Conference

A re-investigation of copper coordination mode in the N-terminal 1-14 fragment of human Ctr1 protein.

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Copper (Cu) is an essential micronutrient for most organisms and serves mainly as a redox-active catalytic centre in enzyme cycling between Cu^{+} and Cu^{2+}. In mammalian cells the membrane transporter Ctr1 regulates the import of Cu into the cytosol (Fig. 1).

Even though the Cu is imported by Ctr1 as Cu^{+}, it may be transferred as Cu^{2+} to the high-affinity N-terminal Cu^{2+} binding site of the h-Ctr1 extracellular domain (ATCUN) and then reduced, for instance by ascorbate or a STEAP reductase on the cell membrane.[1] The critical nature of Ctr1 in human health has spurred interest in structure and function; however details on Ctr1-dependent Cu uptake and transport have to be elucidate.[2] Several studies on Ctr1 model peptides shed light on the identity of the Cu uptake through the extracellular binding site motif, but unresolved questions are yet opened.[3] We examined the copper coordination mode of the Ctr_{11-14} fragment, a most used Ctr1 model peptide, in the presence of an excess of copper (II) (1:2 peptide/copper ratio). Taking in consideration that silver ion may adopt the typical Cu^{+} coordination modes we used Ag^{+} to study the possible formation of ternary complex species with Cu^{2+}. A combined potentiometric, spectroscopic and redox study, revealed that, at physiological pH, no ternary complex species are present, suggesting a crucial involvement of the His 3 as an anchoring point in the coordination of the Cu^{2+} and/or Ag^{+}

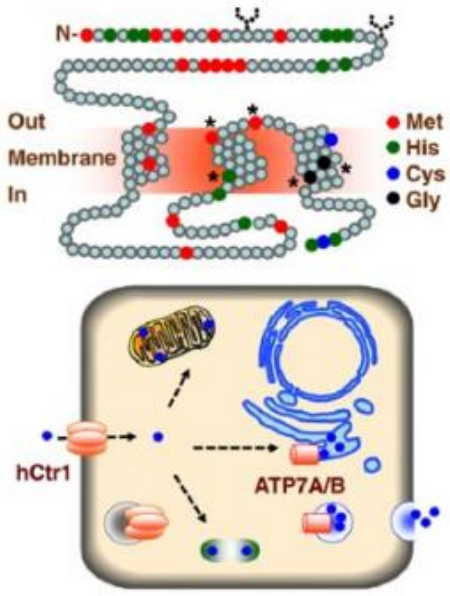

Fig. 1 Schematic illustration of the structure, localization, and function of human CTR1.

References

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