

Polymer chemistry platform for modulating the pharmacokinetics of inhaled therapeutics

KEYWORDS

- Respiratory diseases
- Pulmonary drug delivery
- Long-acting therapeutic agents

Technology Market:

Therapeutics for respiratory diseases

Inhalation is the method of choice to treat respiratory diseases as it allows convenient and efficient delivery of therapeutic agents directly to the primary site of injury. However, rapid clearance of drugs from the lungs limit their efficacy and necessitates the use of high unit doses at a high administration frequency, thereby jeopardizing compliance and treatment outcome. There is thus a high unmet medical need for inhaled therapeutics with a sustained residence time in the lungs of patients suffering from chronic respiratory diseases such as cystic fibrosis (CF). Such long-acting therapeutic agents will not only increase the long-term adherence rates to chronic treatments, but also improve the overall quality of life of patients.

The UCL invention

A polymer chemistry platform provides a highly versatile toolbox to customize the behavior of molecules. Careful selection of the polymer as well as of the active therapeutic agent allows the creation of new drug entities with optimized pharmaceutical properties. Worked performed by the group of Prof. Rita Vanbever has shown that conjugation of a high molecular weight polyethylene glycol (PEG) polymer to a therapeutic agent can significantly extend

the residence time of the composite molecule within the lungs following delivery to the respiratory tract (Fig. 1). As a result, the therapeutic efficacy of the drug-polymer conjugate is enhanced (Fig. 2).

Main advantages of technology

- ✓ Extended availability of the inhaled drug-polymer conjugate within the lungs leads to:
 - improved drug efficacy
 - reduced inhaled unit doses which decrease the number of side effects
 - reduced administration frequency, decreasing COGS and increasing profit margins
- ✓ Technology compatible with any inhaler device (nebulizers, DPIs and soft-mist inhalers)
- ✓ Polymer conjugation can improve several key properties of a drug simultaneously such as its PK, stability and solubility

This work is the subject of a patent application (WO2015107176) and a business plan has been written around the technology.

Relevant references

- Koussoroplis *et al.*, J. Control. Release. 187: 91-100, 2014
- Freches *et al.*, Int. J. Pharm. 521: 120-129, 2017
- Guichard *et al.*, Adv. Therap. p.2000146, 2020

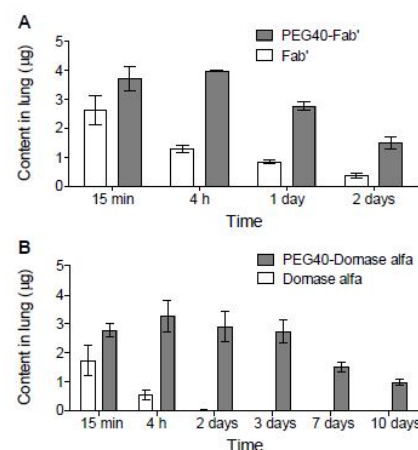


Fig. 1: Assessment of the residence time of native and proteins conjugated to a 40 kDa PEG in murine lungs following delivery to the respiratory tract via intratracheal instillation. A, a Fab' antibody fragment; B, dornase alfa. Mean values (\pm SEM) of 3 to 7 mice per time point.

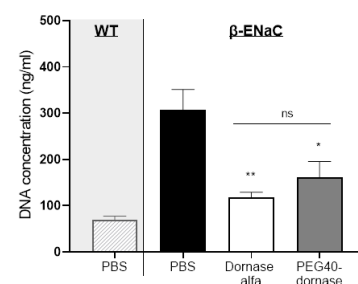


Fig. 2: Assessment of the therapeutic efficacy of native and PEGylated dornase alfa in β -ENaC mice, a CF-like murine disease model with pulmonary inflammation and elevated DNA concentrations. While 10 μ g of rhDNase was administered daily for 5 consecutive days, 1 single dose of PEGylated dornase was delivered on day 1. Mean values (\pm SEM) of 5 to 7 mice per group.