

« Development of chelating chitosan polymers for the oral treatment of contamination by heavy metals »
« Développement de polymères de chitosane chélatants pour le traitement oral des contaminations aux métaux lourds »

Even if regulation has limited the presence of heavy metals (lead, cadmium...) in high income countries, humans are inevitably exposed to the contamination of water and foodstuff due to the inheritance of the industrialized past. Trace levels of blood and cadmium are found in blood in all countries over the world (J. Wang *et al.*, *Front. Public Health*, **2021**; B. Ericson *et al.*, *The Lancet*, **2021**; K. Kim *et al.*, *Nutrients*, **2019**) and are associated with sever diseases including but not limited to cancer, chronic kidney diseases, cardiovascular diseases... (G. A. Lamas *et al.*, *J. Am. Heart. Asso.*, **2021**; A L. Wani, *Interdiscip. Toxicol.*, **2015**; L. J. Yan *et al.*, *Biomolecules*, **2021**).

Low proportion of ingested lead and cadmium can pass through the blood circulation and can be stored in organs including liver, kidneys, brain and bones for long term. Difficulties of elimination of these metals are particularly observed for people suffering from chronic kidney disease leading to more and more damages to the kidneys and to a vicious circle. Current therapies for lead and cadmium poisoning are limited to acute poisoning (>200 µg/L) and cannot be directly applied to trace levels due to lack of efficiency and eventual secondary effects.

Institute of Light and Mater has developed polymers based on the functionalization of natural chitosan by recognized chelating moieties like DTPA or DOTAGA (M. Natuzzi *et al.*, *Sci. Rep.*, **2021**). These polymers can be orally administered to prevent passage of metals from the digestive tract to the bloodstream (**Patent EP22306238**, J. Howard *et al.* *Sci. Rep.* Accepted); they do not pass from the digestive tract to the blood, are eliminated relatively rapidly and display high affinity for lead and cadmium.

During the internship, the candidate will develop such kind of polymer and will optimize the grafting of the chelating moieties on the polymer, will graft fluorophores on it to follow it in the body after ingestion... Analytical tests will be performed to assess of the affinity of the polymer for metals like lead and cadmium. Depending on the advancement of the project, biological experiments can be performed during the internship to assess of the biodistribution and/or the efficiency. This multidisciplinary work will be performed in tight collaboration with at least the start-up MexBrain, Pr Laurent David of IMP for polymer characterization and Dr Eloïse Thomas of LAGEPP for biological experiments.

The competences required for the PhD are basic skills in chemistry, in organic functionalization and in coordination chemistry. Interest and skills in biology are not mandatory but will be appreciated.

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