Helen O McCarthy et al., J Nanomed Nanotechnol 2017, 8:4(Suppl)
DOI: 10.4172/2157-7439-C1-049

The RALA delivery platform: Altering the biodistribution of nucleic acids *in vivo*

Helen O McCarthy, Emma McErlean and **Vicky L Kett**
Queen's University Belfast, UK

RALA is a 30mer cationic amphipathic peptide that condenses nucleic acid cargo into cationic nanoparticles (~50 nm diameter) suitable for gene delivery. However, upon systemic administration of plasmid luciferase-loaded (pLuc) RALA nanoparticles, bioluminescence is largely confined to highly vascularised organs, such as the lungs and liver. This represents a potential limitation of unfunctionalised RALA nanoparticles, which may not reach the tissues requiring the therapeutic cargo. The aim of this project is to functionalise RALA to increase circulation time and improve the pharmacokinetic profile of RALA nanoparticles. Vitamin E Tocopherol Polyethylene Glycol Succinate (TPGS) is a regulatory-approved non-ionic surfactant used in various drug delivery systems to achieve improved stability. TPGS was conjugated with five arginine residues (R5) to form TPGS-R5. Composite RALA/TPGS-R5 nanoparticles were complexed with plasmid DNA (pDNA) at a range of W:W ratios. Characteristics of nanoparticles formed were assessed by encapsulation assay, size and charge analysis. *In vitro* functionality was assessed by transfection studies in MDA-MB-231 breast and PC-3 prostate cancer cells. Stability studies analysing integrity of nanoparticles in serum and at physiological salt concentrations followed. *In vivo* biodistribution studies were performed in BALB/c SCID mice with either PC-3 or MDA-MB-231 xenografts. RALA/TPGS-R5 nanoparticles (W:W ratios 10:4, 8:6 and 6:8) carrying pLuc (50 µg) were delivered via tail vein injection. Bioluminescence was measured using a Bruker *in vivo* Xtreme imaging system 48 h and 96 h post injection. RALA/TPGS-R5 formed nanoparticles with pEGFP-N1 (~150 nm diameter and ~20 mV zeta potential) and transfected MDA-MB-231 and PC-3 cells. W:W ratios 10:4, 8:6 and 6:8 were stable at physiological salt concentrations. Functionalisation of RALA nanoparticles with TPGS-R5 reduced the luciferase expression detected in the lungs, liver, kidney and spleen. Up to a 30-fold increase in luciferase expression was detected in PC-3 tumours 48 h after treatment with 6:8, relative to untreated control. In MDA-MB-231 xenografts, a 12-fold increase in luciferase expression in tumours was detected, which was significantly higher ($P \leq 0.05$) than that of the RALA treatment group. Addition of TPGS-R5 to RALA nanoparticles improves the *in vivo* pharmacokinetics for the delivery of nucleic acids by reducing accumulation in the highly vascularised organs. This indicates the ability of TPGS-R5 to avoid clearance and increase circulation time of RALA nanoparticles in circulation. The enhanced transgene expression in tumours in both prostate and breast cancer models highlights the potential of this composite delivery system for systemic gene delivery, and warrants progression to studies involving delivery of therapeutic nucleic acids for a third generation cancer therapy.

Biography

Helen O McCarthy has her research interest in the development of non-viral delivery systems for nanomedicine applications from last 11 years. These biomimetic systems are designed to overcome the extra and intracellular barriers, so that the macromolecular payload can be delivered at the destination site in order to exert the optimal therapeutic effect. She has designed and patented two delivery systems. Her research team involved in the development of a number of 2nd and 3rd generation multifunctional delivery systems.

h.mccarthy@qub.ac.uk

Notes: