Gene Therapy for Cystic Fibrosis: Going Viral

Jean-François Gélinas
Oxbridge Canadian Conference
June 1, 2013
Cystic Fibrosis (CF)

- Genetic disorder (mutation in the CFTR gene).
- Requires life-long medication and airway clearance therapy.

Source: Adapted from NIH Heart, Lung, and Blood Institute
Cystic Fibrosis in Canada

• Most common lethal inherited disease in Canadian children/young adults.

• 1 in 3,600 children born in Canada has CF.

• Median survival age (2011): 34 years.

• Cumulatively, Canadians with cystic fibrosis (2011):
  • spent over 25,000 days in hospital.
  • attended CF clinics more than 15,000 times.

Source: Cystic Fibrosis Canada
Genetics of Cystic Fibrosis

- 1 in 25 Canadian is a carrier of a defective CFTR gene
UK Cystic Fibrosis Gene Therapy Consortium

Combined Research Programme of UK Groups Performing CF Gene Therapy Clinical Studies

Largest Gene Therapy Research Group for Lung Diseases

www.cfgenetherapy.org.uk
Gene Therapy Approaches for Cystic Fibrosis

- **Gene Repair:**
  - Correct the mutation in EVERY cell of the body.

- **Gene Replacement:**
  - Completely replace the defective gene in EVERY cell of the body.

- **Our approach:**
  - Provide a third, functional, copy of the gene to SOME cells of the lungs.
Our Current Gene Therapy Clinical Trial
Our Current Gene Therapy Clinical Trial

- **Evaluating:** Safety & Efficacy
- **Dose:** 1 per month

CFTR Plasmid + Liposome + Nebuliser → Lung Gene Delivery
Need for a New Platform

• Provide long lasting lung gene delivery
Long Lasting Lung Gene Delivery

What:

• Easily goes into cells?

• Can insert a gene into its host cell DNA?
Long Lasting Lung Gene Delivery

What:

• Easily goes into cells?
• Can insert a gene into its host cell DNA?

HIV!
How to Build Your Own HIV?
1. Genome Plasmid

- CFTR
- Viral Proteins
- Surface Proteins
2. Viral Proteins Plasmid
3. Surface Protein Plasmid
From Plasmids to Viruses via Producer Cells
Virus Production Optimisation

My Project:

• Increase Viral Production
• Reduce Cost
Viral Approach

Lung gene delivery platform:

- Tailored for lung diseases
Tailored for Lung Diseases

CFTR

Viral Proteins

Surface Proteins
Tailored for Lung Diseases

- CFTR
- Viral Proteins
- Surface Proteins
Viral Approach

Lung gene delivery platform:

• Modular
• Flexible
Modular & Flexible

- CFTR
- Viral Proteins
- Surface Proteins
Modular & Flexible

Lung gene delivery platform:

• Different gene to target a different disease
Alpha-1-Anti-Trypsin (AAT) Deficiency

Severe AAT deficiency occurs in 1 in ~5000 in North American population.

Lung Diseases:
- Cystic Fibrosis
- Emphysema
- COPD
- Asthma

Other Diseases:
- Cancer
- HIV
- Diabetes

Source: Marciniuk et al., Can Respir J Vol 19 No 2 March/April 2012
My Project:

- Use AAT as a model for our lung gene delivery platform.
Acknowledgements

• Deborah Gill & Steve Hyde

• Karen Bamford, Mary Connolly, Natasha Davie, Lee Davies, Rebekka Harding-Smith, Laura Moyce, Cathy Oliveira, Ian Pringle, Kristen Pluchino, Stephanie Sumner-Jones

• DPhil Funding: