



## Polypeptide-based Conjugates as Versatile Therapeutics

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*Polypeptides are already playing a major role on a number of different relevant areas such as nanomedicine [1]. 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 [2].*

*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 (including stars, graft and block-copolymers) by NCA polymerization techniques [3]. In addition, post-polymerization techniques allow us the introduction of a variety of functionalities yielding a set of orthogonal reactive attachment sides [4]. 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 [5]. This strategy together with an adequate polymer-drug linker design [6] 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 [5]. 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 [6] 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 or acute kidney injury.*

### References

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**Acknowledgments**

Spanish Ministry of Economy and Competitiveness (SAF2016-80427-R) and the European Research Council (Grant ERC-CoG-2014-648831 MyNano, Grant ERC-PoC-2018-825798 Polymune) for financial support. Part of the equipment employed in this work has been funded by Generalitat Valenciana and co-financed with FEDER funds (PO FEDER of Comunitat Valenciana 2014-2020).

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