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XMaNs

https://www.iocbtech.cz/project/xmans/

A NEW GENERATION OF LNPS

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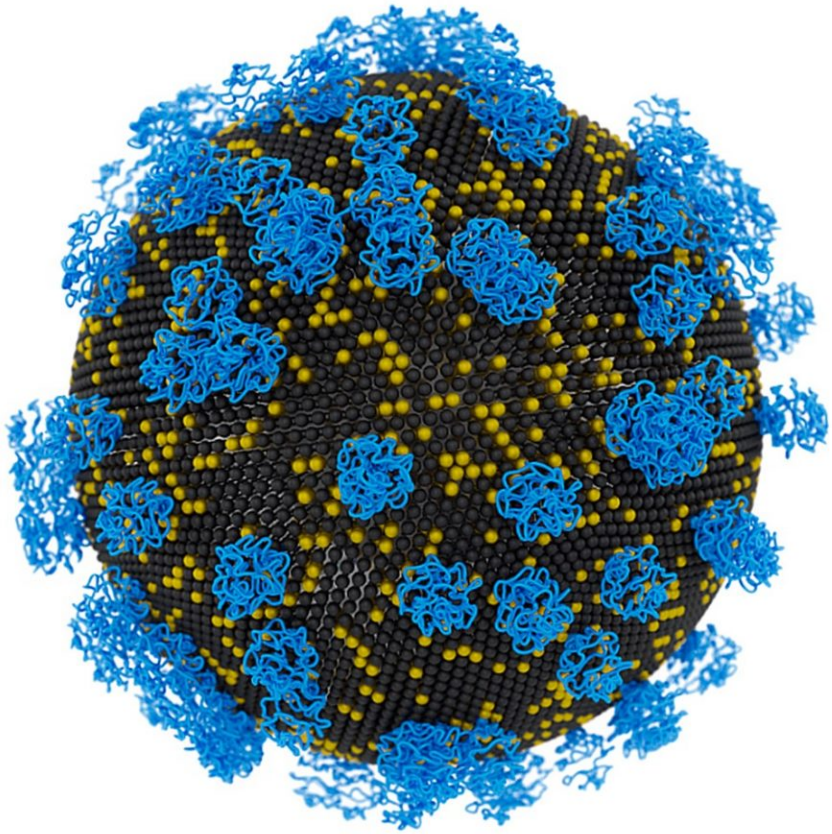
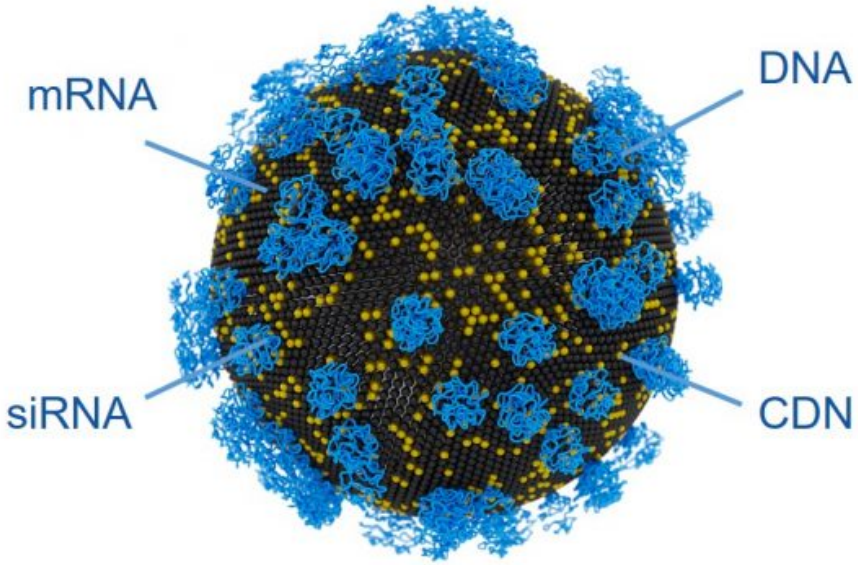
CHALLENGE



In recent years, the development of lipid nanoparticles (LNPs) has gained the pharma industry considerable attention. The general public has further acknowledged that. Especially during the current Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) pandemic, when messenger RNA (mRNA) encapsulated in LNPs proved to be highly efficient as anti-SARS-CoV-2 vaccines and have been recently approved. LNPs, as the most advanced nonviral delivery platform of nucleic acids (NA), significantly improve NA limitations as therapeutics such as their stability, delivery, and increase safety and efficacy.

The majority of known ionizable lipids and lipidoids enabling LNP formulation are optimized to deliver a specific NA (e.g., mRNA or siRNA). Therefore, significant challenges remain, notably how to effectively encapsulate and deliver a wide range of therapeutic NA types without laborious and time-consuming optimization of LNP composition. Therefore, our objective was to develop a highly versatile ionizable lipidoid for efficient encapsulation and delivery of a wide range of NA types that are safe for in vivo applications.

TECHNOLOGY



UNIVERSAL * EFFECTIVE * NON-TOXIC * STABLE AT 4°C

Here, we present LNPs with novel ionizable lipidoids that play a critical part in the NA entrapment. We named our new generation of LNPs, XMaNs. They are highly versatile in entrapment and delivery of mRNA, siRNA, pDNA, and even cyclic dinucleotides (CDNs). They efficiently transfect various cells, such as hard-to-transfect cell lines or human primary hepatocytes. The cGAMP-based XMaN delivered 2´,3´-cGAMP, and activated cGAS-STING pathway at nanomolar levels. The mRNA-based LNPs made of the lead candidate lipidoid, XMaN6, efficiently delivered mRNA in the mouse liver and showed no toxicity.

To our knowledge, such universality has not been described before. Taken together, the XMaNs have the potential to ease the development of LNPs with various payloads and accelerate their translation into the clinical application.

COMMERCIAL OPPORTUNITY

LNPs represent the most advanced nonviral delivery system that pharmaceutical and biotechnology industries had widely accepted since siRNA-based drug Onapattro that FDA approved in 2018. Thus, LNPs will play an inseparable role in medicine where genetic diseases can be effectively treated or cured. Significant opportunities for LNP formulations exist where the antigen can be produced within the body (and without the necessity of adjuvants) rather than by vaccinating with attenuated viruses or recombinant proteins. In addition to RNA-, DNA-, and siRNA-based therapeutics, LNP-based formulations are increasingly considered for use across various other application areas, including anticancer agents and antibiotics, peptide, and protein-based synthetic vaccines, ligand-targeted

formulations, gene editing purposes, and imaging contrast agents.

We thoroughly characterized our siRNA-, mRNA- and CDNs-based XMaNs as universal transfection reagents *in vitro* and *in vivo*. Currently, we look for a business partner who would transfer our universal XMaNs to the therapeutic area. We offer versatile, well-characterized XMaNs to encapsulate any NA cargo type and a team of scientific experts in nanotechnology.

We look for co-development, licensing or research collaboration.

DEVELOPMENT STATUS

Preclinical stage – *in vitro* and *in vivo* testing, defined lead structure, toxicology tests

PATENT SITUATION

Patent Application – 23.9.2020