Nanoparticle Delivery Of Nucleic Acid

Prof. Smadar Cohen, Department of Biotechnology Engineering, Ben-Gurion University of the Negev, Beer-Sheva, Israel

Technology

Prof. Cohen developed anionic polyplex nanoparticles (NPs) for systemic application of gene therapy. This method can overexpress or silence genes (siRNA, miRNA, mRNA, DNA). It can be applied for various applications such as cancer treatment, neurodegenerative, cardiovascular, infectious, or inflammatory disease or disorders. Moreover, the delivery of nucleic acid therapeutics to disseminated and widespread disease sites, can only be achieved by systemic administration. Prof. Cohen developed hyaluronan sulfate (HA-S) and alginate sulfate (Alg-S) carriers for delivering nucleic acids into cells. The first one, HA-S, has inherent biological activity and specificity in the human body that can enhance their targeting and uptake by the cells. HA receptors play important biological roles in endocytosis and single transduction. The latter one, Alg-S, is plant-derived anionic polymers that do not have biological specificity in the human body and thus can be used as blank canvas on which specific groups recognized in the human body can be conjugated or modified. The polyplexes form electrostatic interactions with the nucleic acid and calcium ions (Diameter 50-200 nm; Mw 30-200 KDa). Both types of NPs can be conjugated with specific ligands to generate specific targeting. For example, CD11b-tagged NPs are targeted to heart macrophages, and NPs conjugated with N-acetylgalactosamine (GalNAc) to target hepatocytes.

The method facilitates a systemic drug delivery with a non-toxic response and no mortality or clinical signs throughout the study, compared to the other known methods that cause severe cytotoxicity and serum inactivation. The polyplex uptake was tested in vitro and in vivo and showed significant stability. In vitro studies showed significant cellular uptake and accumulation of siRNA polyplexes in the cytoplasm. In addition, in collaboration with Prof. Etzion, Prof. Cohen targeted cardiac macrophages post-myocardial infraction with the injection of CY5-labeled siRNA/NPs intravenously. They found a significant accumulation of the NPs in infarcted hearts compared with healthy hearts. This treatment caused a phenotype switch from pro-inflammatory to reparative, promoted angiogenesis, and reduced hypertrophy, fibrosis and cell apoptosis in the remote myocardium.

Application

Silencing or overexpressing specific target genes as a treatment for various diseases, such as cancer treatment, neurodegenerative, cardiovascular, infectious, or inflammatory disease or disorders.

Advantage

- Efficient delivery systems suitable for systemic application
- Universal carrier for various cargos - siRNA, miRNA, mRNA, DNA
- Easily adaptable for various targets
- High stability in serum
- Non-toxic
- Can be fit for different administration type
- Biocompatibility
- Simple preparation method at aqueous conditions, which is important for mass production of these carriers.

Patent

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