Fully artificial extracellular vescicles: a biomimicking strategy towards effectvie theranostic tools in nanomedicine

Giada ROSSO - *Polytechnic University of Turin*

Extracellular Vesicles (EVs) have gained significant attention in the nanomedicine field, due to their key role in the delivery of biomolecules throughout the body with incredibly high efficiency and site-selectivity. Consequently, researchers are exploring the use of pristine, or engineered EVs as nano-sized theranostic tools. However, large-scale production of EVs at a consistent clinical grade level is extremely expensive and time-consuming.

To address this problem, we propose an innovative strategy to design fully artificial EV-mimicking vesicles (EV-mimics). Our goal is to produce artificial bilayers, able to host a nanoparticle in their lumen, obtaining a core-shell structure with controllable size, which can be further decorated with peptides to resemble the natural cargo delivery efficacy.

Specifically, we focused on replicating EVs produced by the PC3 prostate cancer cell line, known for their remarkable ability to target bone tissue. We developed three different lipid compositions, starting from a liposomal formulation and progressively approaching the natural composition of EVs. EV-mimics were designed with the help of coarse-grained molecular simulation methods, which provided insights about lipid organization, and experimentally characterized through standard and super resolution techniques.

Although in its early stages, this approach holds a huge potential both in research and industry: EV-mimics can emerge as cost effective, off-the-shelf products, offering reproducibility of morphological and in vivo functional properties, in compliance with regulatory standards.