

New strategies for multimodal cancer therapy based on plasmonic lipogels

Sérgio R.S. Veloso^{1*}, Filipa Costa-e-Sá¹, María Comís-Tuche,² Carlos Spuch,² Elisabete M.S. Castanheira¹

¹ Physics Centre of Minho and Porto Universities (CF-UM-UP), Campus de Gualtar, 4710-057 Braga, Portugal

² Translational Neuroscience Research Group, Galicia Sur Health Research Institute (IIS-Galicia Sur), SERGAS-UVIGO, CIBERSAM, Vigo, Spain.

*Corresponding author: sergioveloso96@gmail.com

ABSTRACT

Enhancing the therapeutic efficacy of chemotherapeutic agents through sequential drug delivery holds immense promise, yet current strategies are mainly dependent on the tumour microenvironment. Natural polymer-based hydrogels present suitable properties for these applications, owing to their inherent biocompatibility [1]. Herein, we present a novel strategy aimed at improving the tunability and real-time control of nanogels, as well as enabling compartmentalization of drugs for on-demand release using NIR light [2]. We hypothesized that combining chitosan/alginate nanogel with lipid-gated mesoporous silica-coated gold nanorods, thus obtaining plasmonic lipogels [3], could enable both the drug loading in different compartments and the sequential release of two chemotherapeutic drugs (doxorubicin and methotrexate). Hence, mesoporous silica-coated gold nanorods (99 ± 11 nm) were loaded with methotrexate, and further coated with a thermoresponsive phospholipid bilayer that works as gatekeeper. These particles were then incorporated in a chitosan/alginate nanogel matrix containing doxorubicin (Figure 1). The nanogels exhibited high loading efficiencies of $\sim 90\%$ and $\sim 85\%$ for methotrexate and doxorubicin, respectively. Notably, the exposure to NIR laser irradiation led to an enhanced release of both drugs, in which doxorubicin released at a faster rate than methotrexate under acidic conditions. Besides, the plasmonic nanogels were found to be cytocompatible across different cell lines. Hereby, this design strategy presents a robust and multifunctional hydrogel platform for NIR-triggered sequential delivery that holds promise for advancing cancer therapy through different drug combinations against multiple targets in tumour microenvironment.

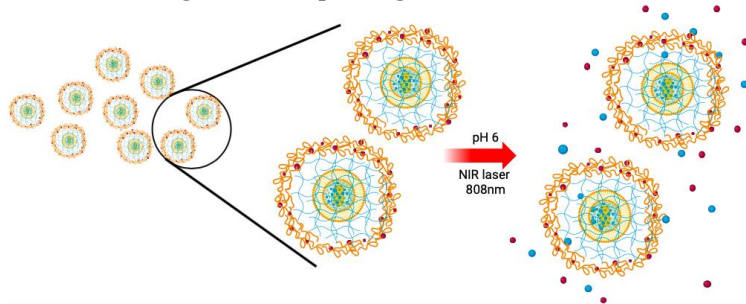


Figure 1. Scheme of the plasmonic lipogel based on silica-coated gold nanorods and chitosan/alginate nanogels.

Keywords: gold nanorods; plasmonic lipogels; drug release; photothermia; multimodal therapy.

Acknowledgements: This work was funded by Foundation for Science and Technology (FCT - Portugal) in the framework of the Strategic Funding of CF-UM-UP (UIDB/04650/2020, UIDP/04650/2020). C.S. was funded by Instituto de Salud Carlos III/FEDER grant number PI20/00937, and “Axencia Galega de Innovación” grant number IN607B-2018/17. S.R.S. Veloso acknowledges FCT for a PhD grant (SFRH/BD/144017/2019 and COVID/BD/153440/2023).

References:

- [1] S.R.S. Veloso, E.S. Marta, P.V. Rodrigues, C. Moura, C.O. Amorim, V.S. Amaral, M.A. Correa-Duarte, E.M.S. Castanheira, “Chitosan/Alginate Nanogels Containing Multicore Magnetic Nanoparticles for Delivery of Doxorubicin”, *Pharmaceutics*, vol. 15, no. 9, p. 2194, Aug. 2023, doi: 10.3390/pharmaceutics15092194.
- [2] S.R.S. Veloso, V. Gomes, S.L.F. Mendes, L. Hilliou, R.B. Pereira, D.M. Pereira, P.J.G. Coutinho, P.M.T. Ferreira, M.A. Correa-Duarte, E.M.S. Castanheira, “Plasmonic lipogels: driving co-assembly of composites with peptide-based gels for controlled drug release”, *Soft Matter*, vol. 18, no. 44, pp. 8384–8397, 2022, doi: 10.1039/D2SM00926A.
- [3] F. Costa-e-Sá, M. Comís-Tuche, C. Spuch, E.M.S. Castanheira, S.R. S. Veloso, “Sequential release of drugs from dual-delivery plasmonic nanogels containing lipid-gated mesoporous silica-coated gold nanorods”, *J. Drug Deliv. Sci. Technol.*, vol. 96, p. 105723, Jun. 2024, doi: 10.1016/j.jddst.2024.105723.