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Sala de Conferencias EDIFICIO I+D

INMA *Impulso*

Polypeptide-based Nanoconjugates as Versatile Therapeutics

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Polypeptides are already playing a major role on a number of different relevant areas such as nanomedicine. The physico-chemical parameters of a polypeptide-conjugate, and hence its biological performance, are defined by an intricate interplay of multiple structural factors. This highlights the need for detailed structure-activity relationship studies to develop the hierarchical strategies of polypeptide conjugate design. However, structural complexity also represents a unique opportunity, since small changes at the structural level might endow nanomedicines with outstanding and unexpected biological performance. In our group, we have overcome the main classical limitations for the synthesis of defined polypeptides using precise controlled reactions followed by an adequate characterization yielding to well-defined polypeptidic architectures. In addition, post-polymerization techniques allow us the introduction of a variety of functionalities yielding a set of orthogonal reactive attachment sides.

Using these techniques and following a bottom-up strategy we have been able to obtain star-based polypeptide architectures with the capacity to self-assemble yielding supramolecular nanostructures with interesting properties. This strategy together with an adequate polymer-drug linker design enabled *in vitro* and *in vivo* evaluation, revealing a lack of toxicity, an enhanced in vitro cell internalization rate and significantly greater terminal and accumulation half-life *in vivo* together with a significant lymph node accumulation. These results allow us to envisage these systems as promising nanocarriers for therapeutic or diagnostic applications, especially in anti-cancer treatments including lymph node metastasis and cancer immunotherapy. Proof of Concept for metastatic breast cancer and for immunotherapy design in melanoma will be also shown as well as the use of this self-assembled architectures in applications such as neurodegenerative disorders, spinal cord injury or acute kidney injury.

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