Gene therapy enabled by nanotechnology: A new era of medicine

NanoMedicines Innovation Network (NMIN) thought leaders contribute to a commentary in the December 2019 issue of *Nature Nanotechnology*

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On August 10, 2018 the US Food and Drug Administration (FDA) approved ONPATTRO™, a nanomedicine for treating the devastating and usually lethal hereditary disease known as hereditary transthyretin-induced amyloidosis (hATTR). The approval of ONPATTRO™ has opened the door to a new era of gene therapies to treat most human diseases—including genetic disorders, infections, chronic diseases and cancer—more effectively.

"It is just a matter of time." This is the implication of a commentary published today in *Nature Nanotechnology* by the scientists and pharmaceutical experts behind the development of ONPATTRO™.

The senior author of the commentary is Dr. Pieter Cullis, Professor of Biochemistry and Molecular Biology at the University of British Columbia (UBC), whose laboratory contributed to the revolutionary lipid nanoparticle (LNP) delivery technology behind ONPATTRO's success.

ONPATTRO™ consists of LNPs containing short interfering RNA (siRNA) that, when delivered to the interior of a target cell, “silences” the gene that codes for mutated transthyretin (TTR) and thus prevents formation of the amyloid plaques characteristic of hATTR. ONPATTRO™ is the first RNA interference (RNAi) drug ever approved by the FDA. This ushers in an entirely new class of gene therapy medicines that have the potential to treat most diseases by silencing proteins causing disease or producing proteins to treat disease.

“These results validate work we have conducted for more than 20 years to develop LNP delivery systems that facilitate intracellular delivery of RNA and DNA polymers," comments Dr. Cullis, who is also the Scientific Director and CEO of the recently launched NanoMedicines Innovation Network (NMIN), a Canadian Networks of Centre of Excellence.

"ONPATTRO builds on experience gained developing LNP delivery systems in my laboratory at UBC since I established it in 1978. In many ways the success of ONPATTRO™ is the highpoint of my career — at least, so far."

"So far" because, as Dr. Cullis and colleagues explain in their commentary this is only the beginning of a new era of medicine enabled by nanotechnology.

"The major advance embodied by ONPATTRO™ is the ability to deliver large nucleic acid polymers into the interior of target cells" note the authors. More recent work has shown that related LNP systems can effectively deliver much larger messenger RNA (mRNA) molecules to produce or “express” therapeutic proteins.

"LNP systems containing mRNA can utilize the liver as a bioreactor producing therapeutic proteins to fight disease," comments co-author Dr. Dominik Witzigmann, a post-doctoral fellow in Dr. Cullis' lab and the administrative lead for NMIN's NanoCore, a facility offering services to assist with the clinical translation of nanomedicines.

"These systems are showing promise as highly effective vaccines for infectious diseases such as the Zika or influenza virus. LNPs containing mRNA coding for programmable nucleases, on the other hand, show considerable potential for gene editing *directly within* patients' bodies."

Challenges remain, the authors acknowledge. However, they add that "the rapid advances of recent years suggest that it is just a matter of time before these challenges are overcome."

The story of ONPATTRO™, detailed in the Nature Nano commentary, illustrates how nanomedicines are increasingly positioned to become the next generation of pharmaceuticals by enabling large molecules such as nucleic acid-based drugs, to be used therapeutically. These gene medicines will dramatically expand the range of diseases that can be treated in a precise and effective manner.

About NMIN

The NanoMedicines Innovation Network (NMIN) is a national research network dedicated to advancing research, innovation & training in nanomedicines to maintain Canada as the world leader in this revolutionary approach to treat & cure disease. Funded by the Government of Canada through the federal Networks of Centres of Excellence (NCE) Program, the Network is hosted at the University of British Columbia in Vancouver, British Columbia.

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