Clinical Development of an Optimal F/HN Pseudotyped SIV Vector for Cystic Fibrosis Lung Gene Therapy


1. The United Kingdom Cystic Fibrosis Gene Therapy Consortium 2. DNAVec, Japan

Introduction
The UK CFSTG is developing gene therapy for Cystic Fibrosis Lung disease. Our rational pathway is currently in a multi-phase phase 1b clinical trial and end of year 2016 (Alton et al., 2013). In parallel, we have been developing a viral vector, SIV pseudotyped with F/HN from membrane proteins from Sato site (SIV-F/HN).

Outcomes
1. Identified lead candidate expression construct for further studies
2. SIV-F/HN can be repeated administered (3 times) to the mouse without loss of activity
3. Demonstrated high levels of transduction efficiency from SIV-F/HN in the mouse lung

Functional Assessment of SIV-F/HN in Mouse Models

Introduction of Lentivirus Vector Construct in Mouse Models
SIV-F/HN vector was introduced in our production system with different transgenes promoters, expressing construct (transgene gene)

- CFTR
- Luciferase
- GFP

Outcomes
1. High levels of transduction efficiency from SIV-F/HN in the mouse lung
2. Demonstrated high levels of transduction efficiency from SIV-F/HN in the mouse lung

Materials and Methods
1. Mice (virus dosed and naive controls) were anaesthetised with isoflurane and 100 µl Luciferin (Caliper Life Sciences, 15 µg/ml) delivered to the lungs by instillation
2. Luciferase assessment by bioluminescent imaging (BLI) in mice
3. TTU was determined by Taqman analysis on integrated copies of the WPRE element in the virus genome

References