INTRACELLULAR COPPER REGULATION: INTERACTIONS WITH IRON.

Miguel Arredondo[1], Héctor Núñez[1], Solange Le Blanc[1], Rodrigo Pulgar[2], Marco Tulio Núñez[3].

[1]Laboratorio de Micronutrientes; [2]Laboratorio de Bioinformática y Expresión Génica, Instituto de Nutrición y Tecnología de los Alimentos (INTA); [3]Facultad de Ciencias. Universidad de Chile.

Copper is a metal both essential and potentially toxic to humans. Because its redox properties copper is a cofactor for proteins involved in essential processes as neural development (dopamine β hydroxylase), photosynthesis and respiration (cytochrome c oxidase), free radical management (Superoxide dismutase) and plasma iron oxidation (Ceruloplasmin). Copper is also toxic, hence, body and cellular copper homeostasis are necessary to achieve a sufficient supplement of copper while avoiding potential toxic effects. Menkes syndrome and Wilson disease represent deficiency and excess of copper, respectively, characterized by a defect in copper distribution to tissues and organs. However, the early effects of marginal deficiency or moderate excess of copper in non susceptible genetic individuals are unknown. Absorption of copper occurs primarily in duodenum and small intestine across de brush border into the cells mediated by hCTR1 and DMT1, two Cu^{1+} transporters. DMT1 also transport Fe^{2+}, suggesting that both metals may compete for theirs uptake. In the present work we studied the a) mechanism of copper uptake and transport; b) intracellular regulation; c) interactions with iron; d) effect of 17-β-estradiol in copper uptake and e) genic expression mediate by copper in intestinal (Caco-2) and hepatic cell lines incubated with different Cu concentrations. The results showed a) a high competition for cellular uptake and transport between Cu and Fe; b) Cu modulate genes involved in Cu and Fe metabolism, and c) Estradiol modified intracellular copper metabolism.