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Phosphonium carbosilane dendrimers: Efficient non-viral vectors for siRNA delivery to adenocarcinoma cells *in vitro*

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Gene therapy is a rapidly growing field of biomedical research which has sparked great interest because it offers the possibility of a permanent cure a variety of genetic-based diseases. The success of gene therapy depends on the development of suitable vectors for the delivery nucleic acids into cells. Our work is focused on the comparative study of the two types of cationic carbosilane dendrimers terminated with the ammonium and phosphonium groups for their use as non-viral vectors for siRNA transfection. We present a part of work devoted to characterization of dendriplexes formed from generation 1-3 (G1-3) of carbosilane dendrimers and model siRNA. We used a number of biophysical methods (e.g. Gel retardation electrophoresis, DLS, ξ (zeta)-potential, AFM) for characterization of dendriplexes. Transfection efficiency was evaluated by Fluorescence Microscopy and Flow Cytometry. Both types of dendrimers G2-G3 form stable complexes with siRNA due to positive charge of surface groups of dendrimers and negative charge of siRNA backbone. Formation of dendriplexes was investigated at different charge ratio (1/5 – 10/1 (+/-)) to find the optimal properties of complexes (e.g. stability, surface charge, dimensions) for transfection of cells. *In vitro* transfection experiments proved the ability of both G3 dendriplex structures to enter the cells, with maximal achieved transfection efficiency at 7/1 (+/-) charge ratio. Ammonium dendrimers achieved max. 30% of transfected cells. More than 70% of cells were transfected under the same conditions with phosphonium terminated dendrimers. With the aim to optimize the properties of phosphonium dendriplexes we incorporated new periphery substituents ($P(Et_2)_2(CH_2)_3OH$, $P(Ph)_3$, $P(C_6H_4\text{-}OMe)_3$, PBu_3) into dendrimer structure. Similar cytotoxicity (except PBu3) and transfection efficiencies were obtained with the exception of P(Ph)3 peripheral substituent. This type of dendrimer exhibits more than 80% transfection efficiency and seems to be the "hot" candidate for further improvements of gene delivery by phosphonium carbosilane dendrimer vectors

Recent Publications

1. Strasak T et al. (2017) Phosphonium carbosilane dendrimers for biomedical applications: synthesis, characterization and cytotoxicity evaluation. RSC Advances. 7(30):18724-18744.
2. Ferenc M et al. (2013) Phosphorus dendrimers as carriers of siRNA: characterisation of dendriplexes. Molecules. 18(12):4451-4466.
3. Biswas S and Torchilin V (2013) Dendrimers for siRNA Delivery. Pharmaceuticals. 6(12):161-183.
4. Dufes C, Uchegbu I and Schatzlein A (2005) Dendrimers in gene delivery. Advanced Drug Delivery Reviews. 57(15):2177-2202.
5. Biricova V and Laznickova A (2009) Dendrimers: analytical characterization and applications. Bioorganic Chemistry. 37(6):185-192.

Biography

Regina Herma is PhD candidate at Jan Evangelista Purkyne University(UJEP),Czech Republic. Her work is mainly focused on the effect of type, generation and surface modification of carbosilane dendrimers on the interaction with selected nucleic acids for applications in biomedicine (transport molecules for drug targeting, vectors for gene therapy, potential treatment of lung cancer). She is part of a research team for a number of projects.

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