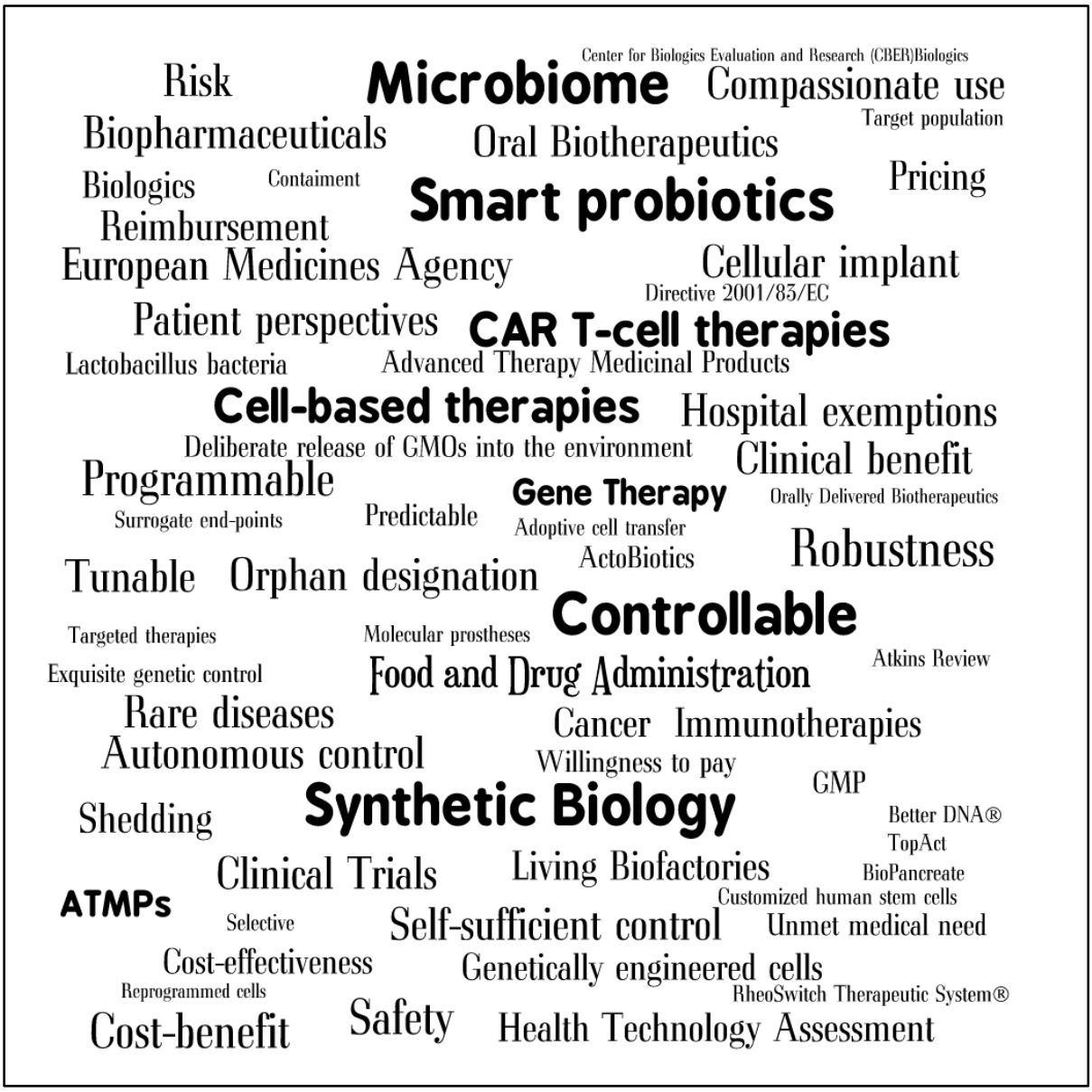
Workshop on the prospects for controllable cell-based therapies

22-23 February 2016

Starts 9:00 on Monday 22nd February, ends 13:00 on Tuesday 23rd February

at City University London

Room AG01, College Building, St John Street, London EC1V 4PB, UK



Imperial College London

CITY UNIVERSITY LONDON

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EPSRC Engineering and Physical Sciences Research Council

Workshop on the prospects for controllable cell-based therapies

Organised by

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This workshop will bring together diverse stakeholders to discuss the prospects for an emerging category of medical applications of synthetic biology that we are calling 'controllable cell-based therapies' (CCBTs) including:

- scientists conducting cutting-edge research to enable CCBTs
- firms seeking to commercialise CCBTs
- staff from agencies involved in the regulation of CCBTs
- independent experts on regulatory frameworks and translation for CCBTs
- staff from patient advocacy groups with expertise in medical innovation and regulation
- social scientists with expertise in medical innovation and regulation

The workshop will provide a unique opportunity for people from these diverse groups to engage with each other in order to identify potential opportunities and challenges for this novel set of medical applications. Questions that will be addressed at the workshop include:

- What is the current scientific, economic and regulatory landscape for CCBTs?
- How do CCBTs compare to alternative approaches to health and medicine?
- How can we ensure that these new therapies reach the clinic and provide actual benefits to patients without generating unreasonable risks?
- What implications might the use of bacterial (as opposed to human) cells have in terms of safety, regulatory frameworks and other challenges for translation to the clinic?

This workshop seeks to encourage interactive discussions among people with different expertise and interests. Emphasis will be given to group discussion, focused around case-studies. A small number of short presentations from experts from different disciplines will help set the scene and provide participants with basic information about: current cutting-edge science, ongoing commercial developments, regulatory frameworks, Health Technology Assessment, patient perspectives and consumer perspectives. The total number of participants will be relatively small (about 25) in order to facilitate constructive discussions. The Chatham House rule will apply whereby "participants are free to use the information received, but neither the identity nor the affiliation of the speaker(s), nor that of any other participant, may be revealed."

The discussions will be audio-taped and transcribed for research purposes. The audio-recording and the transcripts will only be accessible to the research team. They will be used to help in the production of a report summarising the discussion that will be published online. All participants will be provided with an opportunity to comment on a draft of this report before publication. Further publications may also be produced, including articles in academic journals.

What are controllable cell-based therapies?

Cell-based therapies are therapies in which cells are administered to the body to diagnose, prevent or cure diseases. They have been developed over the last two decades and a number are now used at least experimentally for the treatment of cancers and genetic disorders. Advances in scientific research and in particular in the emerging field of synthetic biology will potentially enable cell-based therapies that involve **controlling** the behaviour of cells in more complex, robust and predictable ways. This is particularly important because cell therapies work **within a patient's body**. The general idea is that genes in the swallowed, injected or implanted engineered cells would be switched on and off in response to specific signals that would instruct the cells to perform a programmed therapeutic function at a particular point in time and/or a particular location in a patient's body. This could be the release of a therapeutic compound, the release of a compound to destroy cancer cells or infectious pathogens, or the restoration and maintenance to a desired level of a molecule in the body. More sophisticated forms of control might modulate the amount of therapeutic molecule delivered over time in response to signals from the body, to ensure that the patient receives precisely the dose they need at any given time. We call this **'closed-loop' control**. Control mechanisms could also be designed to increase safety, enabling the engineered function to be switched off or causing the cells to self-destruct in the event of an unintended negative effect. Academic research centres in the USA, Europe and elsewhere are conducting research in this area and some firms are aiming to commercialise CCBTs. Most cell-based therapies that have so far been subjected to clinical trials employ **human cells** (although these do not yet incorporate sophisticated forms of control), but many of the cell-based therapies now being envisaged by synthetic biologists would employ **bacterial cells**.

This workshop will focus on bacterial (as opposed to human) cell-based therapies and will investigate whether and how more sophisticated 'closed-loop' forms of engineered control might be useful to deliver commercially viable medicinal products that deliver real benefits to patients.

Case-Studies

Discussion will be prompted through the exploration of a small number of case-studies.

Smart Probiotics for the treatment of Phenylketonuria (PKU)

So-called 'smart probiotics' would be orally administered, genetically engineered, strains of 'commensal' bacteria (bacteria that are present in the human gastrointestinal and respiratory tract, vagina, skin and constitute the 'microbiome'), designed to deliver therapeutic compounds. One product under commercial development seeks to treat the metabolic disorder Phenylketonuria (PKU). More speculative ideas for 'smart probiotics' include using engineered bacteria to treat obesity, psychiatric disorders (e.g. schizophrenia) or to alter mood and behaviour.

Reprogramming microbes to combat pathogens

Researchers have been attempting to genetically engineer microbes to combat viral and bacterial infections. The 'reprogrammed' bacteria would seek out and kill the pathogenic organisms. They could be used as a prophylactic medicine or to treat infections.

Engineering bacteria to target tumours

Engineered bacteria are being developed to detect cancer cells inside a person's body. This could be for diagnosis purposes: when the engineered bacteria detect a cancerous cell, they would produce a signal, for example in the person's urine. Engineered bacteria could also potentially be used to detect and destroy specific cancer cells.

Other 'oral biopharmaceuticals'

Smart probiotics use commensal bacteria (strains that are already part of our microbiome). Other 'oral biopharmaceuticals' under development use Lactococcus lactis, a species of bacteria that has been widely used for industrial production of fermented dairy products such as milk, cheese and yogurt. One product under commercial development seeks to treat Inflammatory Bowel Disease, while another is an oral rinsing solution for the treatment of oral mucositis, a negative side effect of chemotherapy treatments of cancers of the head and neck.

List of participants

Organisers

Jordan Ang	CSynBI, Department of Bioengineering, Imperial College London
Claire Marris	Sociology Department, City University London
Karen Polizzi	CSynBI, Department of Life Sciences, Imperial College London
Guy-Bart Stan	CSynBI, Department of Bioengineering, Imperial College London

Confirmed Participants

Jacqueline Barry	Cell and Gene Therapy Catapult, Head of Regulatory
Christopher Bravery	Consulting on Advanced Biologicals
Martin Cannell	UK Department for Environment, Food and Rural Affairs, secretariat for the UK's Advisory Committee on Releases to the Environment (ACRE)
Patrick Celis	European Medicine Authority (EMA), secretariat for the Committee for Advanced Therapies (CAT)
Matthew Chang	Synthetic Biology for Clinical and Technological Innovation Program (SynCTI), National University of Singapore
Courtney Davies	Department of Social Science, Health and Medicine, King's College London
Mariette Driessens	European Genetic Alliances Network and member CAT committee
Tom Ellis	Centre for Synthetic biology and Innovation, Imperial College London
Luis Angel Fernandez	Spanish National Biotechnology Centre
Neil Forbes	Department of Chemical Engineering, University of Massachusetts at Amherst
John Heap	Centre for Synthetic biology and Innovation, Imperial College London
Stuart Hogarth	Department of Social Science, Health and Medicine, King's College London
Jesper Jorgensen	Cell and Gene Therapy Catapult, Head of Health Economics
Eric Lange	(UK) National Society for Phenylketonuria (PKU)
Timothy Lu	Synthetic Biology Center, MIT
Pete Lund	School of Biosciences, Birmingham University, member of ACRE (Advisory Committee on Release to the Environment) and SACGM (Scientific Advisory Committee on Genetic Modification)
Tim Reed	Health Action International (Europe)
Paula Salmikangas	Finnish Medicines Agency and Chair of CAT committee
Alison Silva	Synlogic
Richard Stephens	(UK) National Cancer Research Institute Consumer Forum
Hazel Thornton	Independent Citizen Advocate for Quality in Research and Healthcare

Workshop Schedule

DAY 1: Monday 22nd February

8:30 - 9:00 Arrival (coffee, tea fruit juice, pastries and fruit provided)

9:00 - 9:10 Claire Marris - Introduction to the workshop

Session 1: Smart Probiotics for the treatment of Phenylketonuria (PKU)

9:10 - 9:30 Eric Lange: Patient/carer perspectives on PKU

9:30 - 9:50 Alison Silva: Synlogic's pipeline for therapeutics for the treatment of PKU

9:50 - 10:30 Group discussions on smart probiotics for the treatment of PKU

10:30 - 10:50 **Coffee break**

10:50 - 11:10 Feedback from group discussions on synthetic biotic therapeutics for the treatment of PKU

Session 2: Reprogramming microbes to combat pathogens

11:10 - 11:30 Matthew Chang: Reprogramming microbes to combat pathogens

11:30 - 12:10 Group discussions on reprogramming microbes to combat pathogens

12:10 - 12:30 Feedback from group discussions on reprogramming microbes to combat pathogens

12:30 - 14:00 Lunch Break

Session 3: Engineering bacteria to target tumours

14:00 - 14:20 Richard Stephens: Patient perspectives on cancer treatments

14:20 - 14:40 Neil Forbes: Engineering bacteria to target tumours

14:40 - 15:20 Group discussions on engineering bacteria to target tumours

15:20 - 15:40 Feedback from group discussions on engineering bacteria to target tumours

15:40 - 16:00 **Coffee break**

Session 4: Safety regulations

16:00 -16:15 Patrick Celis: The European Union Regulatory framework for Advanced Therapy Medicinal Products (ATMPs)

16:15 - 16:25 Q&A

16:25- 16:40 Christopher Bravery: Regulatory challenges & opportunities

16:40-16:50 Q&A

Session 5: Other examples of bacterial cell-based therapies

16:50 - 17:05 Luis-Angel Fernandez: Overview on the use of engineered bacteria as therapeutic agents

17:05 - 17:15 Q&A

17:15 - 17:30 Tim Lu: 'Closed-loop control' for bacterial cell-based therapies

17:30 - 17:40 Q&A

Session 5: Emerging themes

17:40 – 18:00 General discussion on emerging themes and issues

19:00 - Dinner (all participants invited) at: The Duke of Cambridge Organic Pub
30 St Peters Street, Islington, London N1 8JT
http://dukeorganic.co.uk/

DAY 2: Tuesday 23rd February

Session 6: How to realise benefits for patients, firms and wider society?

9:00 – 9:15 Tim Reed: Consumer advocacy for public health
9:15 – 9:25 Q&A
9:25 – 9:40 Jesper Jorgensen: Health technology assessment and commercialisation
9:40 – 9:50 Q&A
9:50 – 10:00 Jacqueline Barry: Translational challenges & opportunities
10:00 – 10:10 Q&A

Session 7: Moving forward - Advantages and challenges of 'closed-loop control' for cell-based therapies

How useful might bacterial cell-based therapies that involve the 'closed-loop' forms of engineered control be? For what purposes?

How could they be translated into commercially viable medical products that deliver real benefits to patients?

10:10 – 10:25 Guy-Bart Stan: Introduction to final session
10:25 – 10:45 **Coffee break**
10:45 – 12:45 General discussion framed around questions and issues identified
12:45 – 13:00 Wrap up and next steps

13:00 – Lunch and departure

How to get to City University by public transport

College Building, St John Street, London EC1V 4PB

Closest tube/train stations:

Aldgate (Northern Line), 15 mins walk

Farringdon (Circle/Metropolitan lines and National Rail), 15 mins walk

King's Cross & St Pancras International stations, 25 minutes walk

Hotel

We have booked rooms at this local hotel for participants from outside London:

DoubleTree by Hilton Hotel London - Islington

60 Pentonville Road, London, N1 9LA, United Kingdom

Tel: +44 (0)20 7282 5500

http://doubletree3.hilton.com/en/hotels/united-kingdom/doubletree-by-hilton-hotel-london-islington-LONLIDI/index.html

DoubleTree Hilton Hotel