Identification of a novel high affinity copper binding site in the APP(145-155) fragment of amyloid precursor protein.

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Rok wydania

2004

Czasopismo

Dalton Transactions

Strony

16-22

DOI

10.1039/B312411H

Kolekcja

Naukowa

Język

Angielski

Typ publikacji

Artykuł

Streszczenie

The copper(II) binding features of the APP(145–155) and APP(145–157) fragments of the amyloid precursor protein, Ac-Glu-Thr-His-Leu-His-Trp-His-Thr-Val-Ala-Lys-NH_2 and Ac-Glu-Thr-His-Leu-His-Trp-His-Thr-Val-Ala-Lys-Glu-Thr-NH_2 were studied by NMR spectroscopy and NMR findings were supported by UV-vis, CD and EPR spectra. Potentiometric measurements were performed only for the more soluble Ac-Glu-Thr-His-Leu-His-Trp-His-Thr-Val-Ala-Lys-Glu-Thr-NH_2 peptide fragment. The following was shown: (i) the imidazole rings of all the three His residues are involved in metal coordination; (ii) metal binding induces ionisation of Leu-148 and His-149 amide nitrogens that complete the donor set to copper(II) in the species dominant at neutral pH; (iii) the unusual coordination scheme of the His-Xxx-His-Xxx-His consensus sequence justifies the high specificity for Cu(II) when compared to SOD-like or albumin-like peptides or even in amyloid Aβ fragments. The present findings may represent the key for interpreting the observed requirement of His residues conservation for the redox cycling between Cu(II) and Cu(I) by soluble APP.

Adres publiczny

https://doi.org/10.1039/B312411H

Strona internetowa wydawcy

https://www.rsc.org/