

Cu(I) and Zn(II) binding to the Alzheimer peptide

In the "Alzheimer, amyloid and Bio-Inorganic Chemistry" group of the Laboratoire de Chimie de Coordination, we are interested in the study of peptides – ions interactions, mainly Copper and Zinc, since they are at the core of pathological processes involved in many amyloid-related diseases, such as Alzheimer's disease (AD).[1] The description of the interaction between the amyloid- β peptide (A β the one involved in AD) and the metal ions is multiple and includes the environment of the metal ions within the peptide but also the strength of the interaction (e.g. the association constant). While for Cu(II) ion, such parameters have been extensively measured with a consensual value obtained only recently,[2] the Cu(I) and to a lesser extent the Zn(II) affinity are still under debate.

In the present project, we aim at determining those crucial data using a set of complementary methods, mainly fluorescence. To do so, we will first label the A β peptide with a fluorophore, whose fluorescence will be sensitive to the folding of the peptide that is changed by Cu(I) and Zn(II) binding. NMR and circular dichroism will be used in complement. Lastly, the amino-acid residues involved in Cu(I) and Zn(II) binding will be deduced from the affinity study of mutated peptides.[2,3]

References :

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[3] Noël, S.; Bustos, S.; Sayen, S.; Guillon, E.; Faller, P.; Hureau, C.,* "Use of a new water-soluble Zn sensor to determine Zn affinity for the amyloid- β peptide and relevant mutants." *Metallomics*, **2014**, 6, 1220-1222.