Hybrid extracellular vesicles - biomimetic tool for drug delivery to repair endothelial cell dysfunction

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Introduction

In living organisms, extracellular vesicles (EVs) are responsible for delivering biologically active molecules to distant cells. In vitro loading of therapeutic compounds into EVs is still not effective and needs developing new strategies.

Aim

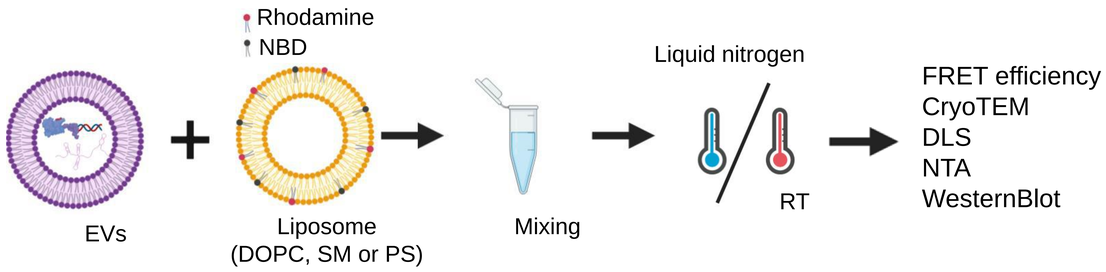
The aimed was to design hybrid extracellular vesicles (hEVs) with high loading capacity for DDS.

Method

For hEV synthesis, we used human endothelial derived EVs. Using freeze/thawing method we fused them with liposomes composed of cholesterol and one of the three lipids: DOPC, sphingomyelin or phosphatidylserine. We evaluated how the number of freeze thawing cycles and lipid to protein ratio influence the fusion efficiency using FRET.

FRET – evaluation of Fusion efficiency

Fusion efficiency was measured as a FRET efficiency between two fluorescent dyes: NBD (*nitrobenzoxadiazole*) and rhodamine after freeze/thawing cycles of liposomes and EVs samples mixed in different ratio.



Acknowledgements

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Summary

- Fusion efficiency is changing with a type of liposomes, number of freeze/thawing cycles and lipid to protein ratio
- After fusion hEVs are conserving their characteristics

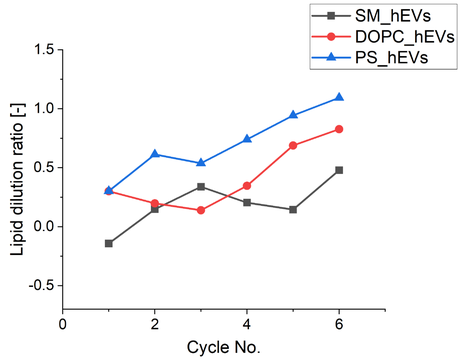

Fig.1. Changes in FRET efficiency presented as a lipid dilution ratio after different number of freeze/thawing cycles.

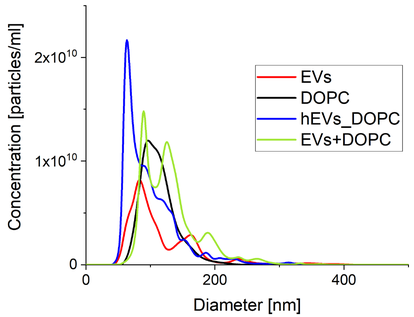

Fig.2. Results of the NTA measurements. The graph presents results for EVs sample, DOPC sample, DOPC_hEVs and mixture of EVs and DOPC without performing freeze/thawing cycles.

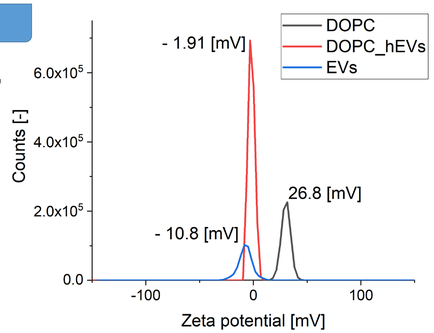

Fig.3. Results of the DLS measurements.

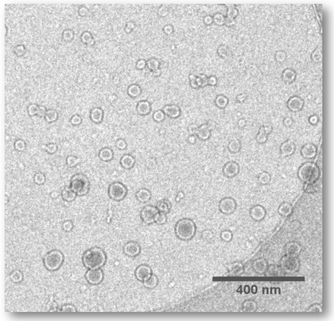

Fig.4. CryoTEM images of DOPC_hEVs.

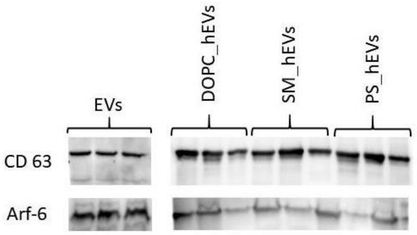

Fig.5. Western blots for typical EVs markers.