CELLULAR VESICLE FOR DRUG DELIVERY: ENGINEERING FOR OPTIMIZED PROPERTIES

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ABSTRACT

Cellular vesicles (CVs) have been developed from the rapidly expanding field of exosomes, representing a class of bioinspired Drug Delivery Systems. Contrary to exosomes, CVs have a higher production yield in a shorter time period, and present similar protein and lipid composition with parental cells [1]. In a recent study [2] CVs demonstrated poor integrity (compared to liposomes), which was increased by addition of polyethylene glycol (PEG) in their membranes; while *in vivo* live-animal imaging studies proved that non-engineered (non-PEG) CVs rapidly accumulated in the liver and lung, while engineered-CVs demonstrated reduced liver uptake. The retention of a small hydrophilic fluorescent dye, calcein, in CVs (the calcein integrity test which is routinely used in the liposome filed), was proven to be useful as a predictive tool for the in vivo biodistribution of CVs. In the present study we elaborated on the methodologies to prepared and engineer CVs, and verified the results obtained previously with calcein. For this, CVs from C57BL/6 mouse B16F10 skin melanoma cells (B16), were prepared by methods used for liposome preparation (sonication, freeze thawing cycles, dehydration rehydration method (DRV)), and characterized for physicochemical properties, and integrity. CV sizes were between 120-160 nm; ζ-potential's were always negative (between -12,6mV and -11,1mV). CVs were loaded with the hydrophilic fluorescent dyes (calcein and FITC-dextran) for evaluation of CV loading efficiency (EE%) and integrity. Furthermore different engineering methods for increasing their cholesterol content and PEGylation were compared. The current results confirmed that: (i) the DRV method confers highest loading to CVs, compared to other commonly applied methods. (ii) Calcein and FITC-leakage from CVs is highest when they are incubated in PBS, compared to fetal calf serum. Optimized engineering methodologies for CVs with increased in vivo integrity are being identified.

REFERENCES

[1] S.G. Antimisiaris et al 2018. *Pharmaceutics*, *10*(4), 218
[2] A. Marazioti et al. 2019. *J Pharmacol Exp Ther,* 370 (3) 772-785

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