Gene Therapy for respiratory diseases

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Chaired by Ian Hollingsworth
Programme Manager, Cell and Gene Therapy Catapult

Funded by

Coordinated by

Who are LAT and the ATTCs?

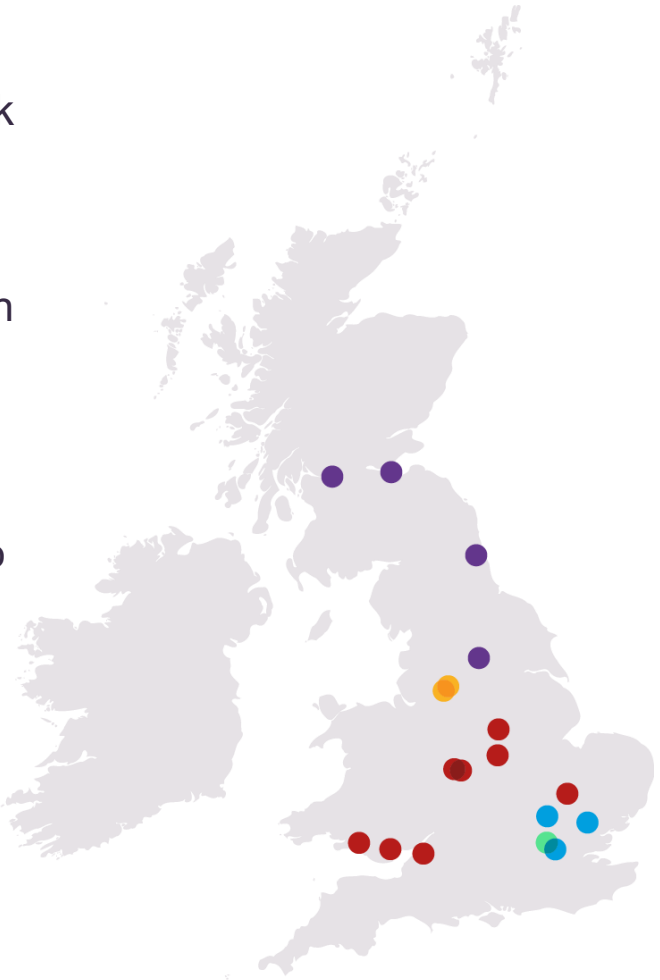
The ATTC (Advanced Therapy Treatment Centre) network is funded by Innovate UK and the Industrial Strategy Challenge Fund

London Advanced Therapies (LAT) is funded by Research England

The centres are working together, along with the Cell and Gene Therapy Catapult to specifically look at the training requirements for the current workforce and what needs to be put in place for them to be ready to deliver the treatments that are currently being developed.

This series of webinars is designed to help increase the awareness of advanced therapies and their impact in the clinic

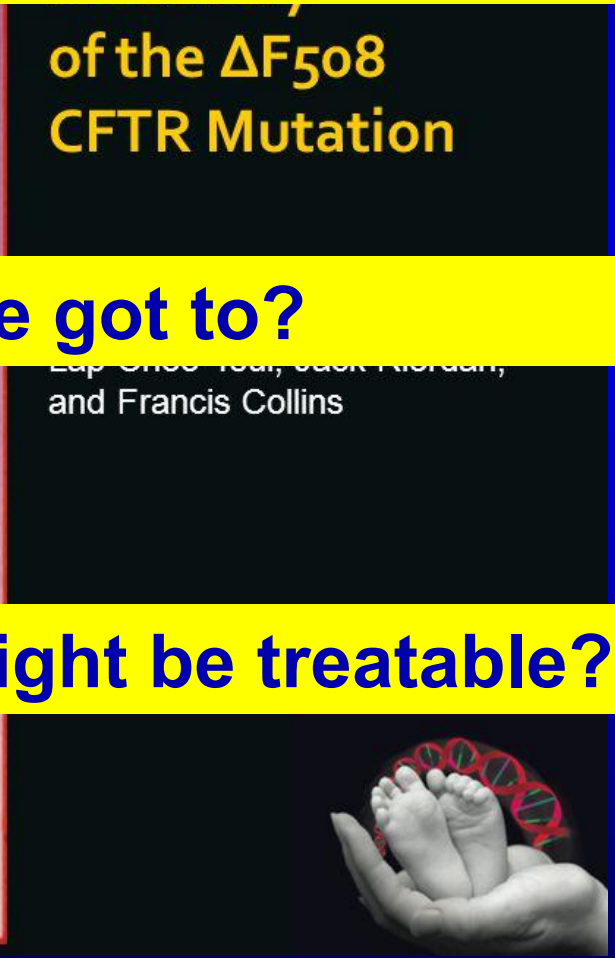
Find out more at https://www.theattcnetwork.co.uk/



Coordinated by

Gene therapy for respiratory diseases

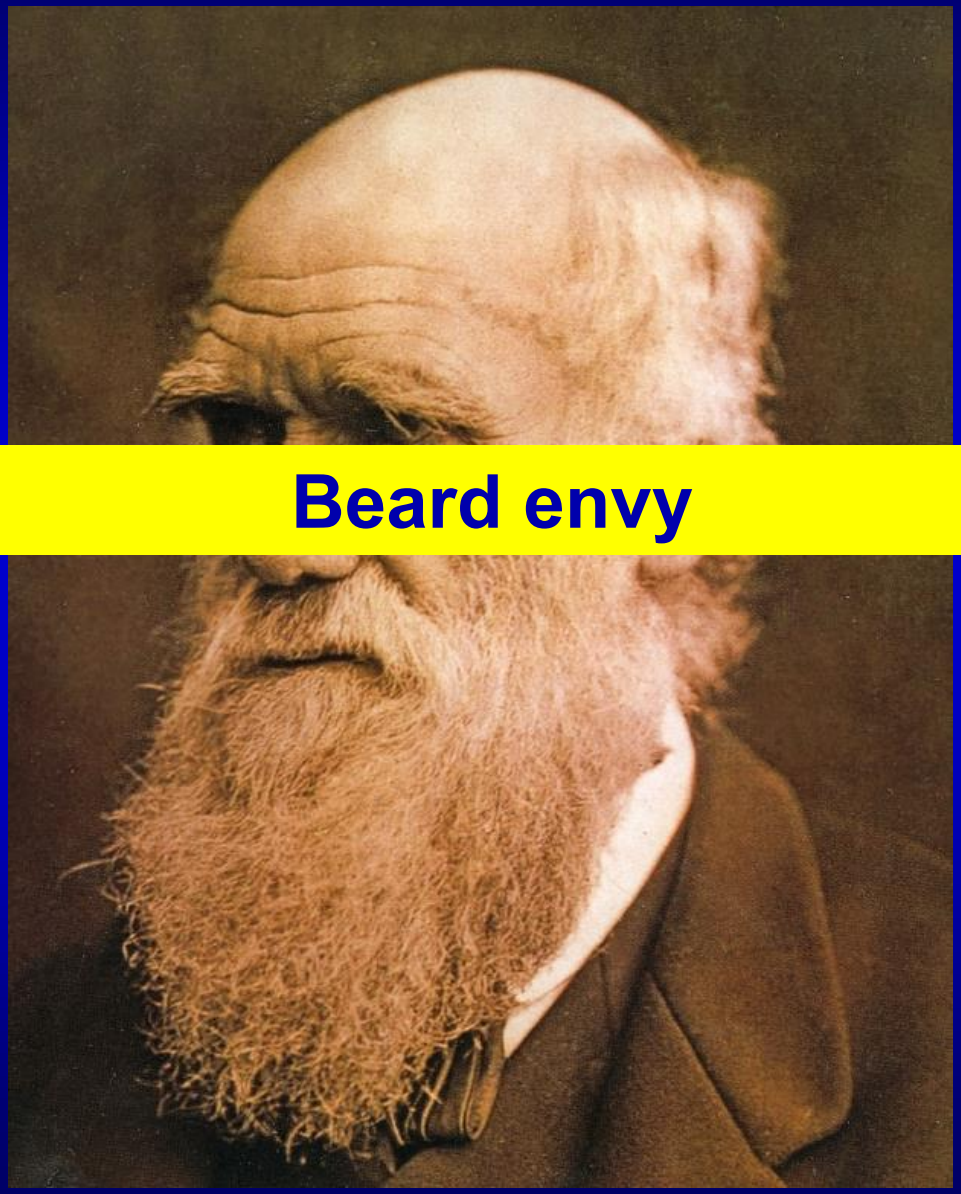
What is the problem?



Where have we got to?

What other diseases might be treatable?

Charles Darwin (1809-1882)



Beard envy

Cystic fibrosis

: Commonest lethal inherited

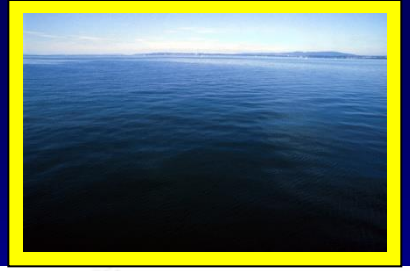
: 1:20 carrier

: 1:2000 disease

: Lung focus

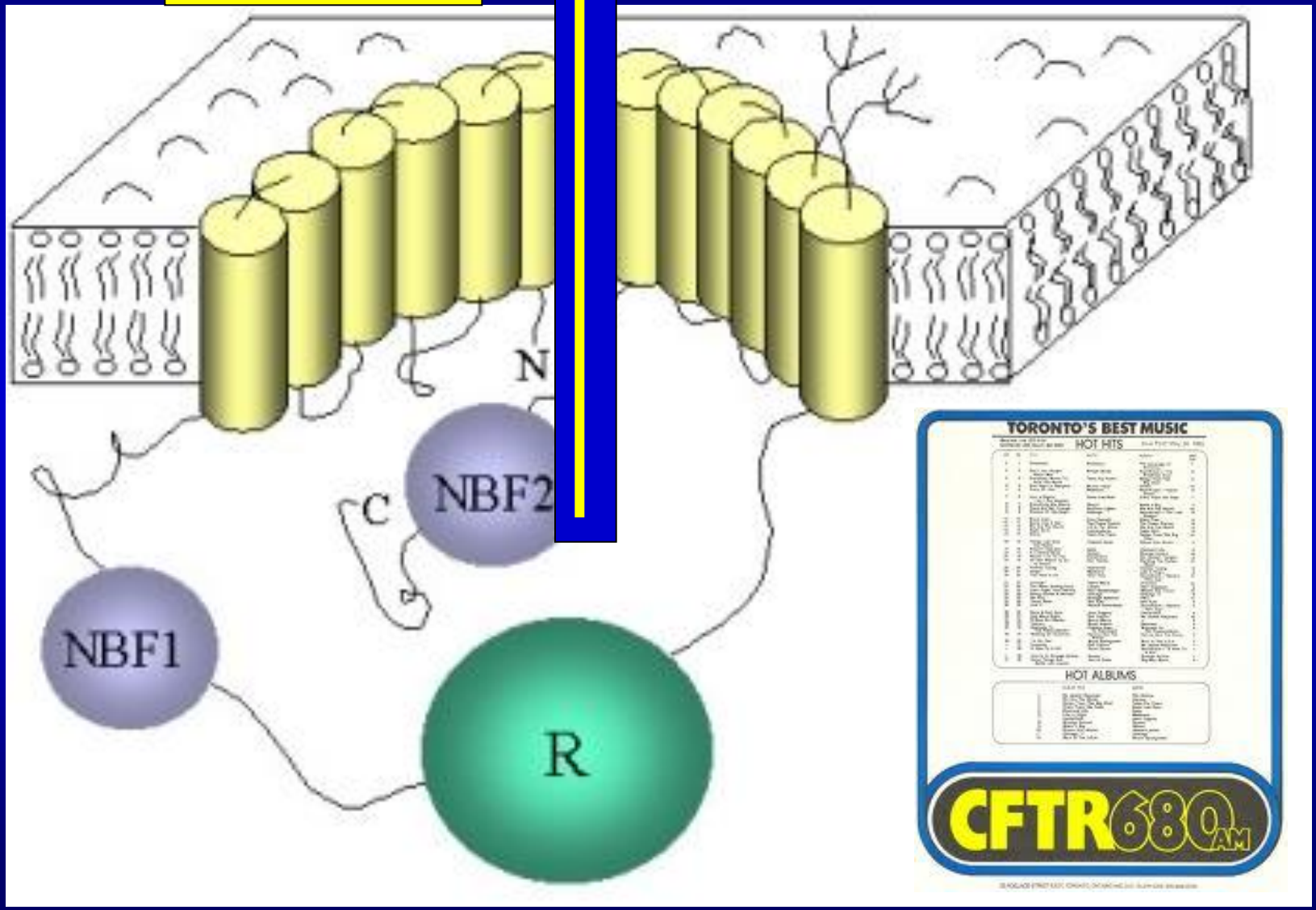
: Sticky secretions – cycles infection

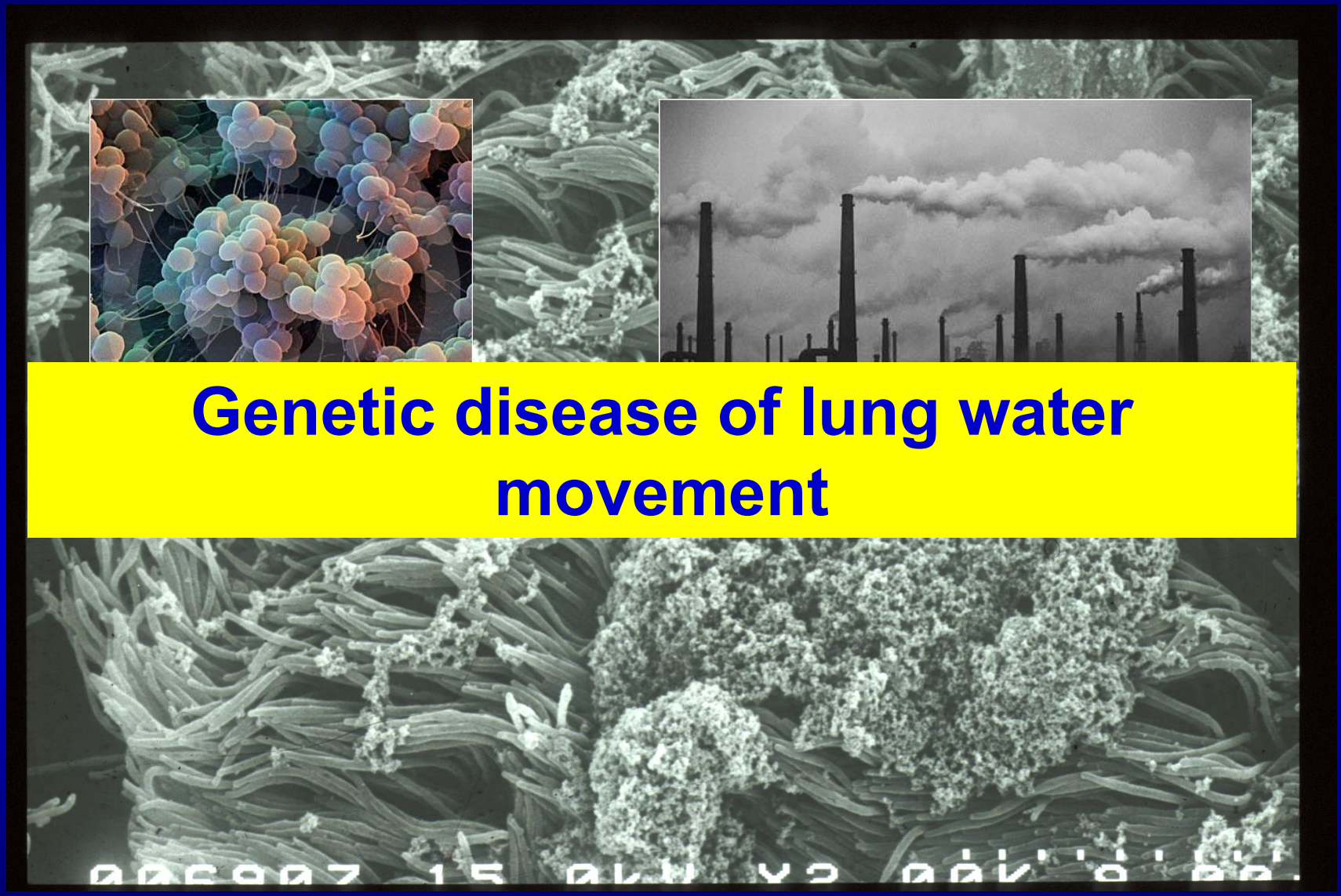
: Survival ~ 38 years



CF Cl-

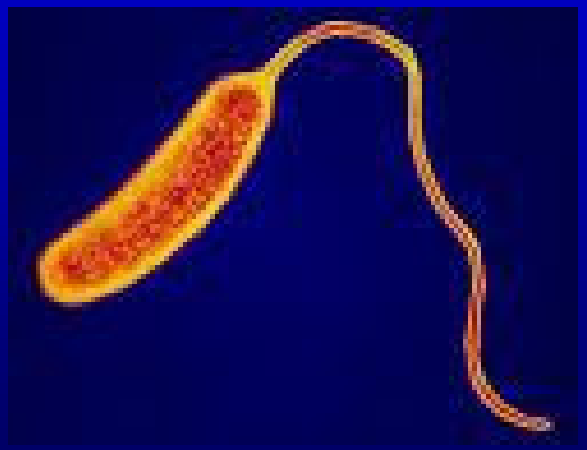

DURACELL
PLUS

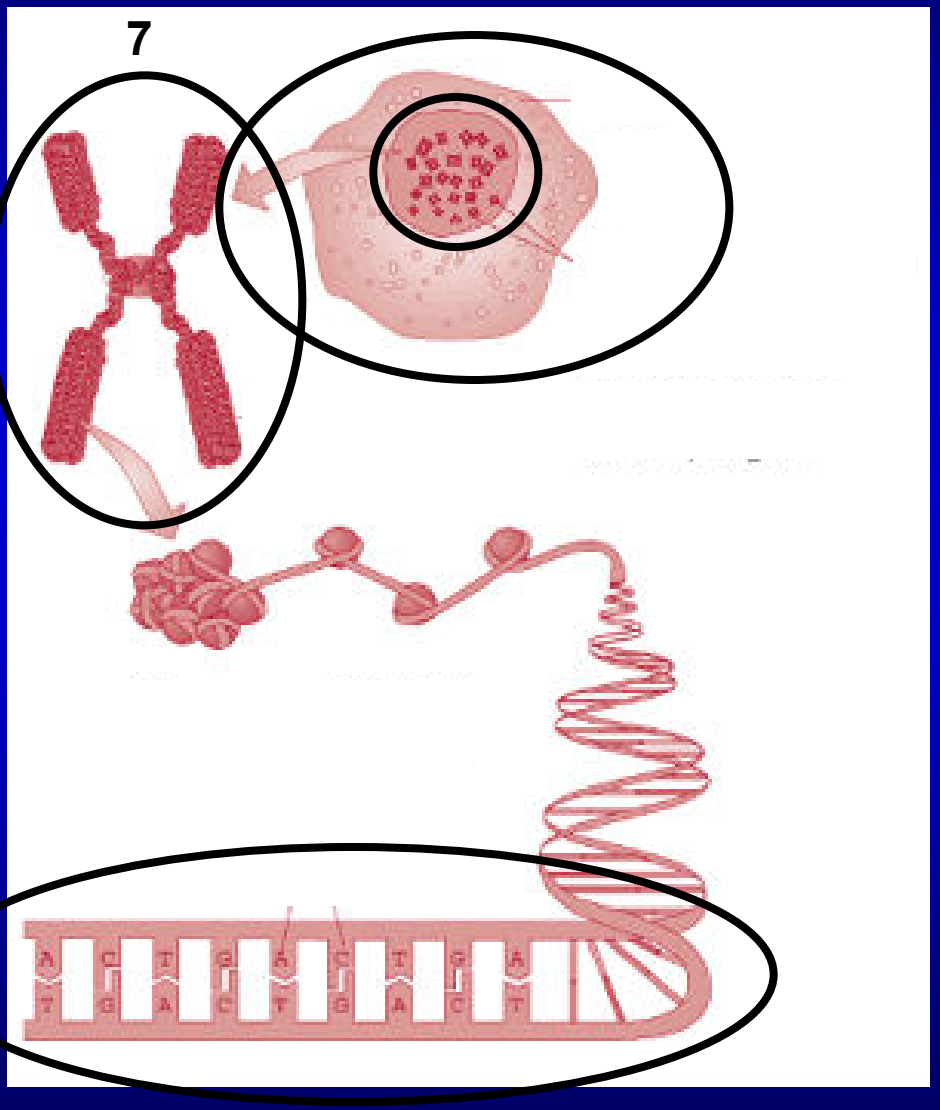

N
C
NBF2
NBF1
R
TORONTO'S BEST MUSIC
HOT HITS
HOT ALBUMS
CFTR680AM



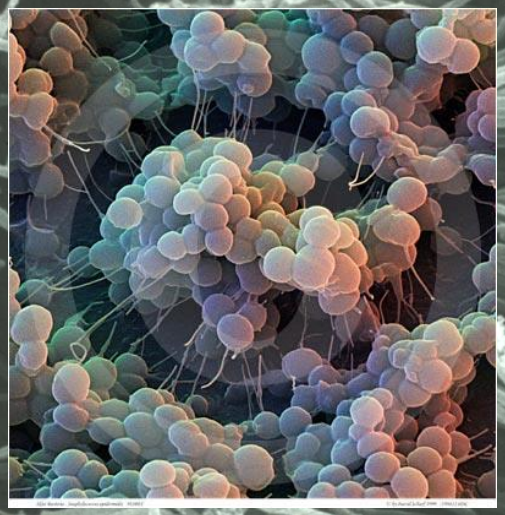
Genetic disease of lung water movement

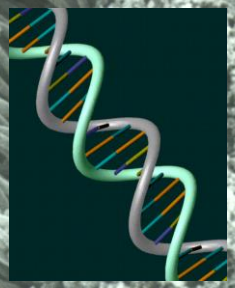
DIY CF gene therapy

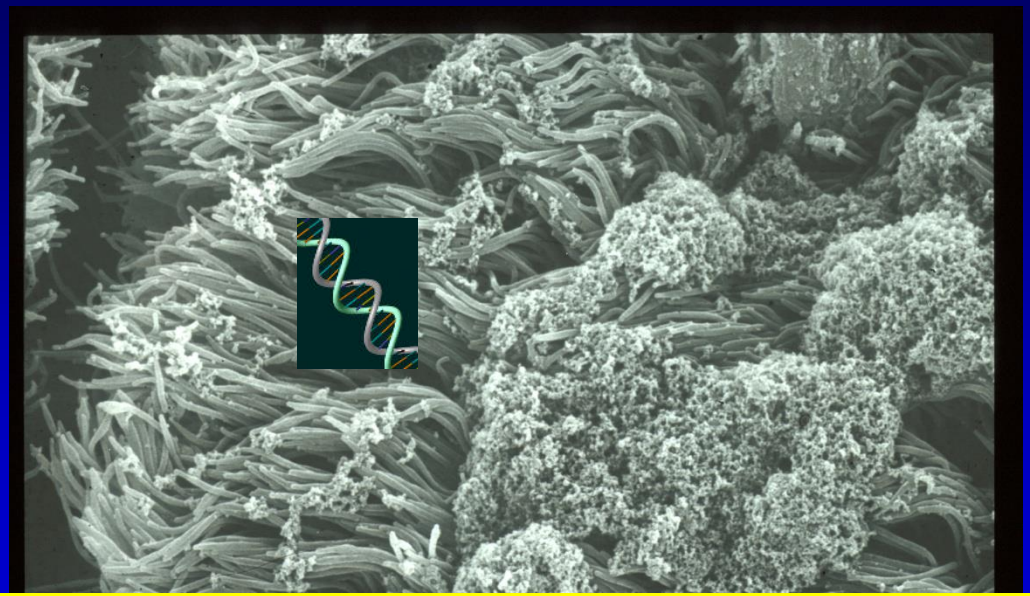





DAKIN
Nebuliser

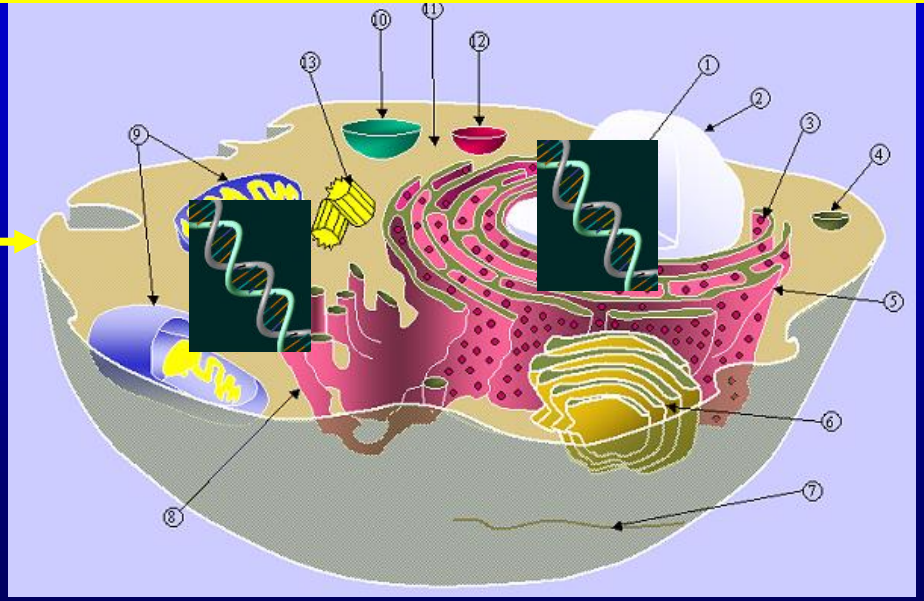






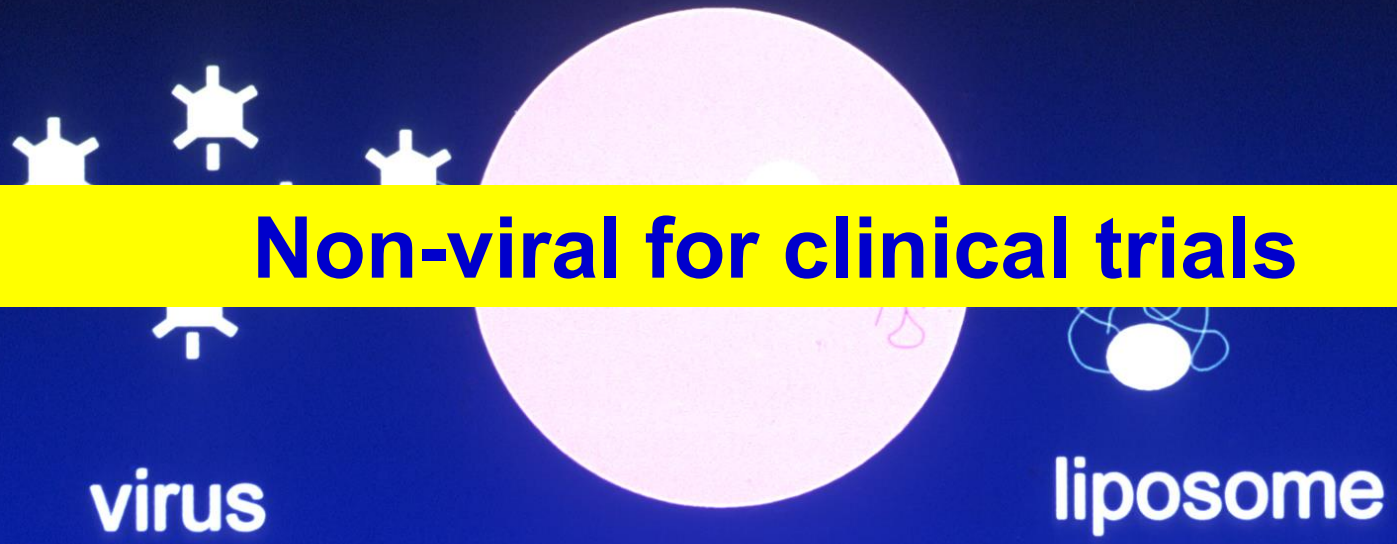
Working against evolution

CFTR protein



GENE THERAPY

Gene transfer into cells



Non-viral for clinical trials

UK Respiratory Gene Therapy Consortium

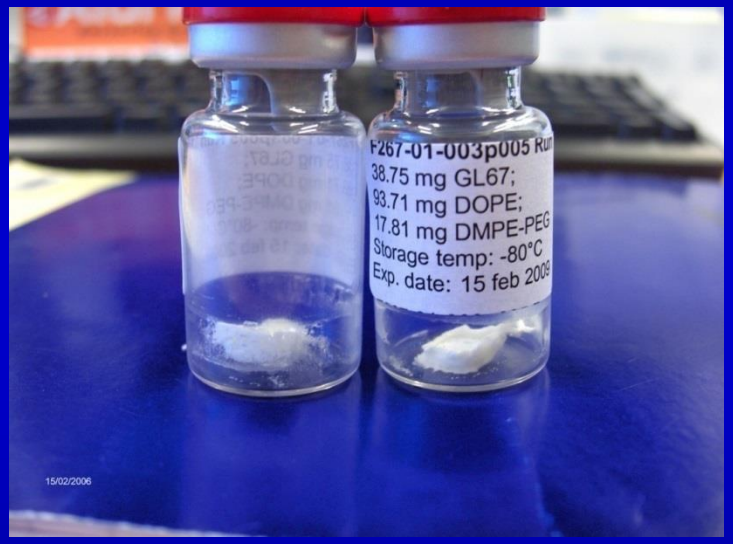
: Focus 50 people

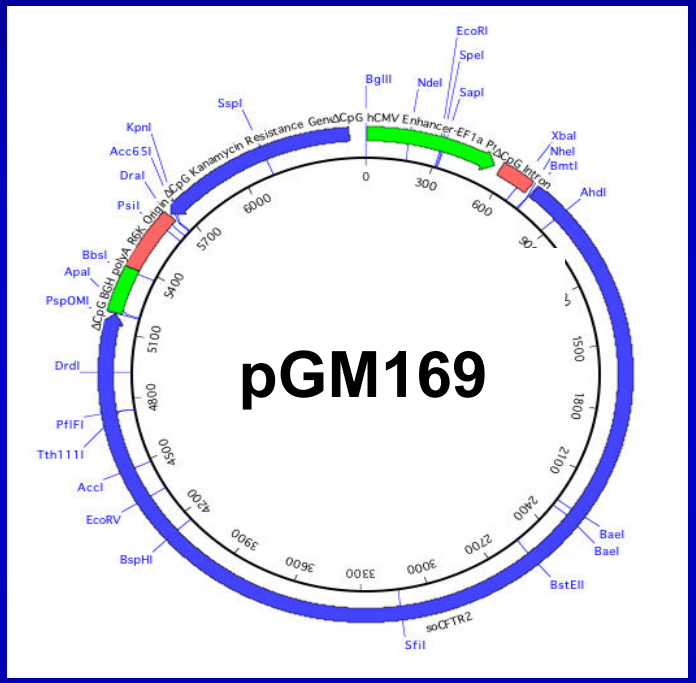
: Common strategy

: Small pharma

Where have we got to?

- Liposome (Wave 1)





- Preclinical, Manufacture, Toxicology, Regulatory
- Multiple early phase trials

Multidose Trial

: Double-blind placebo-controlled (0.9% saline)

: 12 doses at 28 day ± 5 day intervals

: 5 ml nebulised

: Age 12+

: 50% < FEV_1 < 90%

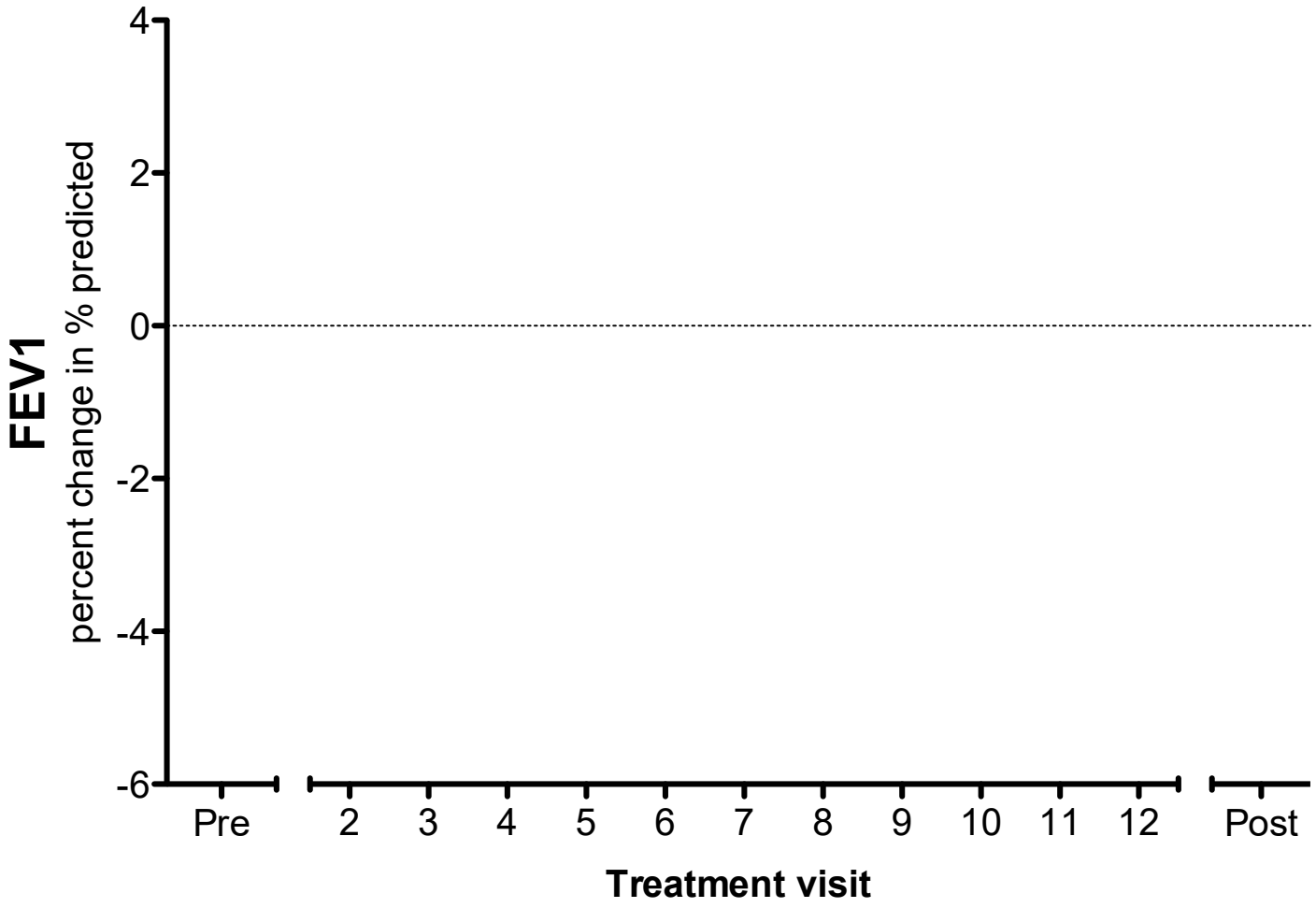
: 1:1 randomisation

: Two sites

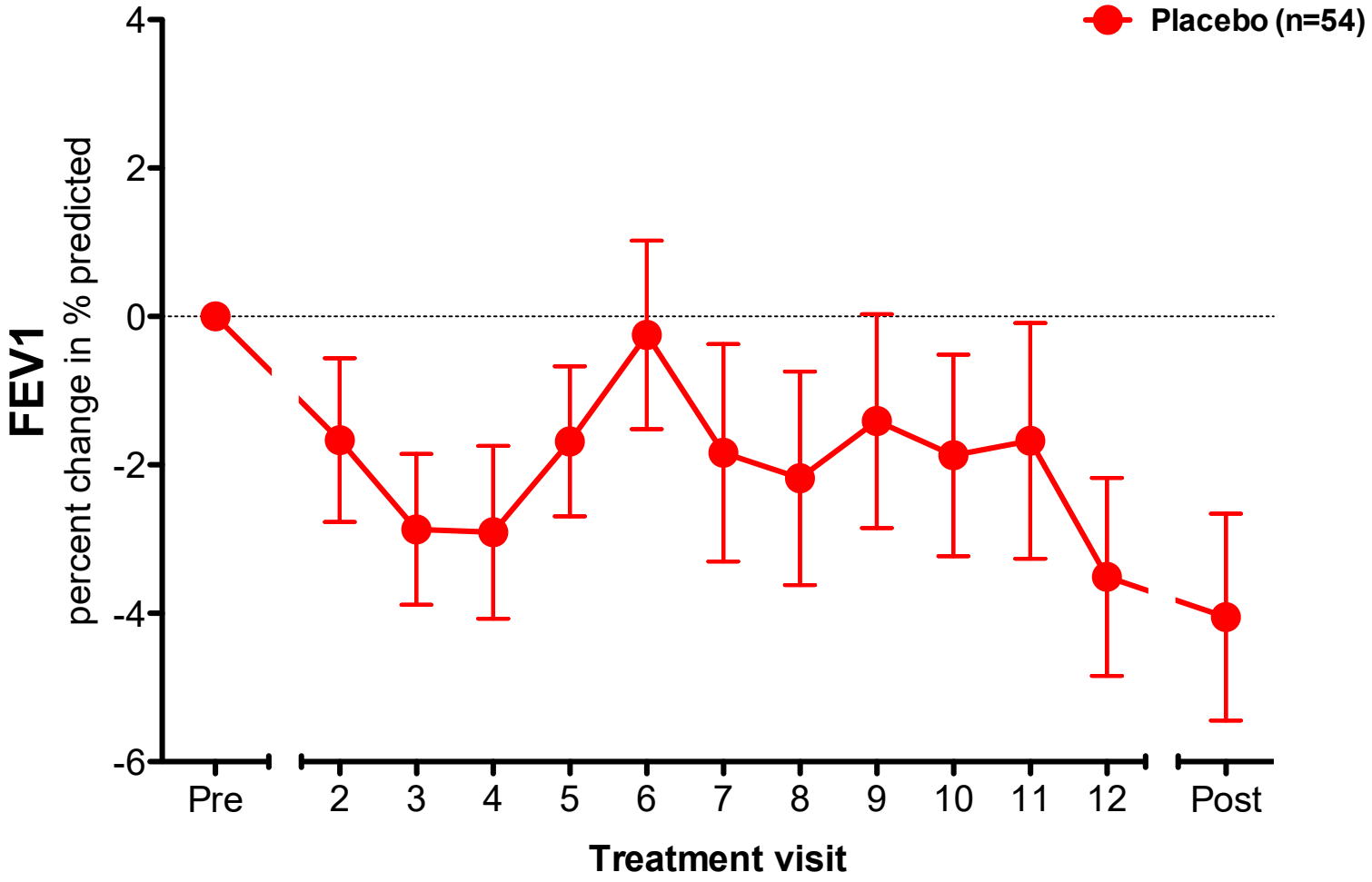
Dosing

3 min on	2 min off	3 min on

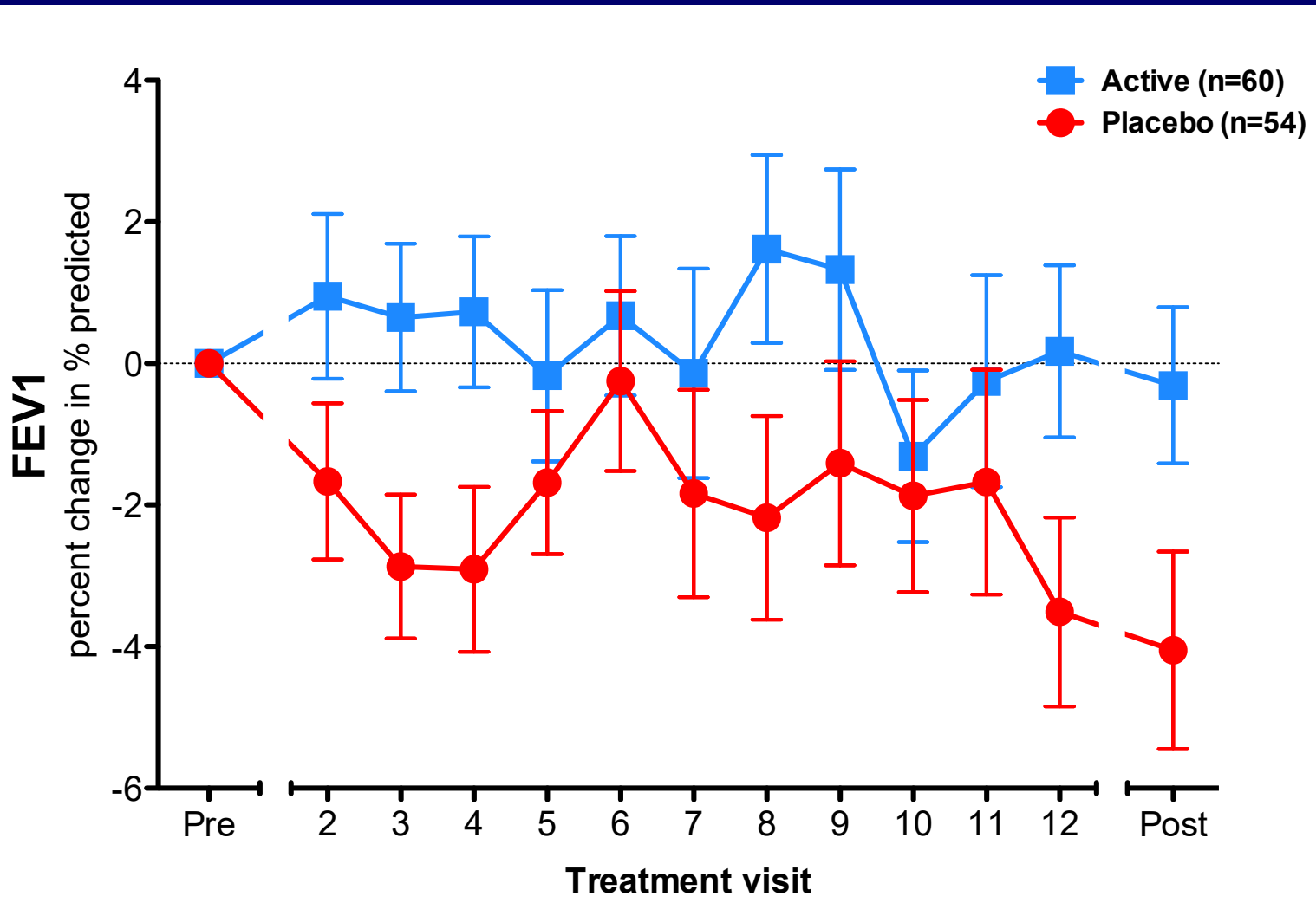
Primary outcome: FEV1



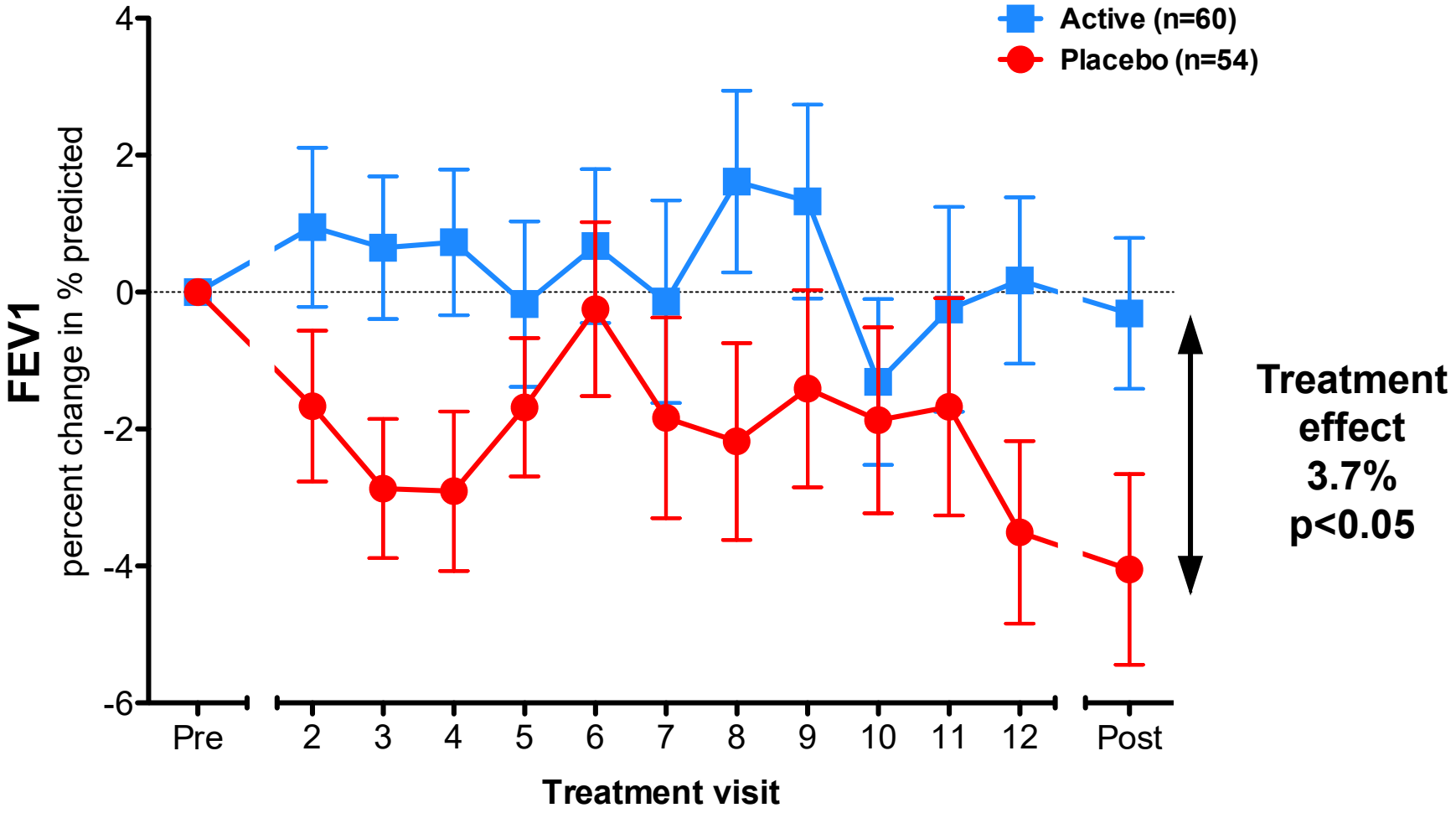
Primary outcome: FEV1



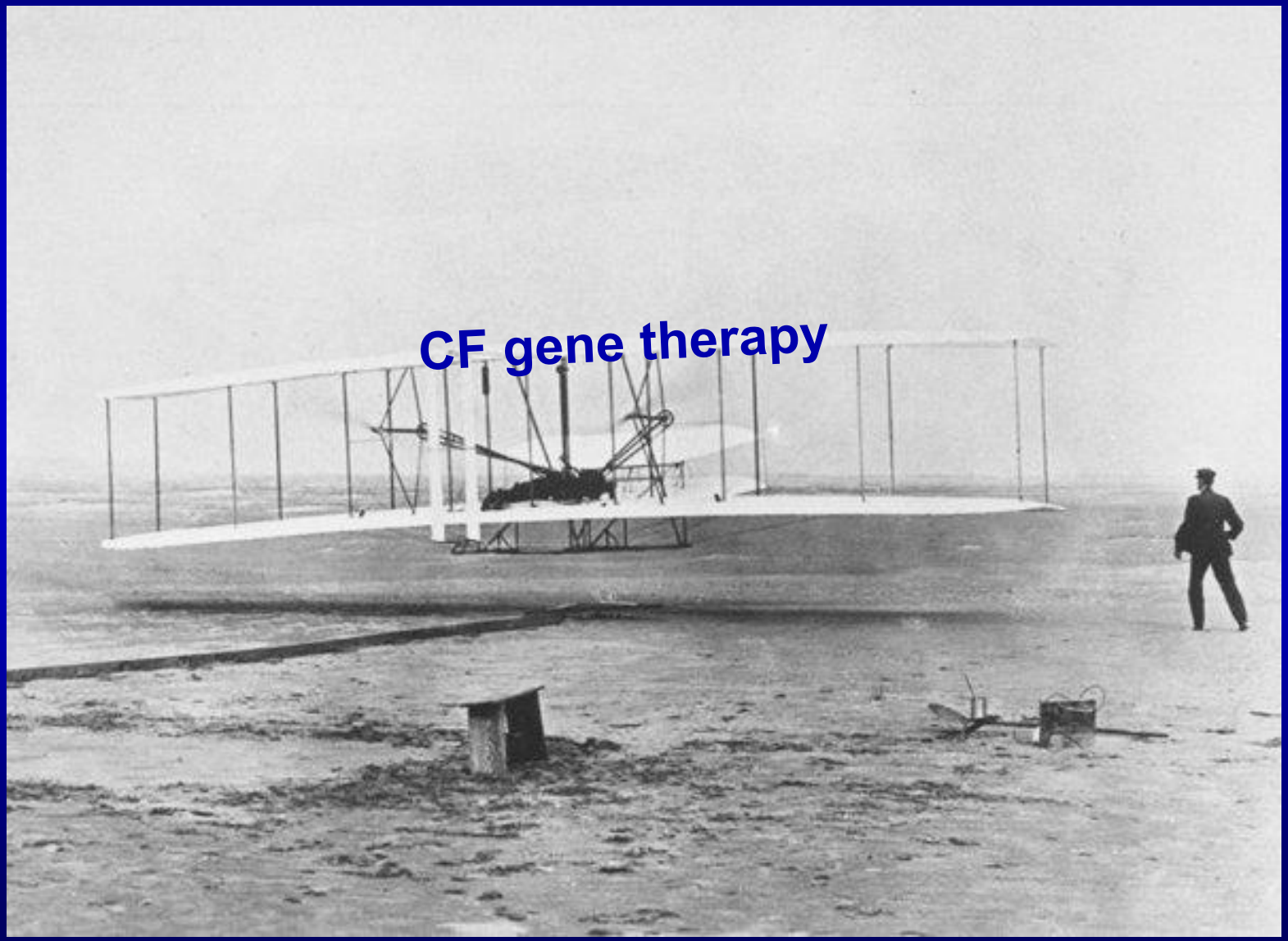
Primary outcome: FEV1



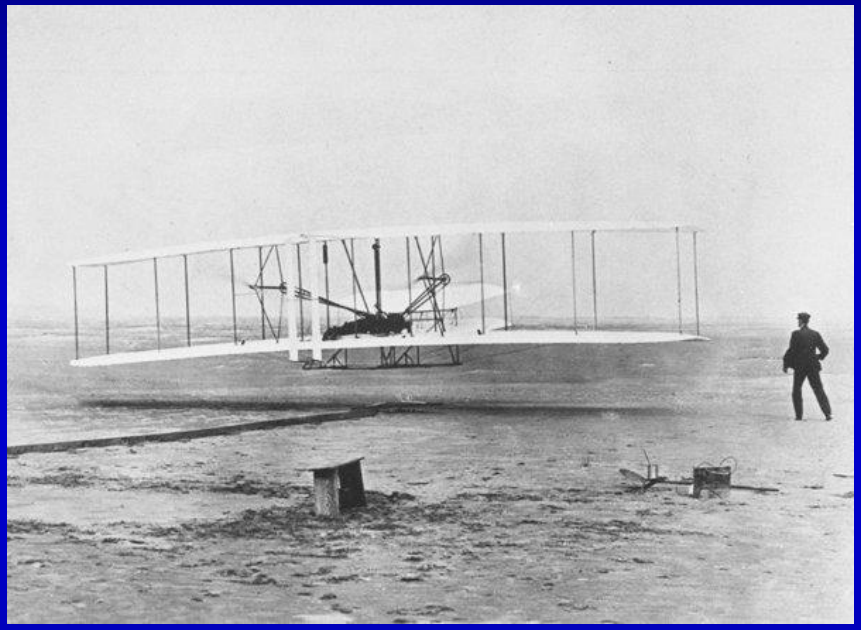
Primary outcome: FEV1



What this is



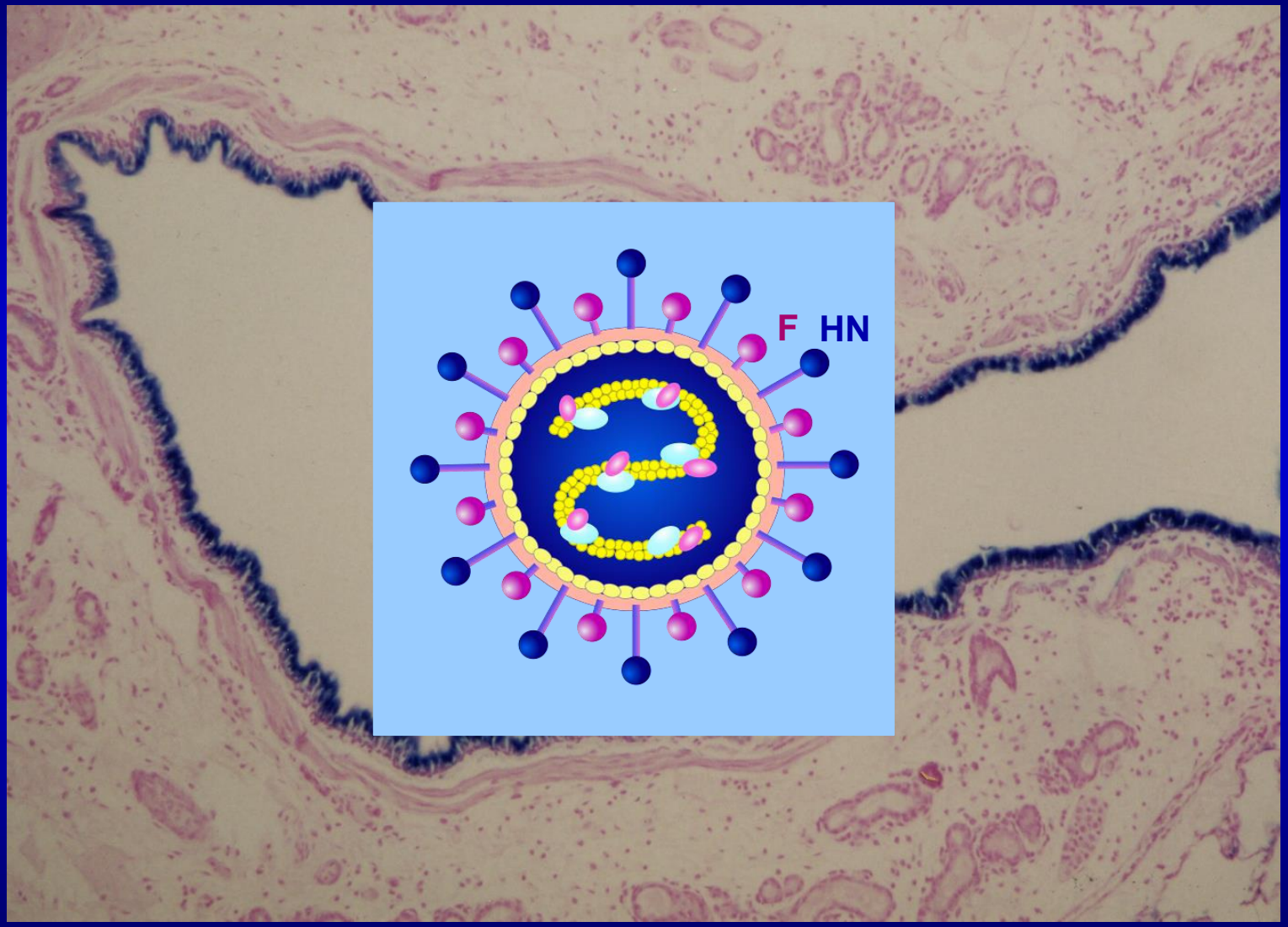
What this isn't



Wave 1

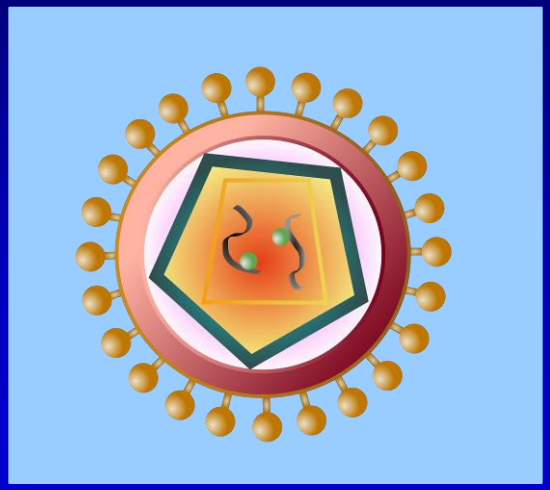
Wave 2

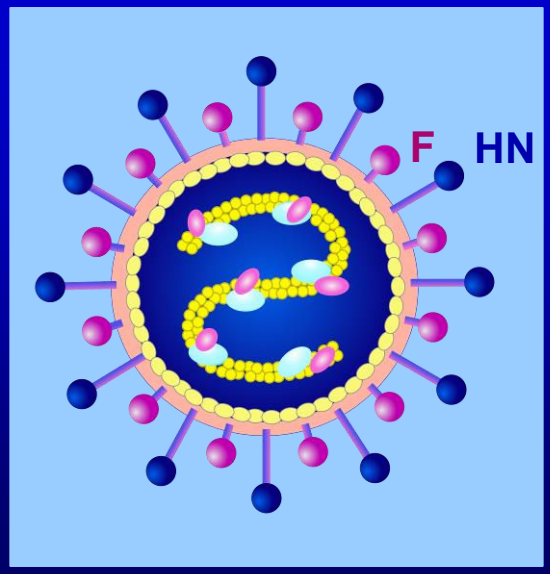
Sendai virus transfects airways

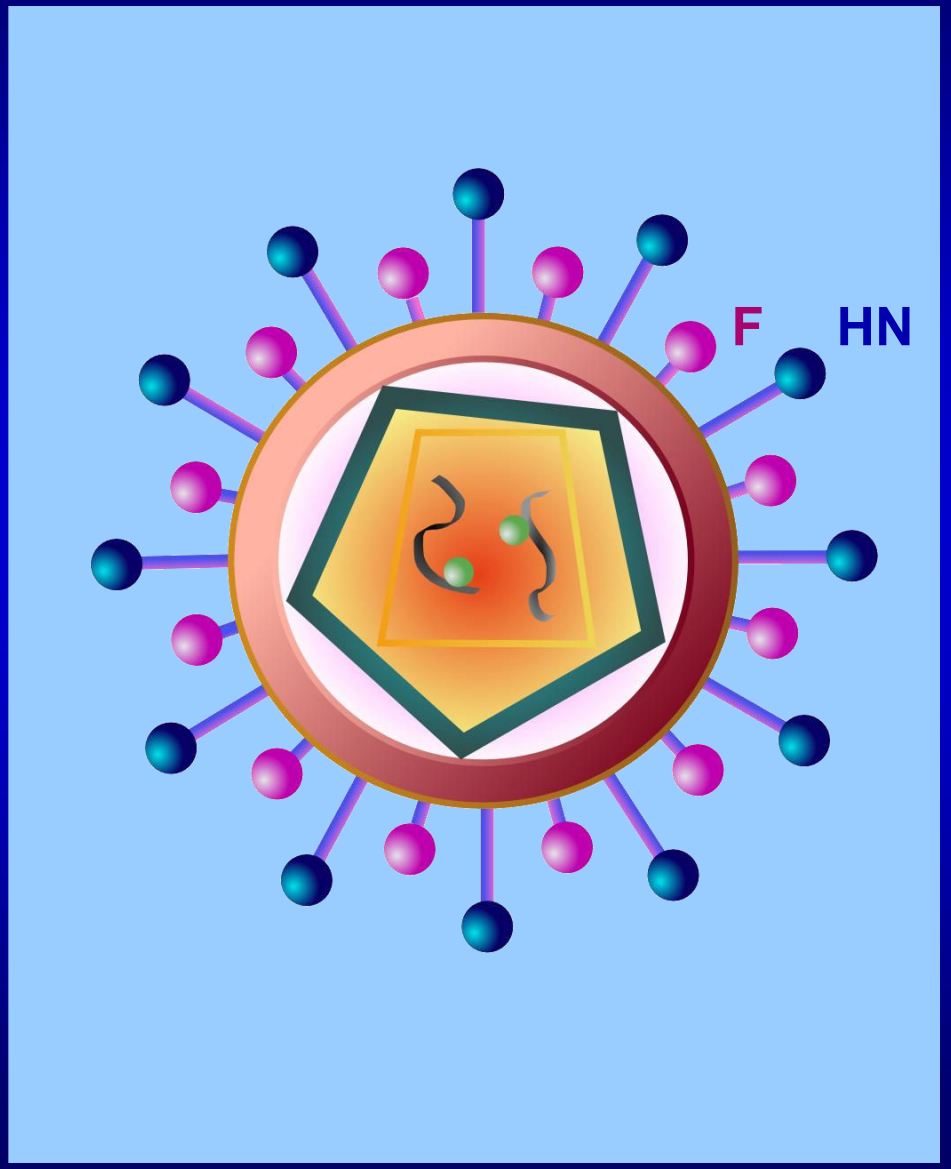


1-2 weeks: can’t repeat

F/HN pseudotyped lentivirus

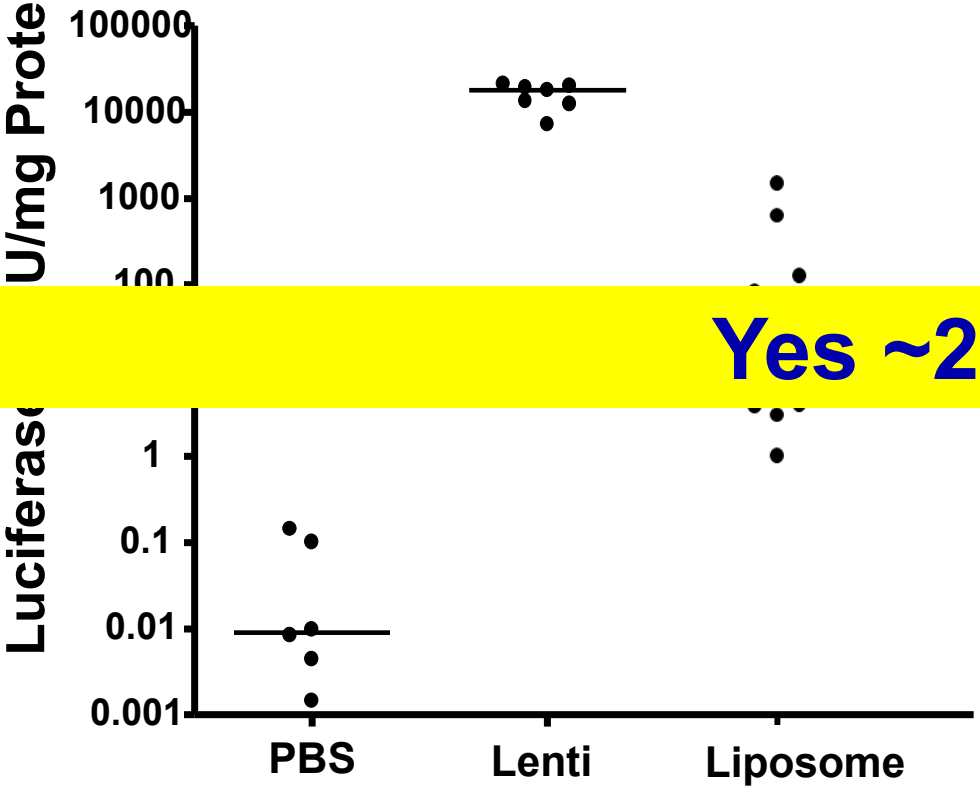




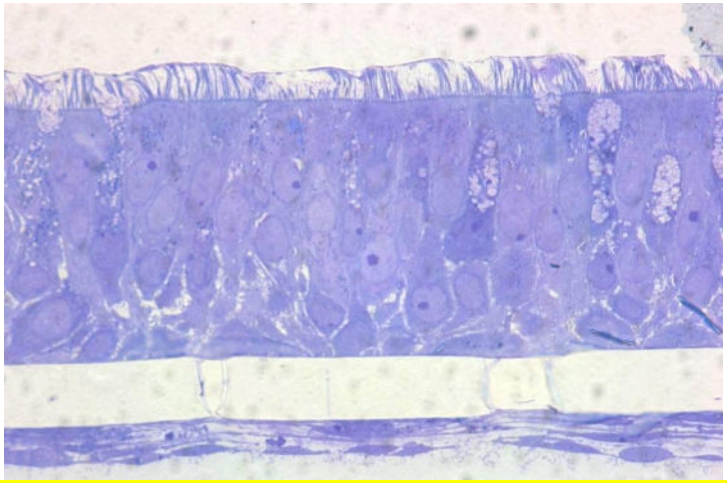


Is it better than Wave 1?

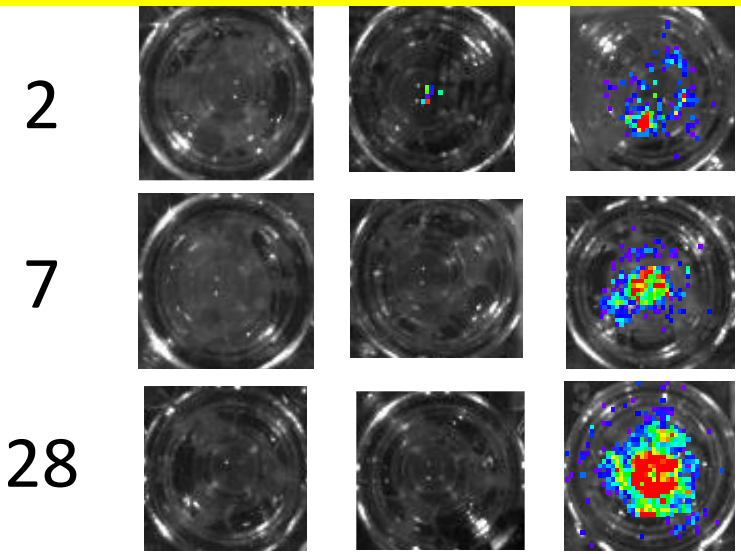
Mouse in vivo



Human ALI



Yes ~2 logs



Long duration expression

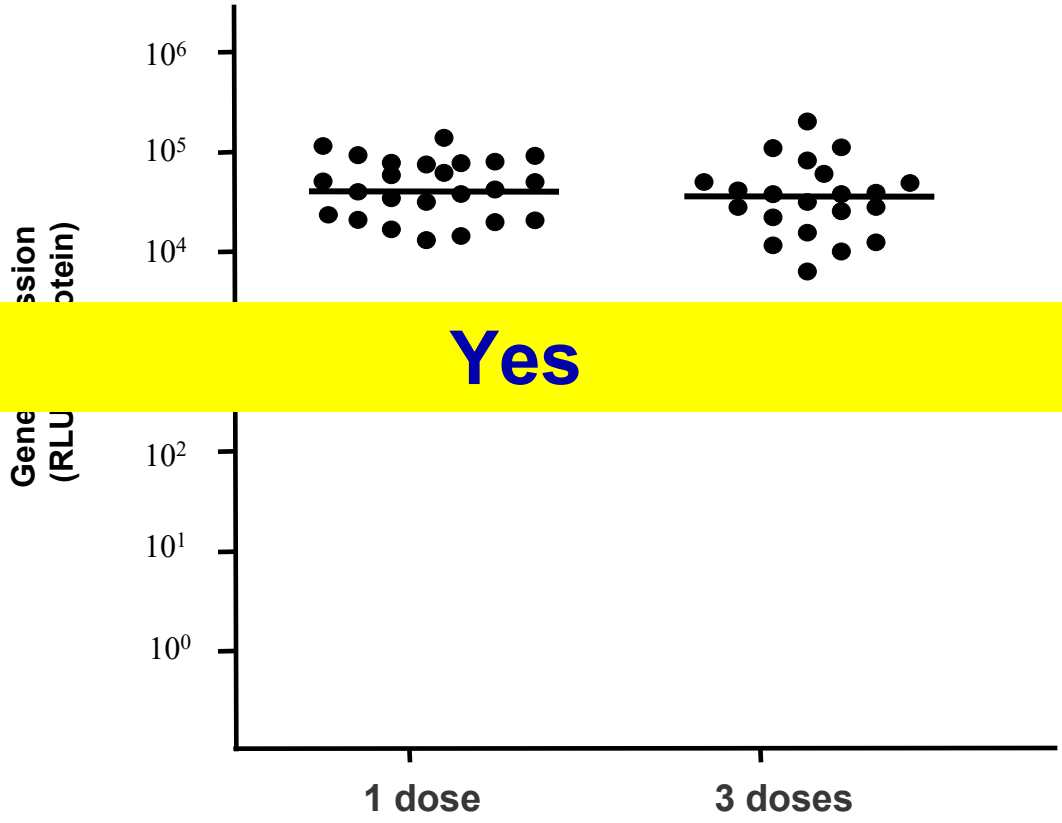
Likely still need repeat dosing

PBS

Lenti

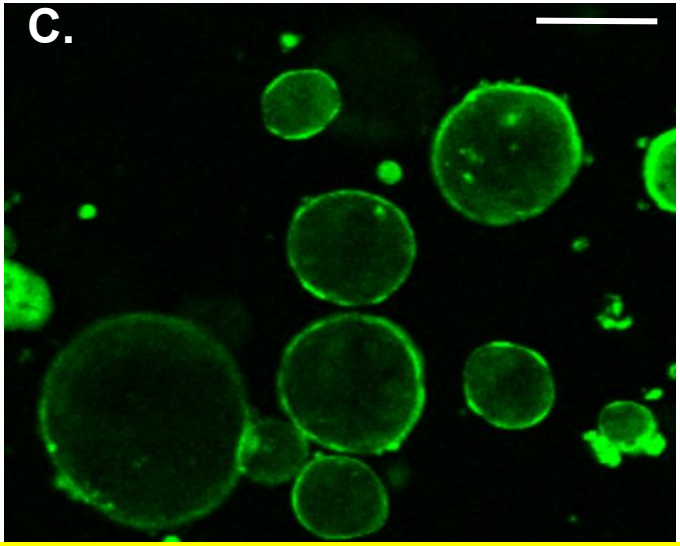
2 years

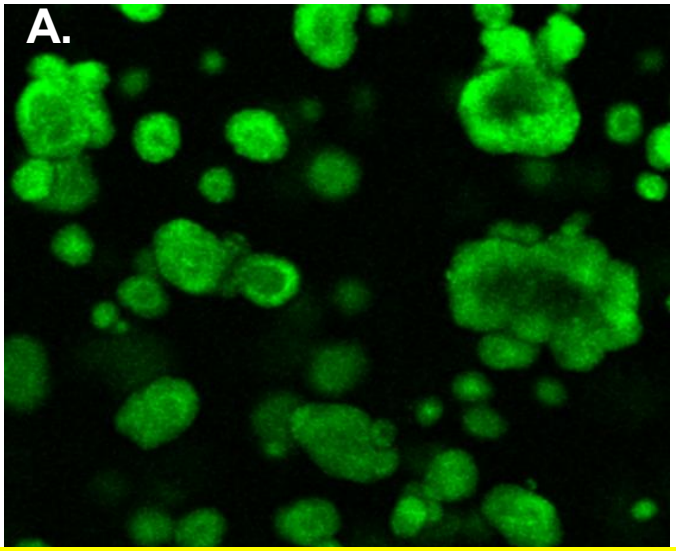
Expression feasible on repeated administration?



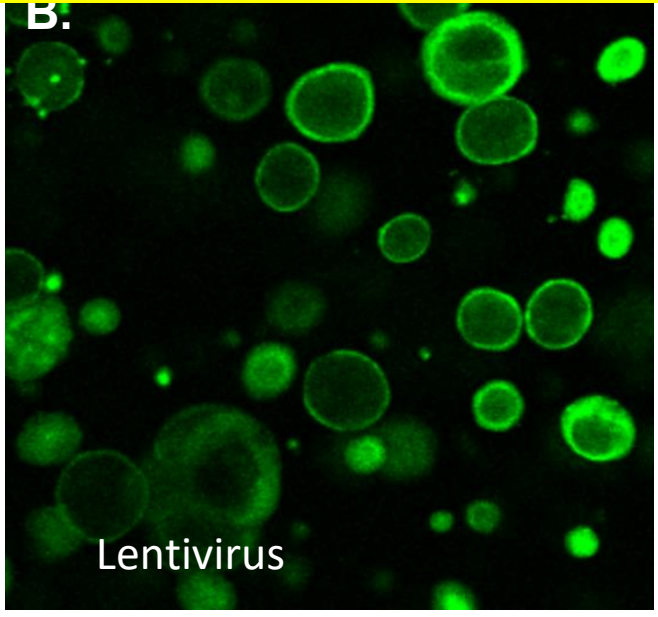
Yes

Produces functional CFTR



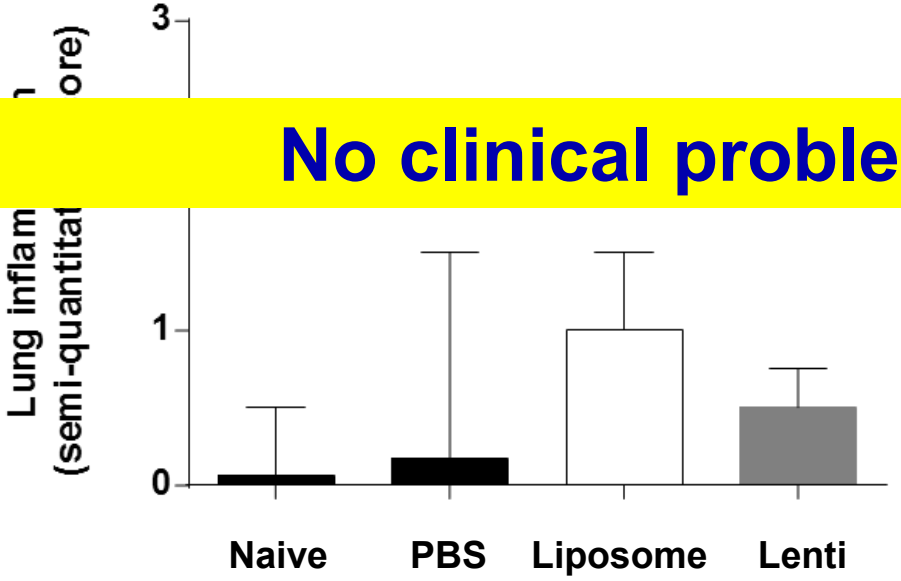


Yes

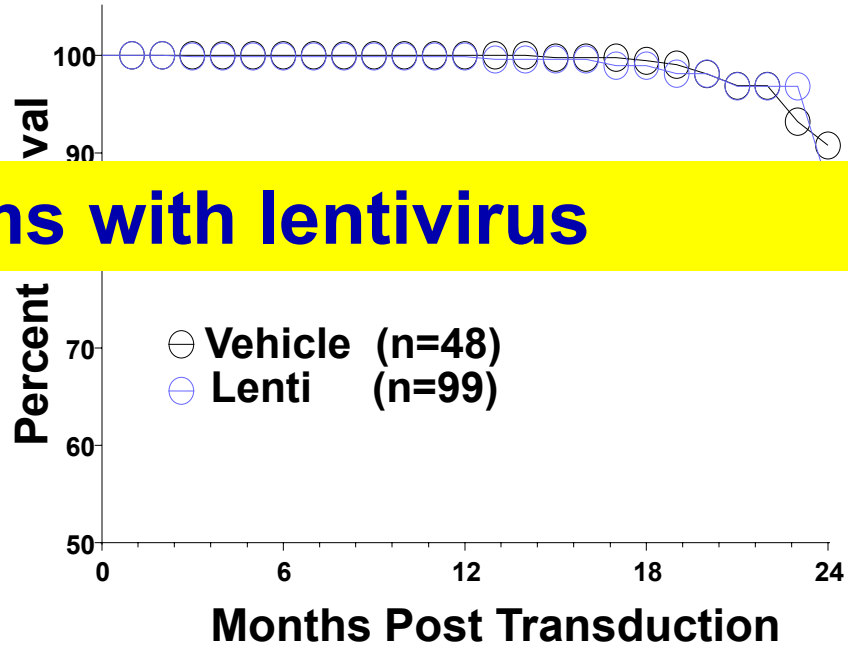


Toxicology

Acute



Chronic



No clinical problems with lentivirus

Next steps: Wave 2

: Defined pharmacopoeia-compliant product

: Academic first-in-man funded (Wellcome: £2.7M)

: Regulatory approved

: Tripartite agreement (Boehringer Ingleheim + Oxford BioMedica)

: Moving rapidly towards trial

Other applications

: Transduce lung

: Secreted proteins into lung/circulation

: Non-CF lung diseases or systemic conditions

: Genomics England

: Rare diseases

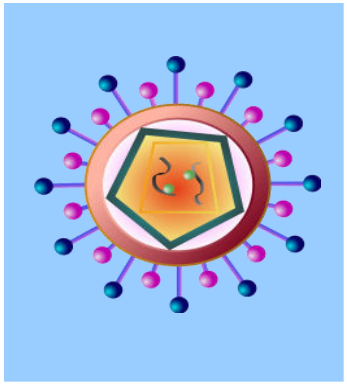
High efficiency vector opens up multiple new clinical targets for gene therapy

Rare genetic lung conditions

Surfactant protein deficiencies

α1-antitrypsin deficiency

Alveolar proteinosis



Systemic conditions

Haemophilias

Thrombotic thrombocytopaenic purpura

Commoner lung conditions

Idiopathic pulmonary fibrosis

COPD

Respiratory anti-viral targets (flu, RSV, COVID-19)

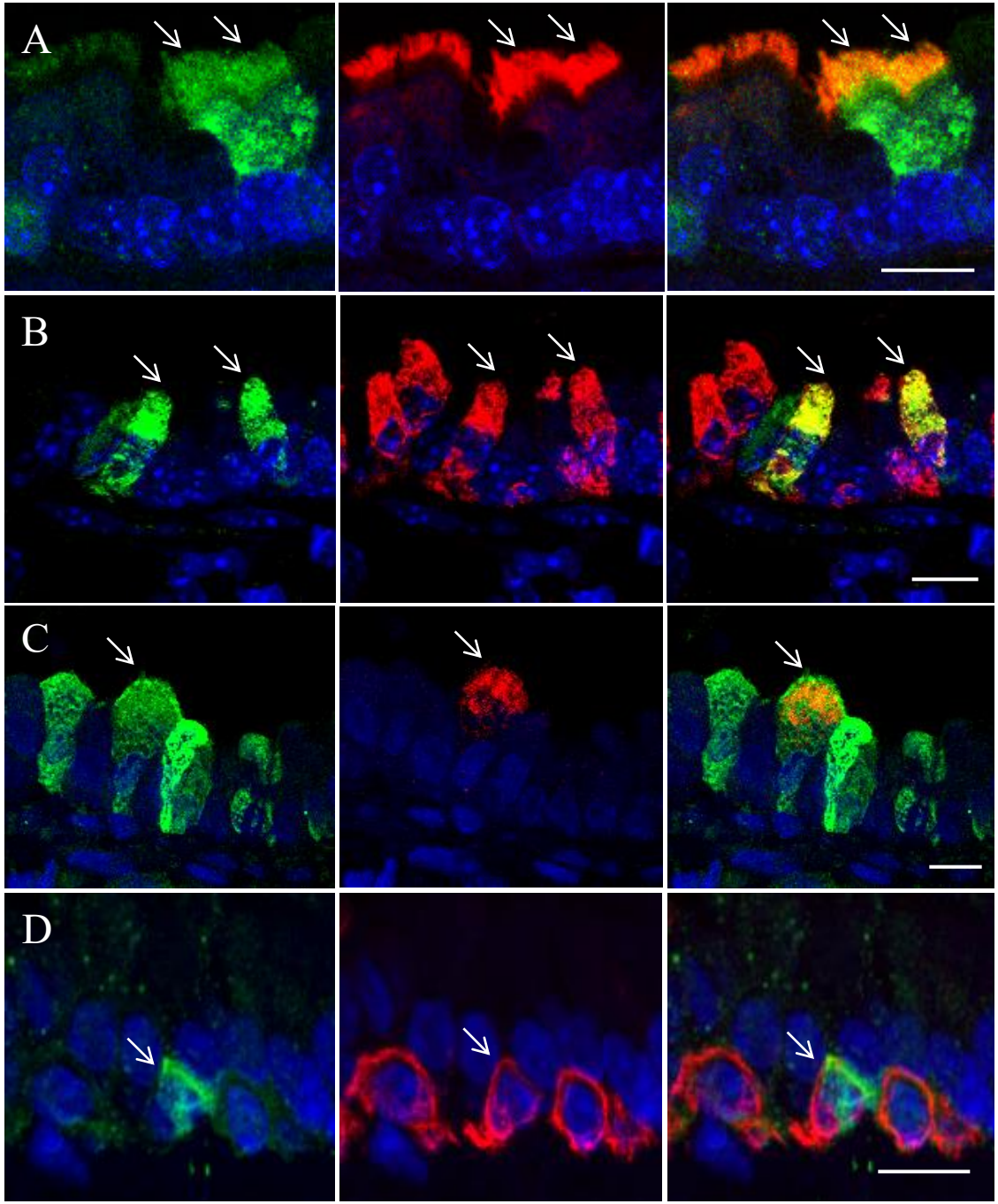
Wellcome Trust awarded £6.4M (2017-2022)

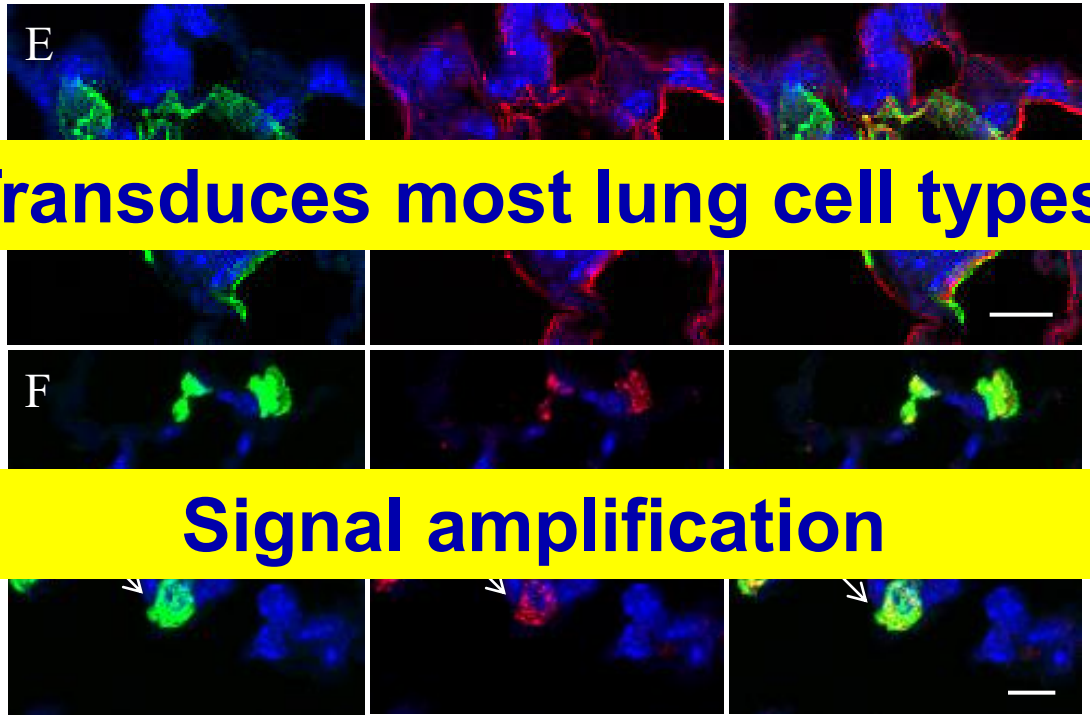
Ciliated

Club

Goblet

Basal

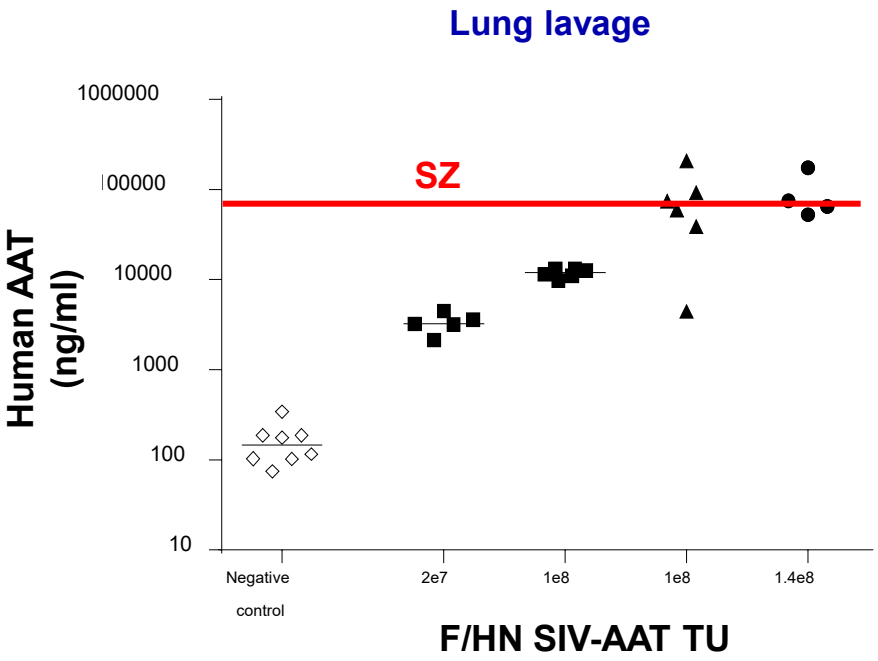


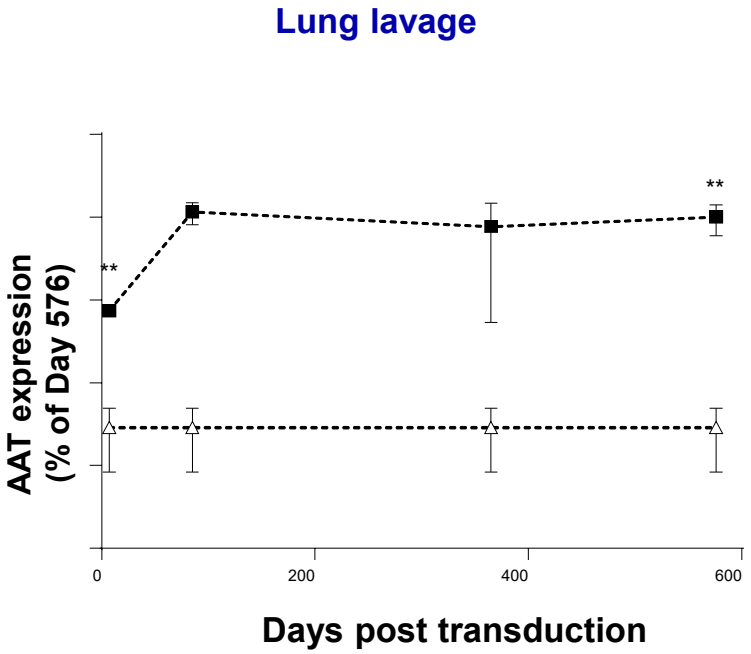


Transduces most lung cell types

Signal amplification

Treatment of α1-antitrypsin deficiency





GENE EDITING

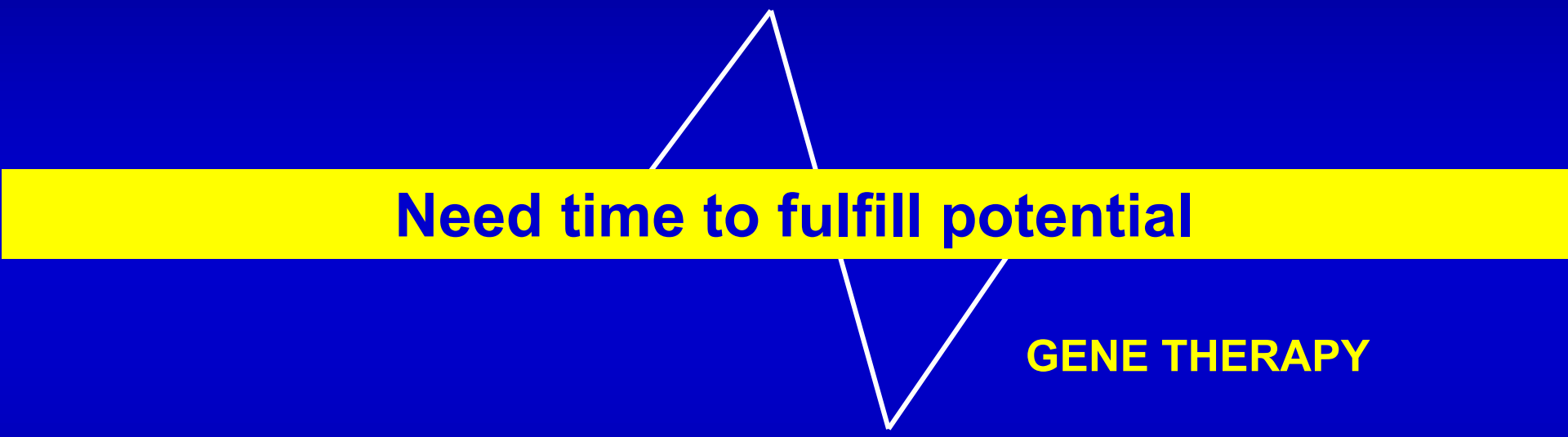
Cures all known diseases

Wouldn’t give it to my dog

GENE THERAPY

GENE EDITING

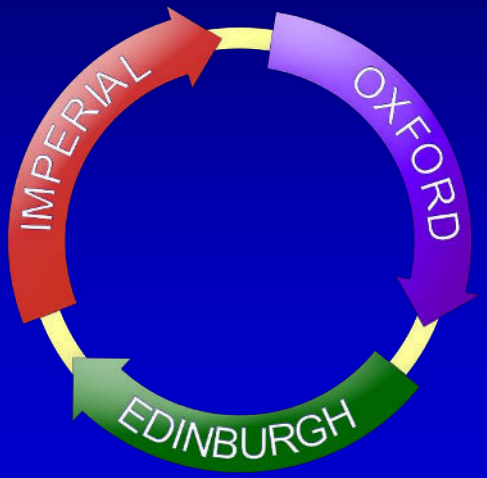
Cures all known diseases



GENE THERAPY

Wouldn’t give it to my dog

Thank you



wellcome trust

CYSTIC FIBROSIS TRUST

cfgenetherapy.org.uk

NHS
National Institute for Health Research

MRC Medical Research Council

Just Gene Therapy

Q&A

Advanced Therapy Treatment Centres

Please add any question you have into the Q&A box

Please fill in feedback survey, your input is really valuable to us

Next webinar,

Gene editing: scientific basis and clinical potential,

4pm 9th February, Kyriel Pinealt (Research Associate, Imperial College