Overexpression of amyloid precursor protein increases copper content in HEK293 cells

Suazo, Miriam

Hodar, Christian

Morgan, Carlos

Cerpa, Waldo

Cambiazo, Verónica

Inestrosa, Nibaldo C.

Gonzalez, Mauricio

Amyloid precursor protein (APP) is a transmembrane glycoprotein widely expressed in mammalian tissues and plays a central role in Alzheimer's disease. However, its physiological function remains elusive. Cu2+ binding and reduction activities have been described in the extracellular APP135-156 region, which might be relevant for cellular copper uptake and homeostasis. Here, we assessed Cu2+ reduction and 64Cu uptake in two human HEK293 cell lines overexpressing APP. Our results indicate that Cu2+ reduction increased and cells accumulated larger levels of copper, maintaining cell viability at supra-physiological levels of Cu2+ ions. Moreover, wild-type cells exposed to both Cu2+ ions and APP135-155 synthetic peptides increased copper reduction and uptake. Complementation of function studies in human APP751 transformed Fre1 defective Saccharomyces cerevisiae cells rescued low Cu2+ reductase activity and increased 64Cu uptake. We conclude that Cu2+ reduction activity of APP facilitates cop