Copper Binding to Human Doppel Protein Fragments

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The Doppel protein (Dpl, downstream prion protein-like) is the first discovered homologue of prion protein (PrP^C) a GPI-anchored glycoprotein which conformational transition causes a class of diseases known as transmissible spongiform enchephalopathies or prion diseases [1]. Dpl resembles a sort of N-terminal truncated version of PrP^C, lacking of the octarepeats motif. It shares 25% identity with the C-terminal two-thirds of PrP^C and an almost superimposible three-dimensional fold, characterized by three α-helices and two short antiparallel β-sheets. Both proteins are able to bind copper in a selective manner in vitro and some reports indicate an antagonism between the Dpl and N-terminal truncated form of PrP for Cu(II) ions [2]. One specific histidine has been identified as Cu(II) binding site and an enhancement of α-helical content of whole protein has been observed after the copper complexation [3]. The unambiguous characterization of the copper(II) coordination binding site has not been yet achieved. In order to investigate the coordination environment of copper and the conformational variation of this part of protein we have synthesized the peptide fragments of human Dpl encompassing residues 122-130 and 122-139 with the N- and C-termini protected by acetylation and amidation respectively. The peptides were characterized by means of NMR and CD spectroscopy. Then copper(II) complexes were studied by means of potentiometry and spectroscopy obtaining copper binding details. The results allow to determine not only the copper(II) species formation, but also the influence of metal ion into the secondary structure of this Dpl region.

References

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