Treatment of Genetic Disorders 2 Symposium

Thursday 11th April 2019

Lecture Theatre 2, Faculty of Medicine,
University of Southampton, Southampton General Hospital

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Welcome!

11th April 2019

Dear Delegates,

Welcome to the 2nd Treatment of Genetic Disorders Symposium (aka TGD2) here at the University of Southampton's Faculty of Medicine.

Since the first symposium in 2016, much has changed in the world of medical genetics and likewise in the world of genome-based therapeutics. The availability of genomic testing continues to expand, bringing with it not only the possibility of ever more genetic diagnoses for patients but also our own responsibility to use such testing appropriately, in the right setting and for the right clinical reasons.

With its docks, double tide and strategic sheltered position on the Solent, Southampton was once known as the "Gateway to the World". I very much hope that today's symposium, featuring talks from our stellar cast of invited speakers, will prove to be a gateway through which you yourselves will come to new ideas of how to treat genetic disorders. I am extremely grateful to all our invited speaker for taking the time to come and tell us about their state-of-the-art research and clinical work and I hope that they too will find the day stimulating and rewarding.

It just remains for me to thank our sponsors, without whom this free educational event would not be possible, and to wish you all an enjoyable and informative symposium.

Yours faithfully,

Dr Andrew Douglas
TGD2 Symposium Organiser

Symposium Programme:

0900-0930 **REGISTRATION & COFFEE**

0930-0945 **Welcome & Introduction**
Dr Andrew Douglas, University of Southampton

0945-1030 **Oligonucleotide therapies for DMD and SMA**
Dr Mariacristina Scoto, UCL

1030-1115 **Making gene and cell therapies happen in the UK**
Dr Kerstin Papenfuss, Cell and Gene Therapy Catapult

1115-1145 **COFFEE BREAK**

1145-1230 **Treatments for mitochondrial disorders**
Dr Victoria Nesbitt, Oxford Rare Mitochondrial Diseases Service

1230-1315 **Gene therapy for motor neurone disorders**
Prof. Dame Pamela Shaw, University of Sheffield

1315-1415 **LUNCH BREAK**

1415-1500 **Gene therapy for cystic fibrosis**
Prof. Uta Griesenbach, Imperial College London

1500-1545 **Ethical issues in gene and cell therapy**
Dr Rachel Horton, University of Southampton

1545-1600 **Closing remarks and discussion**
Dr Andrew Douglas, University of Southampton

1600 **CLOSE & TEA/COFFEE**

Speaker abstracts:

Welcome & Introduction
Dr Andrew Douglas, University of Southampton

Genetic disorders represent a particular challenge when it comes to therapeutics. To correct a genetic mutation in an individual at the DNA level remains technically difficult, despite great advances in gene editing technology in recent years. However, correction through targeted gene addition is achievable for certain conditions and is starting to enter clinical practice, as are therapies that utilise genetic correction of haematopoietic stem cells. RNA is another viable target for therapy of some genetic conditions, particularly with regards the therapeutic manipulation of splicing. The UK is a leading player in the field of novel therapeutics development and the coming years and decades will be pivotal in building research and development infrastructure to allow us to treat rare genetic diseases.

Oligonucleotide therapies for DMD and SMA
Dr Mariacristina Scoto, UCL

Making gene and cell therapies happen in the UK
Dr Kerstin Papenfuss, Cell and Gene Therapy Catapult

The Cell and Gene Therapy Catapult is a non-for-profit organization that has been tasked with developing the UK cell and gene therapy industry. The CGTC was established in 2012 as an independent centre of excellence to advance the growth of the UK cell and gene therapy industry, by bridging the gap between scientific research and full-scale commercialization. Supported by Innovate UK, CGTC's mission is to drive the growth of the industry by helping cell and gene therapy organizations across the world translate early stage research into commercially viable and investable therapies. With more than 180 employees focusing on cell and gene therapy technologies, CGTC offers leading-edge capability, technology and innovation to enable companies to take products into clinical trials and provide clinical, process development, manufacturing, regulatory, health economics and market access expertise. Led by a rigorous market-need based approach CGTC identifies barriers to the growth of the cell and gene therapy sectors and then develops and exploits capabilities to address those barriers.

Treatments for mitochondrial disorders
Dr Victoria Nesbitt, Oxford Rare Mitochondrial Diseases Service

Gene therapy for motor neurone disorders
Prof. Dame Pamela Shaw, University of Sheffield

Update on CF gene therapy
Prof. Uta Griesenbach, National Heart and Lung Institute, Imperial College London

Although a large number of cystic fibrosis (CF) gene therapy trials have been carried out over the last two decades, these have not addressed whether gene transfer to the lungs can ameliorate CF lung disease. The UK CF Gene Therapy Consortium has developed a programme of both non-viral and lentivirus-mediated gene therapy. Efficacy of the non-viral formulation pGM169/GL67A has been assessed in a double-blind, placebo-controlled multi-dose Phase IIb trial in which subjects received 12 doses of pGM169/GL67A or placebo at monthly intervals. The trial met its primary endpoint and showed, for the first time, that non-viral gene transfer can stabilise CF lung disease. However, the response was comparatively modest and further improvements in gene transfer efficiency are required. To achieve this we have developed a novel lentiviral vector (rSIV/F/HN) which leads to efficient (log orders better than pGM169/GL67A) and long lasting expression (~ 2 years) in mice after a single dose. We have recently partnered with Boehringer-Ingelheim and Oxford BioMedica to progress towards a first-in-man lentivirus trial in CF.

Ethical issues in gene and cell therapy

Dr Rachel Horton, University of Southampton

Emerging therapies for previously untreatable genetic disorders are one of the most exciting advances in genomic medicine, but in practice, meaningful treatment remains elusive for many patients and families.

I plan to discuss ethical issues arising in the treatment of genetic disorders, including:

- Consent in the context of experimental treatments – how can we facilitate genuine choice?
- Financial inaccessibility and resource implications – how can we ensure that expensive therapies are made available to people who might benefit?
- Changing options around the care of seriously ill children – navigating new questions in the care of children where previous care focus would have been palliative
- Knowing what we are treating – will unknown penetrance be a future challenge to treatment decisions?

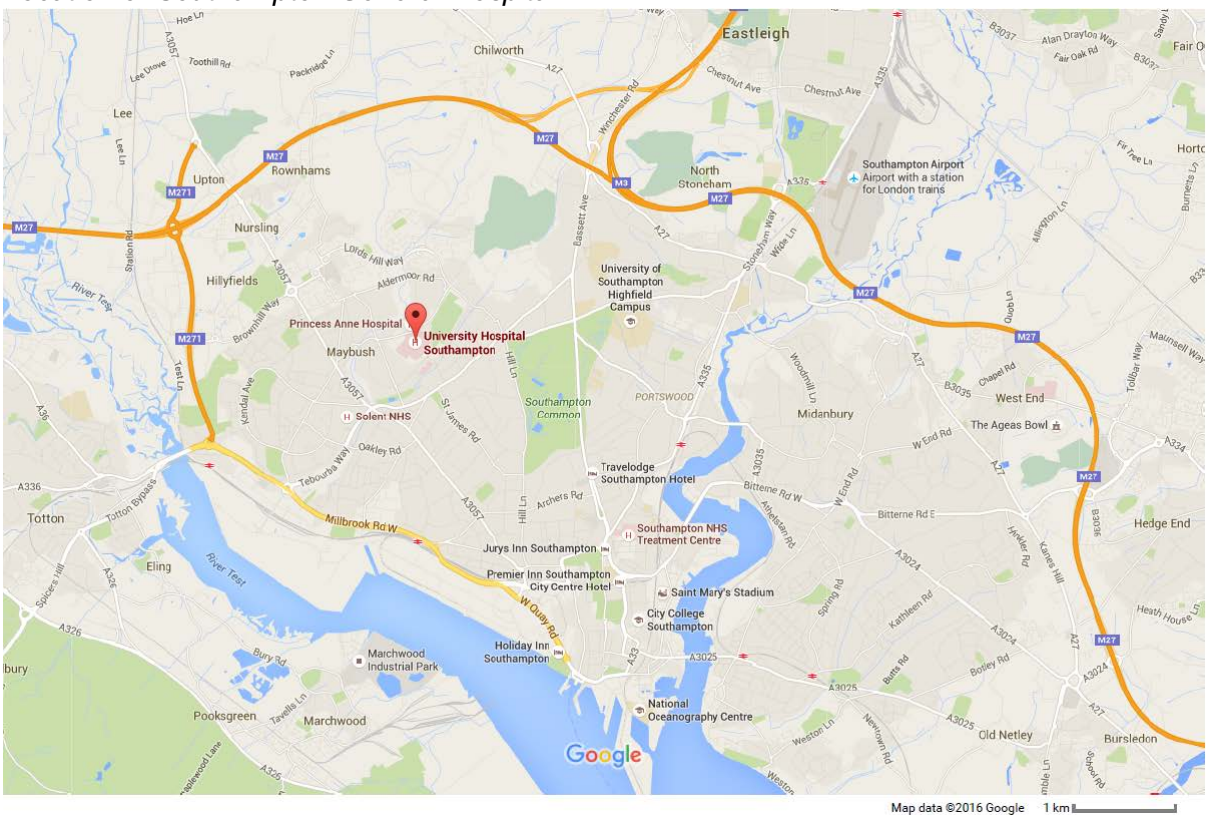
My talk outlines the need for a broader conversation about how we can anticipate and respond to ethical issues when developing treatments for genetic disorders.

Closing remarks and discussion

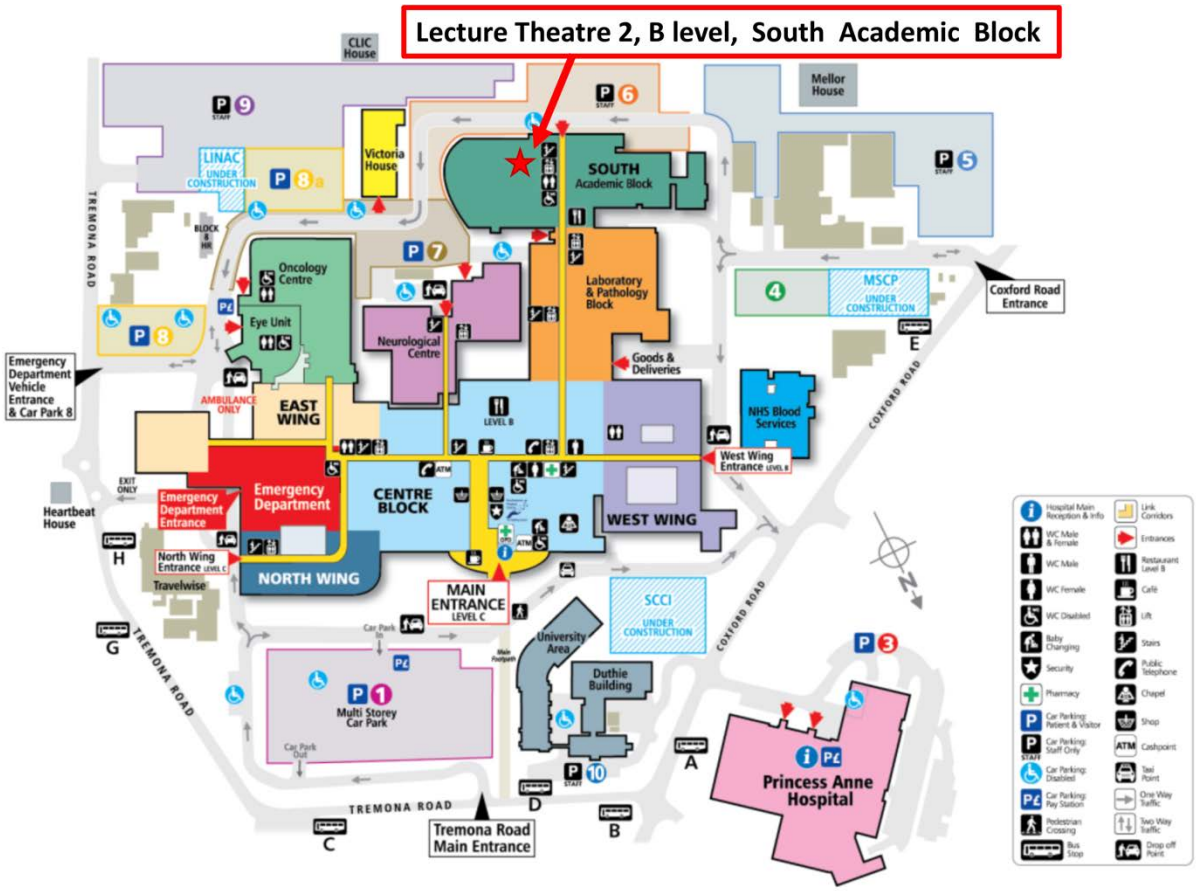
Dr Andrew Douglas, University of Southampton

A summary of the day with opportunities for discussion and thoughts about the future of genomics, genome-based therapeutics and the treatment of genetic disorders.

Location of Southampton General Hospital:



Location of Lecture Theatre 2:



Evaluation Form

Treatment of Genetic Disorders 2 Symposium

11th April 2019
University of Southampton

PLEASE TICK BOXES

1. How useful did you find this event?

Extremely useful	Useful	Fairly useful	Not useful
[ ]	[ ]	[ ]	[ ]

If this symposium was not useful, please explain why…

2. What was your overall impression of this event?

	Excellent	Good	Fair	Poor	Very Poor
Programme	[ ]	[ ]	[ ]	[ ]	[ ]
Organisation	[ ]	[ ]	[ ]	[ ]	[ ]

3. How useful to you personally was each session?

	Very useful	Useful	Fairly useful	Not useful	Not directly relevant but of interest
Andrew Douglas **Introduction**	[ ]	[ ]	[ ]	[ ]	[ ]
Mariacristina Scoto **Oligo therapies for DMD/SMA**	[ ]	[ ]	[ ]	[ ]	[ ]
Kerstin Papenfuss **Cell and Gene Therapy Catapult**	[ ]	[ ]	[ ]	[ ]	[ ]
Victoria Nesbitt **Mitochondrial disorders**	[ ]	[ ]	[ ]	[ ]	[ ]
Pamela Shaw **Motor neurone disorders**	[ ]	[ ]	[ ]	[ ]	[ ]
Uta Griesenbach **CF gene therapy**	[ ]	[ ]	[ ]	[ ]	[ ]
Rachel Horton **Ethical issues**	[ ]	[ ]	[ ]	[ ]	[ ]
Closing discussion	[ ]	[ ]	[ ]	[ ]	[ ]

4. What was the best aspect of this event?

5. What was the worst aspect of this event?

6. What impact will this event have on your future practice?

7. To what extent did the presenters provide a balanced (evidence-based where possible) view of the topic?

8. Were there any examples of bias in this activity?

9. Please write down any additional comments or suggestions:

THANK YOU!