OP-52

DOI: 10.14232/syrptbrs.2021.op52

Protamine-based nanoparticles: an attractive gene delivery system for 2D and 3D glioblastoma models

Sheila Barrios-Esteban[1], Sonia Reimondez-Troitiño[1], Ruman Rahman[2], Cameron Alexander[3], Marcos Garcia-Fuentes[1], Noemi Csaba[1]

[1]Center for Research in Molecular Medicine and Chronic Diseases, University of Santiago de Compostela, Santiago de Compostela, Spain
[2]Biodiscovery Institute, School of Medicine, University of Nottingham, Nottingham, United Kingdom
[3]Boot Science building, School of Pharmacy, University of Nottingham, Nottingham, United Kingdom

Glioblastoma multiforme is one of the most aggressive brain tumors. Its treatment combines surgical resection, chemotherapy, and radiotherapy, at expense of severe side-effects. Gene therapy holds great promise due its capacity to target specific pathways within glioblastoma cells by the introduction of exogenous tumor suppressor sequences, which are rendered therapeutically effective by using nanocarriers. Protamine:Dextran nanoparticles have become an attractive gene delivery system due to their intrinsic ability to encapsulate and protect nucleic acids, and the delivery efficacy. These NPs present spherical morphology, size below 150 nm and positive surface charge. They present long-term stability for one month under storage conditions (4ºC) and short-term stability for 4h when diluted in simulated physiological media (37ºC, pH=7.4). The association of different nucleic acids to these NPs was studied by agarose gel electrophoresis, showing high encapsulation (≥90%). *In vitro* cell-viability studies were optimized using U87MG cells and spheroids models, then followed by assessment using primary patient-derived glioblastoma cells. Toxicity was studied with proliferation and cell-death assays indicating low/non-toxicity for this nanosystem. Particle uptake in both glioblastoma models was tested with fluorescently labelled-nanosystem using confocal microscopy and quantified by Flow Cytometry. The studies revealed an uptake efficiency of 99%. The transfection of different doses of pDNA was carried out with a model plasmid encoding the Enhanced Green Fluorescent and Luciferase Proteins. These studies showed the capacity of NPs to efficiently transfect U87MG cells and spheroids at doses greater than 1 ug/well. This new formulation could be considered as a promising gene-nanocarrier for glioblastoma treatment.

Supervisors: Noemi Csaba, Marcos Garcia-Fuentes