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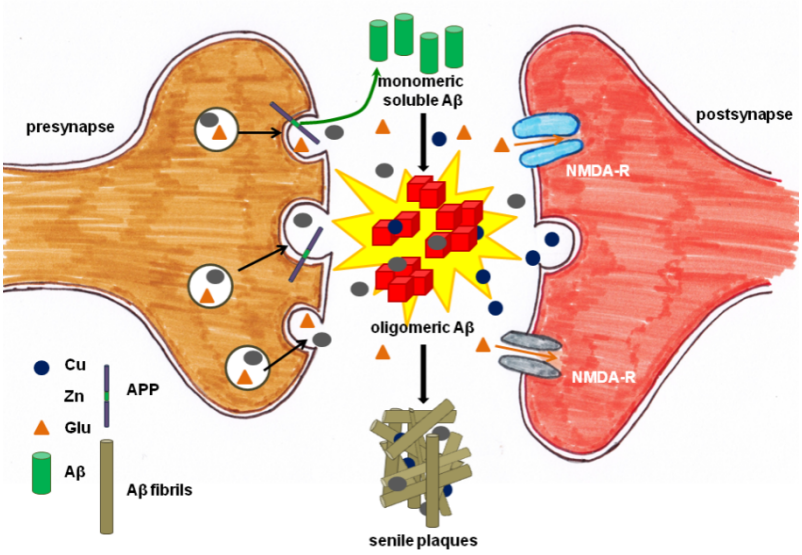
"Cu and Zn impacts in Alzheimer's disease. From fundamental studies to therapeutic strategies"

Alzheimer's disease (AD) is characterized by a global deterioration of mental, cognitive and physical abilities. AD is the most common cause of dementia in the elderly population. As a direct consequence, AD represents a global public health problem that will become even more important in the next years. Two hallmarks are detected in AD patients brains: i) the intracellular neurofibrillary tangles of Tau protein, the protein involved in the "neuronal skeleton", and ii) the extracellular amyloid plaques (also known as senile plaques) made of aggregated forms of the amyloid-β (Aβ) peptide. These peptides are present in soluble (monomeric) form in healthy brains. Hence the route to the formation of the aggregated forms of the Aβ peptide is key in the etiology of the disease. Such phenomenon is known as the amyloid cascade. A role in the amyloid cascade have been proposed for the metallic ions Copper(I/II), Zinc(II) et Iron(II/III). They have also been implicated in oxidative stress production, i.e. in the formation of highly toxic reactive oxygen species (ROS).

In the Biological Chemistry Group, we have recently studied how such metallic ions are bound to the Aβ peptide, which is a prerequisite to understand how they can interfere in the Aβ aggregation process as well as in the ROS production. In particular, we have shown how the nature of the metallic ion and the peptide sequence impact the coordination site.

The good knowledge of these data are crucial for designing new kind of therapeutic tools, which is an emergent axis of our team. Some of these terapeutic strategies will be commented on.



Refs: Coord. Chem. Rev, 2012, *256*, p2164
Act. Chim., 2013, *380*, p31