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Development of Dry Powder Formulations of siRNA Nanoparticles for Inhalation

A platform for spray-drying siRNA nanoparticles to obtain nano-in-microparticles with ideal aerodynamic properties for inhalation

Reference: Dry Powder siRNA Nanoparticles

Source: https://stock.adobe.com/uk/337416078

IP Status

Patent application submitted

Seeking

Development partner, Commercial partner, Licensing, Seeking investment

About **LMU Munich**

Ludwig-Maximilians-Universität München is the University in the heart of Munich. LMU is recognized as one of Europe's premier academic and research institutions. The LMU Munich community is engaged in generating new knowledge for the benefit of society at large.

Background

After the approval of Onpattro and Givlaari, siRNA therapy has become reality – however only for targets in the liver. While the lung is generally easily accessible by inhalation, formulation of siRNA, which generally has to be delivered by a nanocarrier, for inhalation is challenging.

To develop a spray-drying platform for pulmonary siRNA delivery against SARS-CoV-2, other respiratory viruses or genes pathologically (over)expressed in the lung in patients suffering from asthma, COPD, cystic fibrosis, lung fibrosis, or lung cancer, LMU Munich researchers have optimized spray drying process parameters, matrix excipients and tubing materials to decrease siRNA losses, decrease residual moisture of the powder formulation, optimize redispersion, maintain nanoparticle sizes, size distributions and zeta potentials and to ensure efficient gene silencing in lung epithelial cells and T cells.

Tech Overview

To develop stable and inhalable polyplex dry powder formulations, the researchers spray-dried polyplexes consisting of siRNA and a polyethylenimine (PEI) based block copolymer i.e. PEG-PCL-PEI (PPP) at different temperatures in presence of mannitol or trehalose. The team investigated the effect of inlet (T-In) and outlet (T-Out) temperature and of a secondary drying step on the recovery of siRNA as well as adsorption effects within the tubing material. Choosing a low abrasion silicon tubing prevented siRNA loss due to adsorption. It was shown that mannitol and trehalose formulations preserved siRNA integrity regardless of concentration and temperature at T-Out below the siRNA melting temperature. However, trehalose formulations allowed full siRNA recovery whereas mannitol formulations resulted in spray drying induced losses of ~20 % siRNA and of 50-60 % PPP independent of mannitol concentration and T-Out. All formulations showed optimal aerodynamic characteristics as confirmed by next-generation impaction analysis based upon siRNA amount. All spray-dried formulations resulted in comparable or better GFP silencing in GFP expressing lung cancer cells (H1299) compared to freshly prepared polyplexes. Additionally, formulations of siRNA and transferrin-PEI conjugates were spray dried, characterized and used to transfect primary human T cells *ex vivo*. Results confirmed successful silencing of the Th2 transcription factor GATA3 with spray-dried formulations as a potential treatment for severe asthma (Figure 1).

Stage of Development

TRL 5, in vitro and *ex vivo* experiments performed, technical upscaling confirmed, aerodynamic properties for inhalation confirmed.

Benefits

- Development of siRNA quantification techniques in dry powder
- Assessment of aerodynamic properties based on siRNA content (active ingredient vs. powder mass) an optimization or aerodynamic properties for inhalation and residual moisture
- Preservation of nanoparticle characteristics after spray-drying/redispersion
- Preservation of siRNA integrity
- Preservation of bioactivity of both siRNA and nanocarrier system

Applications

- Therapeutic and prophylactic pulmonary siRNA delivery
- COVID-19
- Asthma, COPD
- Cystic fibrosis, fibrosis
- Lung cancer

Opportunity

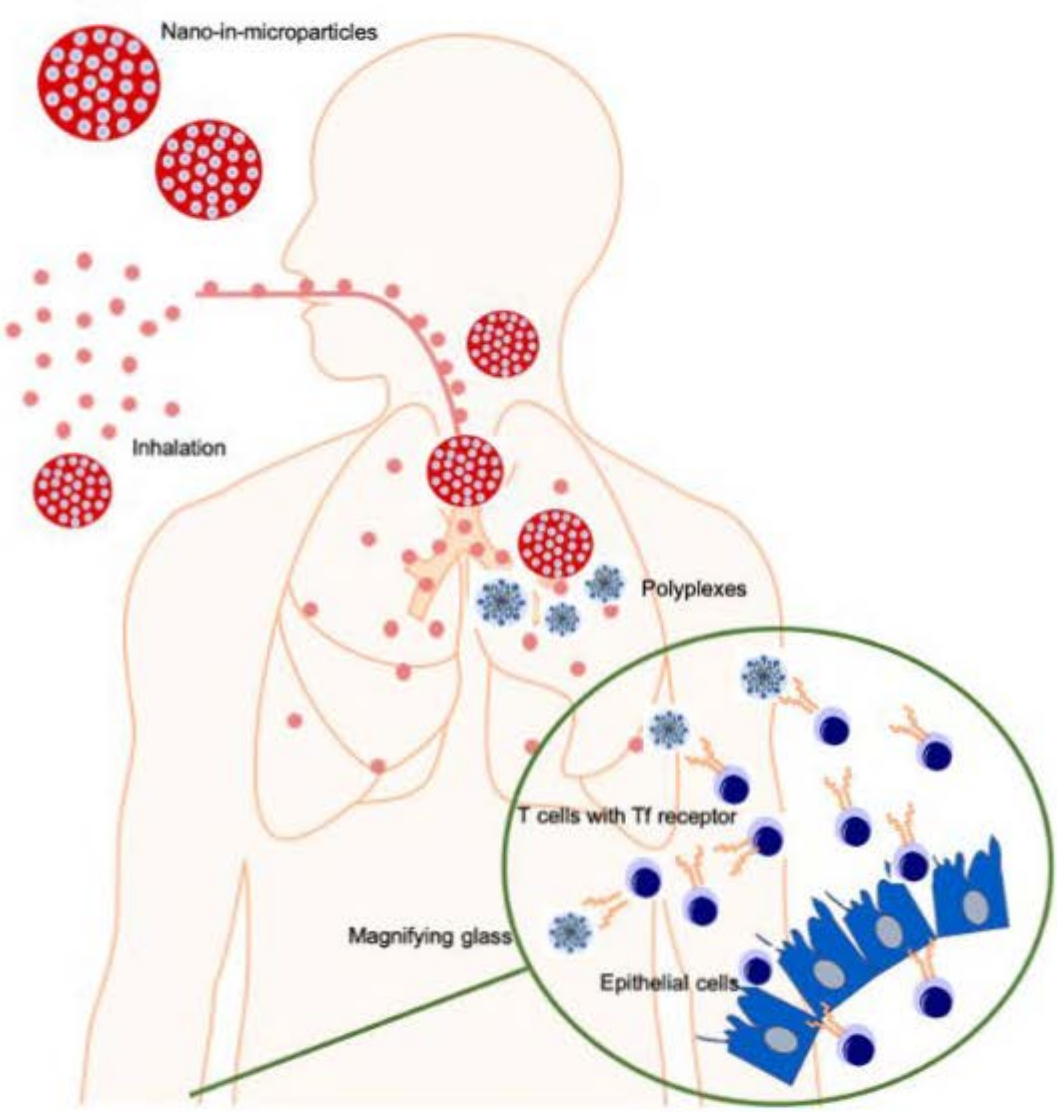
Searching for investors and/or licensing partners to further scale-up production, perform *in vivo* studies and clinical trials.

Patents

- Patent application submitted. Contact TTO for further information.

Appendix 1

Figure 1



For further information, please contact us.

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