Copper-protein interactions in degenerative diseases:
From the brain to the human lens

Liliana Quintanar
Department of Chemistry,
Cinvestav (Center for Research and Advanced Studies),
Mexico City, México ***lilianaq@cinvestav.mx***

Copper is essential for life as cofactor of a wide range of metalloproteins, yet it has also been implicated in several degenerative diseases associated to the deposition of protein aggregates. Examples include Alzheimer´s, Parkinson´s, prion diseases, diabetes type 2, and cataracts, where the implicated proteins are the β-amyloid peptide, α-synuclein, prion protein, islet amyloid polypeptide (IAPP) or amylin peptide, and β/γ-crystallin proteins, respectively. Our research group studies the interaction of copper ions with some of these proteins, using a wide range of spectroscopic tools to understand their coordination chemistry, and the impact of the metal ion in protein folding, stability and aggregation properties. In this presentation, some Cu-protein interactions that are key players in neuroprotective mechanisms at the synapse - and likely affected in Alzheimer´s disease - will be discussed. Also, two stories that illustrate the role of copper coordination features on protein stability and aggregation will be presented. The inhibitory effect of copper ions in the amyloid aggregation of the IAPP peptide – involved in diabetes type 2 – will be discussed, illustrating how the copper coordination chemistry provides the molecular basis to understand the inhibitory effect of the metal ion. This story will be contrasted to the case of human lens γ-crystallin proteins, where copper ions induce their non-amyloid aggregation through different site-specific mechanisms. Overall, understanding how the metal ion impacts protein stability and aggregation provides further insights into the bioinorganic chemistry of copper in these degenerative diseases.