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CiQUS Lecture

Tuesday, April 16, 2024
11:00 am - CiQUS Seminar Room

Prof. Roy Van der Meel
Eindhoven University of Technology

https://www.mulderlab.com/
https://www.tue.nl/en/research/researchers/roy-van-der-meel
https://scholar.google.com/citations?user=4brXEMMAAAAJ&hl

Abstract

Nucleic acid therapeutics harbor great potential for silencing, expressing, or editing genes. However, nucleic acid-based drugs require chemical modifications and sophisticated nanotechnology to prevent their degradation, reduce immunostimulatory effects, and ensure intracellular delivery. Lipid nanoparticle (LNP) technology is the current gold standard delivery platform technology that has enabled the clinical translation of the first siRNA drug Onpattro and the COVID-19 mRNA vaccines. Nevertheless, currently approved LNP systems are mostly suited for vaccine purposes following local administration or hepatic delivery following intravenous administration.

Here, I introduce a nanodelivery platform based on natural lipoproteins, which prevents premature degradation of small interfering RNA (siRNA), ensuring its targeted and intracellular delivery to hematopoietic stem and progenitor cells (HSPCs) in the bone marrow. After establishing a prototype apolipoprotein lipid nanoparticle (aNP) that stably incorporates siRNA in its core, we built a comprehensive library of which we thoroughly characterized the individual aNPs' physicochemical properties. Following the in vitro screening of all formulations, we selected eight siRNA-aNPs that are representative of the library's diversity, and determined their capacity to silence lysosomal-associated membrane protein 1 (LAMP1) in immune cell subsets in mice, using an intravenous administration regimen.

Our data show that using different aNPs, we can achieve functional gene silencing in immune cell subsets and their bone marrow progenitors. Beyond gene silencing, the aNP platform's inherent capacity to engage immune cells provides it with considerable potential to deliver other types of nucleic acid therapeutics to HSPCs.

Biosketch

Roy van der Meel is a biomedical engineer specialized in nanomedicine and RNA therapeutics. After obtaining a PhD from Utrecht University under guidance of prof. dr. Wim Hennink and prof. dr. Gert Storm, and a postdoc appointment at the University Medical Center Utrecht in prof. dr. Raymond Schiffelers' lab, he secured Marie Skłodowska-Curie and Dutch Research Council (NWO) Veni funding to move to prof. dr. Pieter Cullis' lab at the University of British Columbia in Vancouver, Canada. During his 3.5-year postdoctoral tenure, he gained extensive experience with developing lipid nanoparticle (LNP) technology that has enabled the approval of the first siRNA therapeutic Onpattro® and the COVID-19 mRNA vaccines. In 2019, he was recruited to Eindhoven University of Technology by prof. dr. Willem Mulder and appointed Assistant Professor in the Precision Medicine group. His current research is supported by NWO Vidi funding and focuses on establishing platform nanotechnology for delivering RNA therapeutics to specific immune cells and regulating the innate immune response. He has co-authored over 50 publications in leading nanotechnology-focused journals including Nature Nanotechnology, Nature Biomedical Engineering, and ACS Nano.