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Copper chelator from *in vitro* to cellular studies

Copper (Cu) is the third most abundant transition metal in the human body after iron and zinc. It plays a central role in many biological processes (Neurobiology of Disease 1999, DOI : 10.1006/nbdi.1999.0250). When misregulated Cu is however prone to generate reactive oxygen species (ROS) due to its redox ability at physiological potential, which causes catastrophic damage to biologic tissues. Disturbance of its homeostasis is observed in a number of serious diseases including Alzheimer's disease (AD). Moreover, Cu associated with the amyloid beta peptide (CuAβ), a central peptide in AD, keeps its ability to redox cycle between its two biologically relevant redox states and produces ROS. The ROS production originates from the incomplete reduction of the dioxygen fueled by a reductant as ascorbate. Cu would also stabilize Aβ-oligomer forms considered as the most toxic Aβ-aggregates nowadays.

The group is actively working on the development of Cu chelators able to sequester Cu and to froze it under a single redox state (either Cu(I) or Cu(II)) in order to avoid its toxicity in AD context. Several chelators have been synthetized and have demonstrated their ability stop the CuAβ-induced ROS production *in vitro* (in a test tube). The object of the present internship is to (1) translate the positive results obtained with the chelator in vitro to the cellular level and (2) fine-tune the chelator structure to optimize its efficiency, stability, solubility on cells.
The internship includes a part on cell studies to identify the reactive species produced in presence of CuAβ and quantify of their intra and extracellular production using mass spectrometry and EPR spectroscopy.

The internship will be conducted on two different sites between two teams in collaboration.
The candidate should be a motivated and perseverant person, willing to work on an interface biology / chemistry in a multidisciplinary environment. The candidate should have a strong background in organic synthesis, bio-organic chemistry, and be opened minded to cellular studies. Experience in cellular biology is not required but a strong interest and willingness to learn is needed.