the hairpin-like structure that stabilizes the transition states leading to β -sheet formation. On the other hand, since both His sites differ in their ability to Cu(II) sequestration, with His-111 as a preferred binding site, we found it interesting to test the role of Cu(II) coordination to this single site on the structural properties of amyloidogenic domain. The obtained results reveal that copper binding to His-111 site imposes precise backbone bending and weakens the natural tendency of apo peptide to β -sheet formation.

Słowa kluczowe

Prion protein, Copper, His-111, Amyloidogenic region, β -sheet

Adres publiczny

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