at a 1:1 stoichiometry to test the lung transduction functionality of the peptide using the 53 kDa dendrimer as a model macromolecular cargo. Phage peptide-dendrimer conjugates were labelled with a fluorophore and characterised by ^{1}H NMR and quantitative amino acid analysis prior to administration into the airways of the IPRL model. The extent of absorption of PAMAM G5.5 alone equalled 17 ± 6% of lung deposited dose absorbed by 90 min. G5.5 dendrimers displaying one syn-LTP-1 peptide per polymer (termed G5.5-syn-LTP-1) displayed a 1.8-fold greater extent of absorption ($p < 0.05$) cf. G5.5 alone; G5.5 dendrimer displaying one equivalent of the syn-NB3 peptide showed no evidence of enhanced absorption ($p > 0.05$). The enhanced absorption of G5.5-syn-LTP-1 absorption was competitively inhibited by co-administration of 100-fold molar excess of syn-LTP-1 peptide ($p < 0.05$) but not by syn-NB-3 peptide ($p > 0.05$), an observation consistent with the participation of a specific receptor-mediated transport mechanism. As such the LTP-1 peptide motif may serve as a platform for enhancing macromolecule absorption from the airways.

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doi:10.1016/j.drudis.2010.09.439

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Differential transport of anionic PAMAM dendrimers across *in vitro* biological barriers

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Polyamidoamine (PAMAM) dendrimers are a class of branched polymers that have the potential to serve as drug carriers. This is primarily due to their extremely low polydispersity index, the ability to precisely control their size and charge, and the multiple functional groups that they bear on their surfaces giving the ability to conjugate a wide range of therapeutic molecules. The transport across *in vitro* biological barriers of cationic PAMAMs has been widely studied with reports often indicating high barrier permeability, although interpretation of such data in the context of cation-induced barrier toxicity is often omitted. We are investigating the intrinsic biological activity of intact stable anionic dendrimer-drug conjugates where the dendrimer moiety not only confers a backbone for attachment of multiple phamacological ligands but also offers a means to physically modulate *in vivo* tissue disposition, for example, affording access to intestinal submucosa but excluding BBB penetration. In this abstract we report the differential *in vitro* barrier permeability of a molecular weight series of anionic PAMAM dendrimers, that is, G1.5, 2935 Da; G3.5, 12,931 Da; G5.5, 52,907 Da which has supported our ongoing *in vivo* investigations. Dendrimers were fluorescently labelled and added to the apical surface of epithelial cell monolayers grown on a semi-permeable inserts (Transwell). Permeability coefficients (ρ) were determined for transport in the apical to basal direction. The epithelial models included the highly restrictive MDCK-I (TEER 5000 Ω cm^2), the moderately restrictive Caco-2 (TEER 600 Ω cm^2) and the low restrictive MDCKII (TEER 200 Ω cm^2). For CACO-2 and MDCKII an inverse relationship was evident between dendrimer transepithelial transport and dendrimer molecular size, with dendrimer ρ decreasing approx. 5-fold G1.5 ⇒ G3.5, and decreasing approx. 10-fold G1.5 ⇒ G5.5. The permeability of the cell models to dendrimer transport declined as the paracellular restrictiveness of the monolayers increased. Indeed, for MDCKI monolayers dendrimer concentrations in the basal chamber remained at all times below the limit level of detection, but could be readily enhanced by briefly adding EDTA to the media. Nevertheless, predicted (based upon LLQ) ρ for dendrimer transport across MDCKI were at least ×10–15-fold lower than in the other cell models. Significantly, even for the smallest dendrimer, that is, G1.5, the maximum predicted (based on LLQ) ρ across MDCKI was no greater than 15% of the ρ obtained for the paracellular marker F-Na. Whereas ρ for G1.5 was 51% and 56% of that for F–Na in CACO-2 and MDCKII models, respectively. Biocompatibility studies show no affect of the anionic dendrimers upon overall barrier properties. The paracellular route is the major pathway of dendrimer transport across biological barriers. Stable pharmacologically active conjugates of dendrimer – drug are an interesting experimental therapeutic with potential to provide differential tissue distribution/exclusion based upon physical characteristics.

doi:10.1016/j.drudis.2010.09.440

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Non-toxic, highly efficient delivery of nucleic acids into challenging cells using safectin transfection reagent

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Deliverics Ltd. has developed a novel cationic lipid-mediated transfection reagent for DNA and siRNA delivery into both easy and challenging to transfect eukaryotic cells: SAFEctin Transfection Reagent. This reagent is a water-based formulation of cationic and neutral lipids with programmed biodegradability. SAFEctin allows for the highest transfection efficiency of nucleic acids into many cell types (e.g. immortilized cells, mESC, hMSC) with the simplest-to-use and fastest procedure in the market: (i) mix SAFEctin and the nucleic acid (ii) followed by direct addition to cells, either in the presence or absence of serum and antibiotics. The formulation has been developed to have very low toxicity to cells and as such it is not necessary to remove or change culture medium following transfection. Combination of the highest/safest transfection rates on the market with the simplest to use protocol ensures optimal performance and fast results. The SAFEctin Transfection Reagent is a universal system that outperforms competitor's products in each of the three defining features any researcher seeks in this kind of product: efficacy, safety and ease of use.

doi:10.1016/j.drudis.2010.09.441