P5.6: Colloidal dispersion of niosphingosome vesicles as an efficient non-viral vector for gene delivery to retina and brain

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Developing new non-viral gene delivery systems into target cells in a safe and efficient way is an essential issue in the search of more efficient strategies to face retina and brain diseases [1]. Low transfection efficiency of non-viral vectors is a major challenge to overcome in gene therapy approaches to reach clinical practice [2]. Therefore, we elaborated a novel non-viral vector in order to improve the transfection efficiency and cell viability in retina and brain. Two formulations referred as niosphingosomes and niosomes devoid of sphingolipids, as control, were prepared by the oil-in water emulsion technique. Both, the formulations and the corresponding complexes obtained after the addition of the reporter EGFP plasmid at different cationic lipid/DNA ratios (w/w), were physicochemically characterized in terms of particle size, superficial charge, dispersity and morphology. Cellular uptake and intracellular trafficking studies were performed in retinal pigment epithelium ARPE-19 cells in order to further evaluate transfection efficiency. Additional studies regarding endosomal scape of the complexes were carried out by elaborating anionic micelles based on PS, as an analogue of the lysosomal compartment [3]. The main finding of this study is that compared to niosomes, niosphingosomes at 3/1 ratio increased 33% the transfection efficiency, with high cell viability. Such niosphingosomes entered into cells mainly by the macropinocytosis-mediated route and reached endosomal compartment, suggesting that sphingolipids could be promoting gene delivery by other mechanisms, such as signaling and regulatory machineries in the cell nucleus. Moreover, *in vivo* administration showed that niosphingoplexes transfected successfully different cells in rat retina, depending on the administration route, and brain. Our preliminary results suggest that niosphingosomes represent a promising non-viral vector for the treatment of both retinal and brain diseases by gene therapy approach.

References

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