

Biomimetic Cloaked Nanobiomaterials for Controlled Drug Delivery and Tissue Repair and Regeneration

H. A. Santos¹

¹ *University Medical Center Groningen, Biomaterials and Biomedical Technology, Groningen, Netherlands*

The recent cutting-edge advances on nanomaterials is anticipated to overcome some of the therapeutic window and clinical applicability of many drug/peptide molecules and can also act as innovative theranostic platforms and tool for the clinic in the future [1-4]. In the last decade, research on cancer and cardiovascular diseases resulted in a new set of potential treatments with promising results in the clinics [5-12].

Amongst the different experimental treatments, active cancer immunotherapy and targeted to cancer microenvironment hold great promise for the future treatment of this disease. In this work, we have demonstrated that prominent nanosystems, such as biohybrid nanocomposites made of different nanomaterials (e.g., porous silicon and metal-organic framework nanomaterials) and cancer cell-based membrane materials are potential platforms for the individualization of medical intervention and biomedical applications.

Furthermore, we demonstrated that a pH-responsive lipid nanoshell-based zeolitic imidazolate frameworks, under the tumor microenvironment, increased their uptake in cancer cells and accumulation in cancer tumor *in vivo*. The nanoparticles induced reactive oxygen species, inhibiting tumor growth and increasing the survival rate in mice by activating the tumor microenvironment and improving the infiltration of macrophages and T cells in the tumor.

In addition, we have combined polyvinylpyrrolidone and cross-linked poly(methyl vinyl ether-alt-maleic acid) to obtain a double-layered formulation with a dissolvable layer and one that formed a hydrogel for hydrophobic drugs [13, 14]. We demonstrated *in vivo* and *ex vivo* that the microneedles double-layer allows for a more extended bioavailability was achieved compared to the oral commercial drug formulation. Furthermore, the incorporation of cancer membrane in MNs was achieved through coating of the MNs using a multi-step layering procedure or the micromolding technique, making it a promising device for immunotherapy and cancer applications.

Overall, our results suggest that biohybrid nano/micro-materials are a versatile and advanced platforms for enhanced cancer therapy with potential clinical impact given and clinical translatability.

References

1. H. Zhang, [...], H. A. Santos*, M. Hai*, D. A. Weitz*, PNAS 2019, 116, 7744.
2. Z. Liu*, [...], H. A. Santos*, Adv. Mater. 2018, 30, 1703393.
3. M. P.A. Ferreira*, [...], H. A. Santos*, Adv. Funct. Mater. 2018, 28, 1705134.
4. M. P.A. Ferreira*, [...], H. A. Santos*, Small 2017, 13, 1701276.
5. F. Fontana*, [...], H. A. Santos*, Adv. Mater. 2017, 29, 1603239.
6. F. Fontana, [...], V. Cerullo*, H. A. Santos*, ACS Nano 2019, 13, 6477.
7. T. Yong, [...], H. A. Santos*, X. Yang*, Nature Commun. 2019, 10, 3838.

-
8. M. Fusciello, [...], H. A. Santos*, V. Cerullo*, *Nature Commun.* 2019, 10, 5747.
 9. J. Zhang, [...], Xinjian Fang*, Hélder A. Santos*, Xu Zhang*, *Sci. Adv.* 2022, 8, eabj8207.
 10. Z. Liu, [...], Q. Zhao*, X. Ye*, X. Deng*, H. A. Santos*, *Adv. Funct. Mater.* 2022, 32, 2204666.
 11. R. Cheng, [...], W. Cui*, B. Shen*, H. A. Santos*, *Adv. Mater.* 2022, 2203915.
 12. J. Li, [...], Z. Luo*, H. A. Santos*, B. Xia*, *Adv. Mater.* 2022, 34, 2108012.
 13. T. Bauleth-Ramos, [...], H. A. Santos*, *Mater. Today* 2023, 63, 239-287.
 14. H. Amani, [...], H. A. Santos*, *J. Control. Release* 2021, 330, 185-217.

Acknowledgment

Prof. H. A. Santos acknowledges financial support from the Academy of Finland (Grant no. 331151), the UMCG Research Funds, and the European Union's Horizon 2020 research and development programme under the Marie Skłodowska Curie Grant agreement no. 955685.