

Stable nanovesicles for the delivery of microRNA in cancer treatment

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Credit: ICMAB

Researchers at ICMAB present a study on new nanovesicles, known as quatsomes, which have been successfully engineered to encapsulate and deliver microRNAs for the treatment of tumors. These nanovesicles are

produced by a simple GMP compliant process, an unavoidable requirement for the clinical use of new drug candidates. The study, published in *Small*, has been highlighted in the Women in Materials Science issue of *Advanced Materials*.

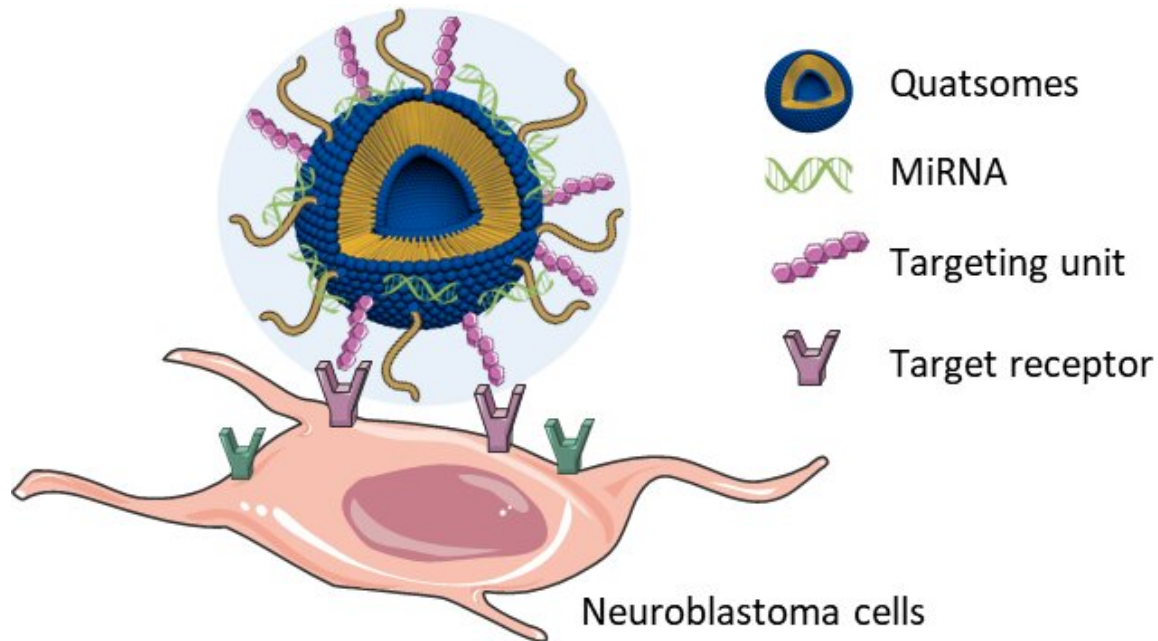
"The beauty of these quatsomes nanovesicles is that they can be easily engineered for the delivery of a variety of nucleic acids. Importantly, they are stable at [room temperature](#), which avoids problems associated to cold chain requirements," says ICMAB researcher Nora Ventosa at the Nanomol-Bio Group.

MicroRNAs (also known as miRNAs) are small RNA molecules that can interfere with the stability of other RNA molecules (specifically, messenger RNA). They have many potential therapeutic uses due to the central role they play in major diseases. However, these molecules are still infrequently used in patients due to their instability in the bloodstream and their poor ability to reach specific tissues. A potential strategy to improve the clinical delivery of miRNAs in the body is to encapsulate them in tiny carriers that compensate its current shortcomings, without side effects and offering other complementary functions.

To this end, researchers have developed and designed especially for this application nanostructures, known as quatsomes, composed by two closed lipid layers. In the new publication, the researchers present a newly engineered formulation of quatsomes that have a controlled structure, composition and pH sensitiveness.

The study is the result of an interdisciplinary team of researchers from the Institute of Materials Science of Barcelona, ICMAB-CSIC, the Vall d'Hebron Research Institute (VHIR)-UAB, the Institute for Bioengineering of Catalonia (IBEC), the Barcelona Institute of Science and Technology (BIST), the CIBER network on Bioengineering,

Biomaterials and Nanomedicine (CIBER-BBN), the company Nanomol Technologies SL, the Technion-Israel Institute of Technology and the Institute for Complex Molecular Systems (ICMS).



Scheme of the functionalized quatsome and the interaction with a neuroblastoma cell. Credit: ICMAB

"In this study we have collaborated with hospitals, research networks and companies. The successful results obtained illustrate the importance of collaboration across fields and beyond the academic system," says Ventosa.

These new quatsomes can be coupled with the miRNA and injected intravenously into the body to be delivered in neuroblastoma primary tumors or in frequent sites of metastasis, such as the liver or lung, with a higher success and stability than if the miRNA were injected by itself.

Once delivered, the miRNA has an effect on the cell proliferation and survival-related genes in the tumors, decreasing the tumor's growth rate.

Many properties make quatsomes a good fit for these applications: they are less than 150 nm in size and are stable in a liquid solution for more than six months; they also have tunable pH sensitiveness, which means that different pH levels around can trigger different responses.

The production of these nanovesicles has been optimized with their final application in mind and to make sure they can be used in clinics.

Through a green and scalable one-step process, named DELOS, researchers have designed a procedure that is fully compliant with Good Manufacturing Practice (GMP) guidelines established by the European Union. "It is time to translate our scientific findings for the benefit of patients," says Ariadna Boloix, VHIR researcher.

In this publication, the functionality of quatsomes in delivering miRNAs is demonstrated with a specific extracranial solid tumor common in pediatric cases of cancer known as neuroblastoma, which is responsible for roughly 15 % of all pediatric cancer deaths and lacks therapies for high-risk patients. The results show that quatsomes protect the miRNA from degradation and increase its presence on liver, lung and xenografted neuroblastoma tumors, amongst other tissues.

More information: Ariadna Boloix et al, Engineering pH-Sensitive Stable Nanovesicles for Delivery of MicroRNA Therapeutics, *Small* (2021). [DOI: 10.1002/sml.202101959](https://doi.org/10.1002/sml.202101959)

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