



UNIVERSITY OF
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Exploring the potential of lipidoid-polymer hybrid nanoparticles to deliver oligonucleotides to intracellular pharmacological targets

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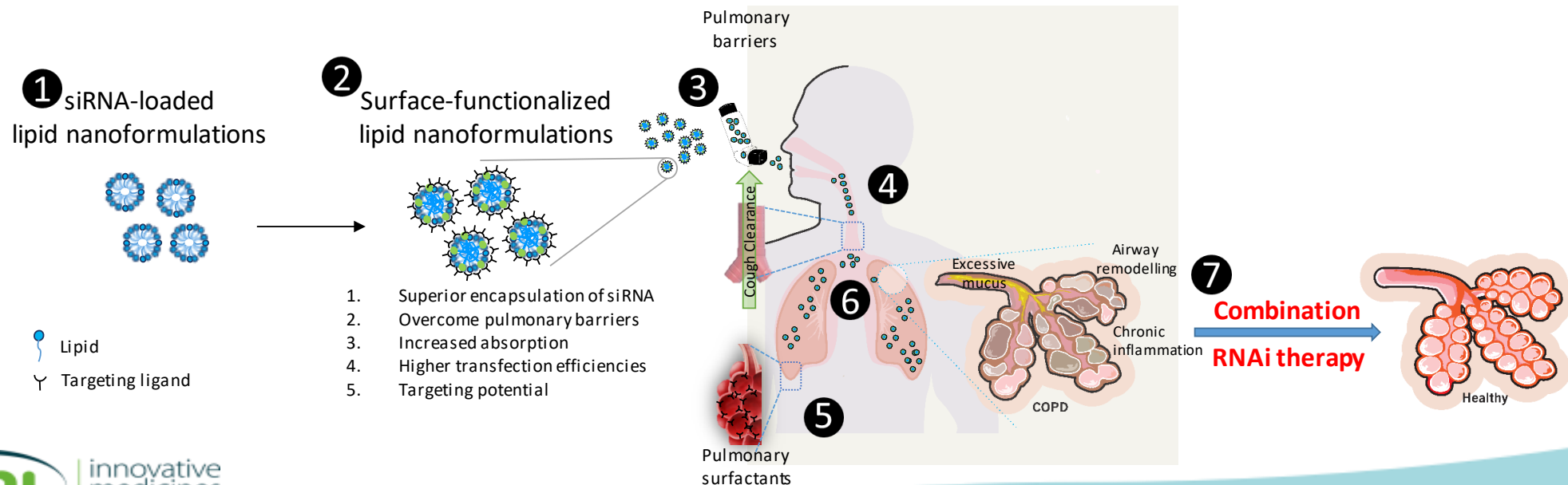
22 & 23 October 2018 • IMI Scientific Symposium • Brussels, Belgium

Research aim

Engineering of lipid-polymer hybrid nanoparticles with lipidoids as lipid component and PLGA as polymer component for local delivery of oligonucleotides (small interfering ribonucleic acids, siRNA) to lungs.

Disease target: Chronic obstructive pulmonary disease

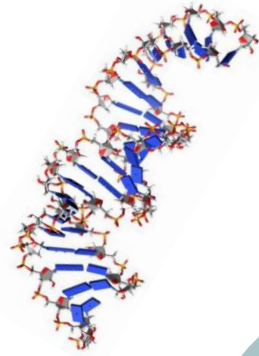
Pathophysiological manifestations: Inflammation, mucus hypersecretion and emphysema



Major findings

Platform technology

Components: Cargo, lipidoid, and poly(DL-lactic-co-glycolic acid)

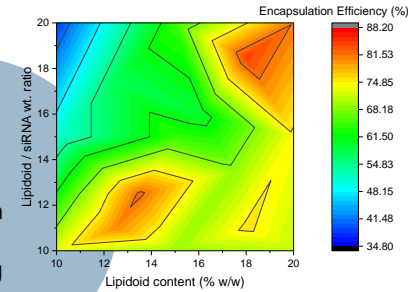


Cargoes

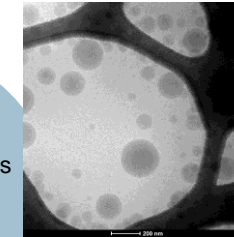
- Small interfering RNA (siRNA)
- Antisense oligos
- Micro RNA
- Messenger RNA

Quality-by-design optimization

- Particle size
- Zeta potential
- Encapsulation efficiency
- siRNA loading

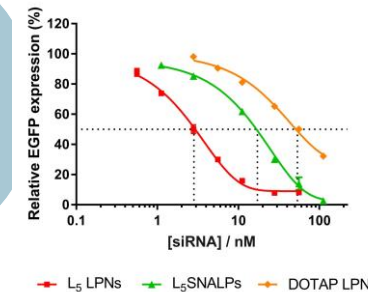


Morphological analysis and structural understanding of particle formation



In vitro evaluation

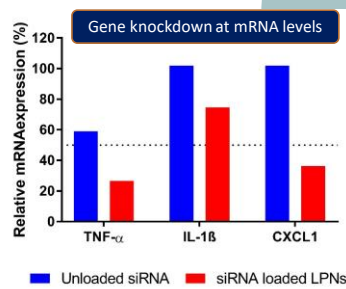
Potent *in vitro* transfection efficiency and high cell viability



Lipidoid-polymer hybrid nanoparticles (LPNs)

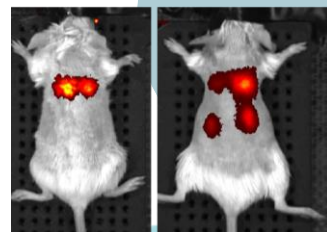
In vivo efficacy using TNF- α siRNA

- Acute lung injury model



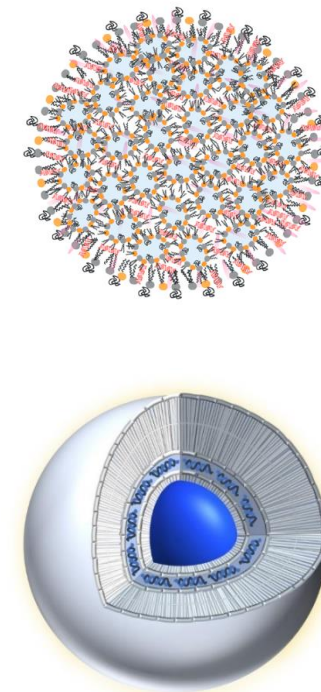
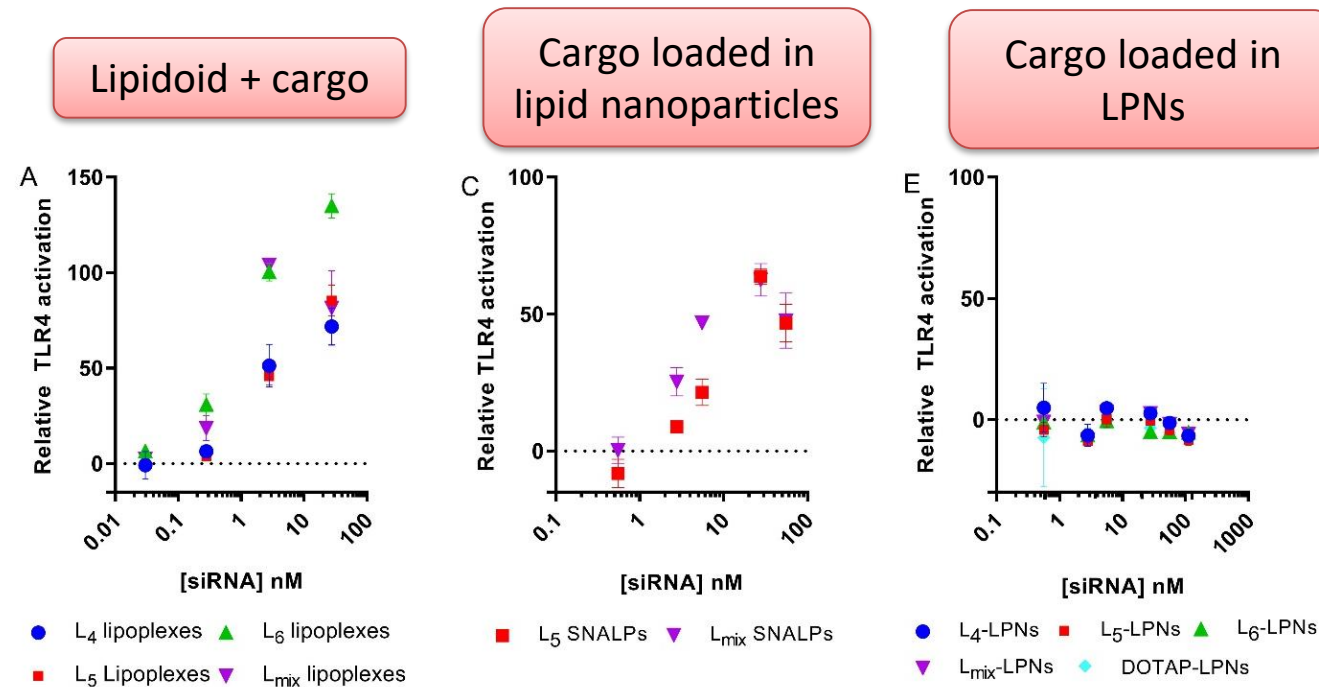
In vivo biodistribution after lung administration

In vivo studies



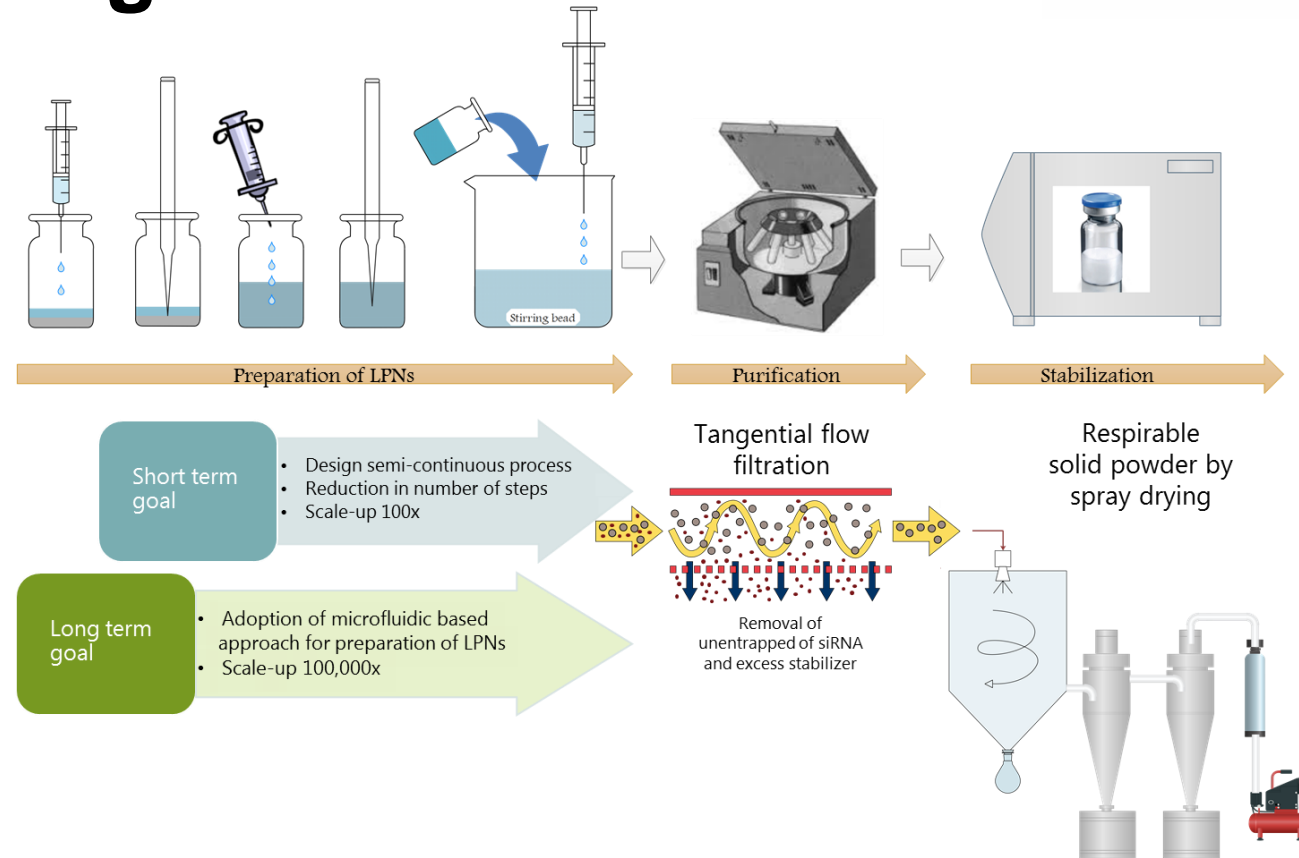
Example of the potential of the developed technology (LPNs)

Toll-like receptor 4 (TLR4) activation (marker of immunogenicity) is dependent on the type of formulation used



On-going activities

Scale-up



Two active industrial collaborations for loading of clinically relevant cargos in LPNs