

Copper binding to the neurotoxic peptide PrP₁₀₆₋₁₂₆: thermodynamic and structural studies.

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Streszczenie

The human prion protein fragment PrP(106-126) is a highly fibrillogenic peptide, resistant to proteinases and toxic to neurons; it derives from the normal prion protein (PrP(C)), with which it can interact, thus inhibiting its superoxide dismutase-like activity. The same properties are also shown by the abnormal isoform of the prion protein (PrP(Sc)), and this similarity makes PrP(106-126) an interesting model for the neurotoxic action of PrP(Sc). A role for copper in PrP(106-126) aggregation and toxicity has recently been evidenced, and the interaction of terminal Lys, His and Met residues with the copper ion at neutral pH has been suggested. In order to shed more light on the complex-formation equilibria of PrP(106-126) with the copper ion, a thorough investigation has been carried out by means of several experimental techniques: potentiometry, solution calorimetry, VIS spectrophotometry, circular dichroism, EPR and NMR spectroscopy. A shorter and more soluble fragment-PrP(106-113), which lacks the hydrophobic C-terminal domain of PrP(106-126) but contains all the potential donor groups-has also been considered for the sake of comparison. The involvement of terminal amino, imidazolic and amido nitrogens in complex formation has been confirmed, while no evidence was found for the interaction of side chains of Met and Lys residues with the copper ion. Solution structures for the main complexes are suggested.

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