Max-Planck-Innovation

Technology Offer

Bottom-up assembly of synthetic extracellular vesicles for biomedical applications

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Natural extracellular vesicles (EVs) are lipid vesicles that carry a plethora of biologically active molecules including soluble and membrane proteins, nucleic acids and metabolites. They have recently been recognized as a promising cell-free alternative to cell transplantation or as a novel therapeutic tool in various diseases. Many in vitro and in vivo studies have shown beneficial effects of EVs from different cell types in diseases ranging from cardiovascular conditions to immune disorders and skin regeneration. Additionally, EVs are being investigated as a potential tool for targeted drug delivery. They are secreted by most cell types and conventionally isolated from cell culture medium. However, their clinical application is limited due to high heterogeneity and batch-to-batch variations of these preparations as well as their limited scalability. Procedures for natural EV isolation are often cost and time intensive and require specialized equipment, for example for differential ultracentrifugation or tangential flow filtration. Additionally, the composition of EVs cannot be precisely manipulated and their mechanisms of action remain largely elusive, both of which is unfavorable for clinical application.

Technology

Scientists from the Max-Planck-Institute for Medical Research developed a bottom-up approach that allows the assembly of synthetic EVs in a two-step process. First, small unilamellar vesicles (around 100 nm in diameter) are formed from commercially available synthetic lipids according to the desired lipid composition by dehydration and rehydration. By tuning the lipid composition, vesicles of different charge and mechanical properties can be designed and fluorescent lipids can be included. These small vesicles can then be fused into larger vesicles of about 500 nm up to several micrometers in diameter by using a surfactant-stabilized water in oil emulsion. During this step, hydrophilic molecules, such as soluble drugs, dyes or nucleic acids, can be encapsulated into the aqueous lumen of the vesicles. After release of the vesicles from the surrounding oil phase, their surface is modified with recombinant proteins or extracellular domains thereof. Different strategies for protein binding are available including His tag binding to NTA(Ni^{2+})-functionalized lipids as well as Biotin-Streptavidin or NHS chemistry-based binding. In principle, reconstitution of transmembrane proteins into the vesicles could also be considered. This approach allows us to precisely control the lipid and protein composition as well as encapsulated compounds of the synthetic EVs.

Therefore, a bottom-up approach to assemble synthetic EVs from chemical building blocks can offer a faster, more precisely defined, reproducible and scalable approach to engineer many different types of synthetic EVs for different biomedical applications.

We are looking for a collaboration partner to further develop this exciting project.

Patent Information

A European priority establishing patent application was submitted in January 2020 and followed by a PCT application in 2021.

Publication

Staufer *et al.,* Bottom-up assembly of biomedical relevant fully synthetic extracellular vesicles, *Science Advances* **2021**, **7**(36)

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