Uniwersytet Wrocławski

Repozytorium

Plik pochodzi z repozytorium Wydziału Chemii Uniwersytetu Wrocławskiego

Specific binding of Cu^{2+} ions by a pentapeptide fragment present in the cysteine-rich region of amyloid precursor protein.

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Rok wydania

2002

Czasopismo

Journal of the Chemical Society, Dalton Transactions

Strony

2266-2268

DOI

10.1039/B203284H

Kolekcja

Naukowa

Język

Angielski

Typ publikacji

Artykuł

Streszczenie

The βA4 amyloid precursor protein fragment situated in the cysteine-rich region is a very effective binding site for Cu^{2+} ions due to the presence of three His residues in the His–Xaa–His–Yaa–His sequence.The βA4 amyloid precursor protein (APP), a multifunctional glycoprotein, is a source of the characteristic βA4 amyloid deposits found in Alzheimer's disease.[1] APP is known to bind to Zn^{2+} ions, which may modulate its interactions with heparin.[2] Studies by Multhaup *et al.*[3–6] have shown that the βA4 amyloid precursor protein binds very effectively to Cu^{2+} ions and then reduces them to Cu^{+}, producing hydrogen peroxide. The copper-binding also results in a site-specific fragmentation of APP, which could be an important process during Alzheimer pathology.[5] The main cause of the specific Cu^{2+} ion binding seems to be the presence of His residues in the cysteine-rich region of APP, while redox reactions are induced by two cysteine residues at positions 144 and 158.[5,6] The –His–Xaa–His– sequence, present in the SOD1 copper-binding centre for example, could be a major factor for metal ion binding by APP.[3] In this work we have tested the specificity of a three His residue site, –His–Leu–His–Trp–His–, which is present in a cysteine-rich region of APP, using potentiometric and spectroscopic techniques (absorption, EPR and CD spectra). To model the protein binding site we have used a pentapeptide fragment protected at the N- and C-termin.

Adres publiczny

https://doi.org/10.1039/B203284H

Strona internetowa wydawcy

https://www.rsc.org/

Plik został wygenerowany dnia 2026-10-31 21:01:16

Adres w repozytorium https://old.chem.uni.wroc.pl/pl/repozytorium/_JIW27x.