

Enhanced RNA or DNA Delivery

Biodegradable multilayer nanocapsules:
highly efficient gene delivery to target cells

Technology

One of the rapidly developing directions of biomedical research & nanotechnology is the design of new delivery systems for bioactive materials and, in particular, for genetic material into target cells. The biodegradable multilayer nanocapsules presented here are of homogeneous size (100 nm diameter in average) but considerably smaller than commonly used microcapsules (3-5 µm diameter). Nanocapsules of this small size, similar to small extracellular vesicles, e.g. exosomes (60 - 280 nm), are traceable in the same cellular compartments as exosomes, indicating not only similar uptake mechanisms but also a similar intracellular traffic, and results in an utmost uptake efficiency and significantly reduced toxicity. Functional analysis of loaded siRNA molecules revealed over 80% knockdown efficiency in any cell type tested (e.g. primary T & tumor cells, adult primary stem cells and primary hematopoietic cells), indicating target cell universality and exceptionally high efficiency. Biocompatibility tests showed no cytotoxicity and no influence of these capsules on viability or metabolic activity of the target cells when treated with more than 20 capsules per cell.

Similar to conventional capsules, in our nanocapsules CaCO₃ builds the core, but by a layer-by-layer coating technique, the core is surrounded by multilayers of biodegradable dextran sulfate and poly-L-arginine hydrochloride. Hence, positioning functional nucleic acids not in the core but between the layers, enables a continuous release during degradation and sustainable knockdown effects within target cells. The system also allows for a simultaneous load of different cargos. Several different siRNA e.g. proofed a simultaneous knockdown of several targets. Furthermore, the negatively charged surface could be functionalized with particular proteins, specifying the nature of target cells.

Taken together, these novel biodegradable multilayer nanocapsules offer high potential as a therapeutic delivery system for any functional RNA & DNA to desired target cells *in vitro* and *in vivo*.

Innovation/ Status

- small nanoscaled capsules of homogeneous size (Ø 100 nm in average)
- exosome like cellular uptake & trafficking mechanism
- reduced toxicity & near to 100% efficiency in various cell lines tested
- target cell universality: loaded siRNA or CRISPR/Cas9 RNA molecules revealed over 80% knockdown efficiency in any cell type tested
- simultaneous load of different cargos feasible, e.g. small molecule inhibitors, miRNAs, siRNAs, mRNA, DNAs, ...

Application

- highly efficient delivery of any nucleic acid to target cells for research & clinical purposes (*in vitro* or *in vivo* - near to 100% efficiency)
- high potential for the application in patients /clinical trials

Furtehr ongoing Developments

- "ready-to-use" tool-box for nucleic acid transfer into target cells, incl. SOPs
- capsule testing in animals (mice or rats), incl. SOP development
- targeted delivery to specific cells using functionalization

Responsible Scientist

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Note: Joint Invention with Queen Mary University of London, UK

Branch

Gene delivery in target cells;
Gene therapy, Oncology & Biotechnology

Patent Status

EP (PRD) filed 26 July 2016
- withdrawn in favour of enhanced PCT

PCT/EP2018/070111 filed 25 July 2018
- Nat/ Reg. due Jan. 2020

Reference Number

ZEE20170530

Status: October 2018



CTF – The R&D Company of the
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