

Nanoparticles for Intracellular Delivery of Nucleic Acids Therapeutics

Nucleic acid compounds such as small interference RNA (siRNA), micro RNA (miRNA), antisense RNA, mRNA and decoy oligodeoxynucleotides (ODN) can be used for the therapeutic modulation of gene expression as well as for the replacement of defective or missing genes and proteins. However, most nucleic acid therapeutics are not applicable for systemic application due to their very short half-life in the bloodstream and inability to cross cell membranes. Since the delivery of nucleic acid therapeutics to disseminated and widespread disease sites such as metastasized tumors and inflamed tissues can only be achieved by systemic administration, the development of efficient delivery systems suitable for systemic application is crucial to the success of nucleic acid-based therapies.

The Technology

We have developed nanoparticles targeted for intracellular delivery of nucleic acid therapeutics, such as siRNA, mRNA and plasmid DNA. We demonstrated excellent cell uptake for nanoparticles encapsulating siRNA, mRNA or plasmid DNA, resulting in nearly 100% knockdown of targeted mRNA when using siRNA, and high protein expression when using mRNA or plasmid DNA. Preclinical studies showed that systemic administration of such nanoparticles is biocompatible and does not elicit toxicity.

Advantages

- ✓ The nanoparticles are made of biocompatible materials, calcium ions and polysaccharides.
- ✓ Fabrication is easy and simple requiring only mixing the components together at aqueous conditions ("green") and room temperature.
- ✓ The mechanism underlying their formation is based on electrostatic interactions between the components.
- ✓ The nanoparticles have an average diameter of 100 nm with a narrow size distribution and have a mild anionic zeta potential (-6 mV). These features enable their efficient entry into the cell cytoplasm.

Applications

- ✓ Targeted delivery to liver cells (hepatocytes)
- ✓ Cardiovascular miRNA therapeutics
- ✓ Localized delivery of therapeutics

Patent Status

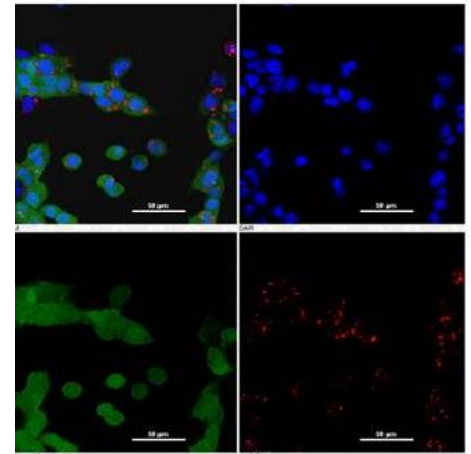
Patent pending

Research Team

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

Contact for Licensing and Investment Information

Ora Horovitz Ph.D, Senior VP Business Development, BGN Technologies, E-mail: orabgn@bgu.ac.il



Evaluation of siRNA cellular uptake by imaging flow cytometry and confocal microscopy. Confocal images of uptake of siRNA in eGFP-CT26 cells, 3 h after addition in unfixed live cells (5 mM Ca²⁺+50 nM siRNA).