The Cu⁺-chaperone Atx1 can be replaced by Cd²⁺- or Hg²⁺-binding proteins in delivering copper to the secretory pathway in yeast

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The Cu⁺-chaperone Atx1 delivers copper to Ccc2 - the Golgi Cu⁺-ATPase - and therefore to the secretory pathway. Atx1 belongs to a family of proteins (or protein domains) of about 70 amino acids that bear a soft-metal binding site including the CxxC consensus sequence and that display a ferredoxin-like fold. Some of these proteins (or protein domains) such as Atx1 participate to Cu⁺ homeostasis, but others are involved in Cd²⁺, Zn²⁺, Pb²⁺ or Hg²⁺ resistance. We investigated Cu⁺-delivery to the secretory pathway *in vivo*, replacing Atx1 by various proteins of this family in an *atx1-?* yeast strain. Five proteins known as Cu⁺-, Cd²⁺- or Hg²⁺-binding proteins in their genuine organism were able to replace Atx1. Therefore, these proteins could all bind Cu⁺ and transfer it to Ccc2, suggesting that Ccc2 is opportunistic and able to gain Cu⁺ from many different proteins. The possible role of electrostatic potential surfaces in the docking of Ccc2 with these Atx1-homologues is discussed.