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seminar

Wednesday, 28th April, 9.30am, Online

Host: Dr. Jesús Ruiz-Cabello

Applications of Oligosaccharides in Nanomedicine strategies

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An important part of nanomedicine research is devoted to the development of **multifunctional nanoparticles (NP)** for **targeted drug delivery** or else as **imaging tools** for both, advanced therapeutic and diagnostic applications.[1] However, even if huge progress has been made in the field, **many obstacles remain to be addressed** toward full utilization of these powerful NP in the clinic and **to improve their translational value**.[2] A more **cross-disciplinary and comprehensive vision** of this **multifaceted research** is now recommended, including **new considerations in: i) clearance pathways, ii) targeting strategies, iii) personalized/predictive medicine and iv) high-scale GMP production.**[3,4]

After a review of these new considerations through a succinct presentation of previous works**, this seminar will focus on the application of novel oligosaccharides (OS) as very promising coatings for the design of NP intended for targeted and personalized therapy in oncology**. We will show in what way **OS preparation by depolymerisation of their native polysaccharide parents**, already widely used in nanomedicine, could overcome the limitations of these natural polymers and **open new exciting perspectives.** In particular, we will discuss **how OS-based functional coatings** could answer major criteria for successful development of NP **such as: an optimal renal clearance**, **a targeting enhancement** through interactions with tumour microenvironment's components with resultant therapeutic effect, or **simplification of the NP synthesis** by achieving a number of simultaneous specific functions.

To illustrate these strategies, we will give details of a pioneer study that use different heparin oligosaccharides (HEP-OS) combined with a new generation of extremely small iron oxide nanoparticles (ESIONP) able to perform positive contrast in magnetic resonance imaging (MRI).[5] This study has demonstrated that the **HEP-OS length** controls the core size during the synthesis and the polymer conformation at the ESIONP's surface, **allowing to achieve optimal MRI contrast**. Also, **HEP-OS coated ESIONP were endowed directly with a** discriminated **specific bioactivity** according to the HEP-OS used. The most relevant point was the *in vivo* nuclear imaging-based **biodistribution study that revealed drastic changes in the probes behaviours: the shortening of HEP-OS promoting a shift from hepatic to renal clearance.** Overall, by fine tuning of the HEP-OS length, we were able to identify a candidate showing prolonged vascular lifetime and accumulation in a tumour xenograft, balanced with a low uptake by non-specific organs and favourable urinary clearance.

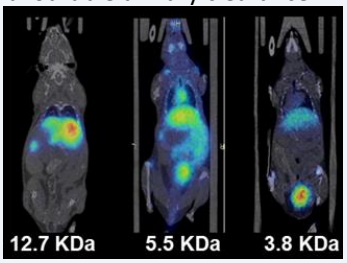

Figure 1 : Effect of the HEP-OS length (related to its molecular weight) on the ESIONP biodistribution 1h after i.v.a

References : (1) *Doane T et al. Chem. Soc. Rev. 2012, 41 (7) : 2885;* ***(2)*** *Greish K et al. Ther. Deliv. 2018, 9 (4), 269–285 ;* ***(3)*** *Shi J et al. Nat. Rev. Cancer 2016, 17 (1), 20–37 ;* ***(4)*** *Rosenblum D et al. Nat. Commun. 2018, 9 (1) : 1410;* ***(5)*** *Groult H et al. Nanoscale 2021, 13(2): 842-861.*