UNIVERSITÉ DE NANTES
FACULTÉ DES SCIENCES ET TECHNIQUES

Chimie Et Interdisciplinarité Synthèse, Analyse, Modélisation
CEISAM
UMR CNRS 6230
UNIVERSITÉ DE NANTES

Séminaire – CEISAM – UMR CNRS 6230

Vendredi 09 février 2018 – 10h30
Salle Marie Curie

Dr. Olivier SANDRE
Chercheur au CNRS
olivier.sandre@enscbp.fr

LCPO – UMR CNRS 5629, ENSCBP, Université de Bordeaux

Thermosensitive Diblock Elastin-Like Peptide (ELP) and Cell-Penetrating Peptide (Tat) Brush Grafted on Magnetic Iron Oxide Nanoparticles: De-Swelling by Magnetic Hyperthermia, Internalization in Tumor Cells and Strong Disruption Effect on Lysosome Membranes

We have recently developed the grafting on iron oxide nanoparticles (IONPs) of recombinant polypeptides made of di-block elastin-like peptide (ELP_{40-60}) and cell-penetrating peptide (Tat) sequence.[1] The ELP_{40} block is thermosensitive and undergoes a water de-swelling transition at a critical temperature around 42 °C in solution while the ELP_{60} block is hydrophilic and provides colloidal stability to the resulting γ-Fe_2O_3@ELP_{40-60}-Tat core-shell IONPs. Cellular internalization and toxicity assays were performed on a human glioblastoma (U87) cell line in view of applications for drug delivery activated magnetically. Superior cellular uptake of the IONPs@ELP_{40-60}-Tat was evidenced compared to IONPs@PEG control nanoparticles prepared from the same magnetic cores,[2] synthesized by a polyol pathway. Since the latter display suitable heating efficiency under an alternating magnetic field (AMF), large temperature variations of the sample (up to 30 °C) could be obtained in a few minutes by applying an AMF.[3] Cellular toxicity after AMF application with these core-shell IONPs was ascribed to lysosomal membrane rupture and leakage into the cytosol. The intra-cellular fate of such IONPs, from their internalization to the effect of an AMF application, validates the use of thermosensitive peptide brushes on IONPs as drug delivery systems, addressing lysosomal compartments and triggering leakage of their content by external AMF application. Long term fate (after 48 h) is discussed in view of the cell division with equal sharing of the magnetically loaded lysosomes among daughter cells, possibly envisioning the successive application of magnetic hyperthermia on time scales superior to the cellular life cycle.

[1] E Garanger, S MacEwan, O Sandre, A Brûlet, L Bataille, A Chilkoti, S Lecommandoux, *Macromol.* 2015, 48, 6617.
[2] G Hemery, C Genevois, F Couillaud, S Lacomme, E Gontier, E Ibarboure, S Lecommandoux, E Garanger, O Sandre, *Molecular Systems Design & Engineering* DOI: 10.1039/C7ME00061H.
[3] G Hemery, A Keyes, E Garaio, I Rodrigo, J A Garcia, F Plazaola, E Garanger, O Sandre, *Inorg. Chem.* 2017, 56, 8232.