P36

Bioinspired polymers for siRNA delivery by lipid based nanovectors

Eleonora Traficante,[a] Emanuela Di Cola,[a] Elena Del Favero,[a] Valeria Rondelli,[a] Laura Cantù,[a] Paola Brocca,[a] Federica Lazzari[b]

[a] Dipartimento di Biotecnologie Mediche e Medicina Traslazionale, Università degli Studi di Milano, via Fratelli Cervi 93, 20090, Segrate (Milano), Italy;
[b] Dipartimento di Chimica, Università degli Studi di Milano, via C. Golgi 19, 20133, Milano, Italy;
eleonora.traficante@studenti.unimi.it

The airway delivery of genetic material inside the cell requires the design of vector nanoparticles (NPs) showing low cytotoxicity, high efficiency in cellular absorption and ability to penetrate the mucus barrier before releasing material to the nucleus. Polyamidoamines (PAAs) are promising condensing structures for DNA and siRNA delivery, since they show good biocompatibility, biodegradability and the ability to form stable polyplexes both with DNA and RNA strains [1,2]. Among these we exploited the potential of the 4-aminobutylguanidine-deriving PAA named AGMA1 to transport siRNA and to target the enzyme β-glucocerebrosidase GBA2 from primary Human Bronchial Epithelial cells (hBEC) of patients affected by Cystic Fibrosis (CF). CF patients' mucus is a strong viscoelastic barrier leading to respiratory disease and high infection risk. We're testing lipid coating on AGMA1-siRNA complexes as a possible strategy to cross the CF mucus barrier. Transfection efficiency, cytotoxicity and siRNA efficacy have been investigated on primary cellular cultures (ALI hBEC cultures). Besides, the structural properties of the nanoparticles have been studied by Light Scattering experiments.

References

1. R. Cavalli, A. Bisazza, R. Sessa, L. Primo, F. Fenili, A. Manfredi, E. Ranucci, P. Ferruti, *Biomacromolecules*, **2010**, *11*, 2667.
2. R. Cavalli, L. Primo, R. Sessa, G. Chiaverina, L. di Blasio, J. Alongi, A. Manfredi, E. Ranucci, P. Ferruti*, J. Drug Targeting*, **2017**, *25*, 891.