

Discussion Workshop: STEM CELLS

The Penridge Suite, 470 Bowes Road, London, N11 1NL, United Kingdom: **6th May 2011**

This event is discussion workshop, focused on the rapidly moving area of pluripotent cells. The aim is to bring together scientists to discuss important areas of work in this field with specific emphasis on practical technology. It offers participants a chance to explore aspects of the biology with the experts during round table and one-to one discussions.

Meeting Chair: **Dr Glyn Stacey**, UK Stem Cell Bank, Division of Cell Biology and Imaging.

This event has CPD accreditation

On registration please submit your questions to the panel that will be asked by the chair on the day of the event

9:00 – 9:30

Registration

9:30 – 9:35

Introduction by Meeting Secretariat

9:30 – 9:45

Introduction by the Chair: Dr Glyn Stacey, UK Stem Cell Bank, Division of Cell Biology and Imaging

Talks by Invited Experts:

9:45 – 10:05

Cardiomyocytes from Human Pluripotent Stem Cells

Dr Chris Denning

*Associate Professor & Reader in Stem Cell Biology
University of Nottingham, UK*

The ability to maintain human pluripotent stem cells (hPSCs) for extended periods of time in culture and yet induce their differentiation to a wide range of cell types offers new opportunities in biomedicine. We will discuss our progress in producing human induced pluripotent stem cells from patients with genetic heart disease and our efforts to model disease using in vitro derived hPSC-cardiomyocytes, including in drug evaluation. We will also consider issues of scale up and defined culture / differentiation.

10:05 – 10:25

Differentiation of hESC/iPSC into Cardiomyocytes

Dr Nadire Ali

*Senior Research Fellow
NHLL, Imperial College London, UK*

ES cells (ESC) and iPSC are potentially good sources of cardiomyocytes. These cells and their derivatives can be used in several applications including as model systems, as a test bed for drug toxicity assays, screening for therapeutic targets, functional genomics studies and in future cell therapies. However, there are several hurdles which need to be overcome. These relate to pluripotent stem cells themselves, the methods of generating cardiomyocytes, and some aspects of the derived cardiac cells themselves. I will discuss these challenges, giving examples from our work and of others.

10:25 – 10:45

Characterisation of Human Pluripotent Stem Cells

Dr Paul Gokhale

*Research Associate
Centre for Stem Cell Biology Sheffield, UK*

Characterisation of pluripotent stem cells is critical if reliable cell lines are to be created for drug screening and therapeutic uses. This talk will describe the characterisation of human embryonic stem cells that has been carried out by the International Stem Cells Initiative at the level of gene expression, imprinting, methylation, karyotype and copy number variation. Attention will be drawn to key properties that mark bona fide human ES cells

10:45 – 11:15

Mid-morning Break

11:15 – 11:35

Principles of Cryopreservation

Dr Charlie Hunt

*Operations Manager
UK Stem Cell Bank, National Institute for Biological Standards and Control*

An essential pre-requisite to the commercial and clinical application of stem cells are suitable and effective protocols for cryopreservation and long-term storage. Whilst effective methods for cryopreservation have been developed for haematopoietic and mesenchymal stem cells, embryonic and iPSC cells have proved more refractory. Effective cryopreservation requires an understanding of the basic physical principles that underly the freeze/thaw process and the cells response to the imposition of such a process. Basic principles and their application to stem cells will be discussed.

- 11:35 – 11:55 **Of Mice (Rats) and Men - How Stem Cell Identities and Culture Systems have Evolved.**
Dr Paul Bello
*Head of Stem Cells & Media Systems; Director of Technology Transfer
 Stem Cell Sciences (UK)*
 Recent publications have opened the door to a real possibility that human ES and iPS cells can be derived or re-programmed into the equivalent counterparts of true mouse pluripotent stem cells rather than what some researchers regard as 'primed' or more mature. Strikingly, the stem cell culture media conditions for this naive, 'ground state' is becoming increasingly defined and reliant on discrete, potent kinase inhibitors rather than growth factors. Indeed, there is now a distinct possibility that all mammalian pluripotent stem cells with germ line competency are attainable in inhibitor-based media.
- 11:55 – 12:15 **The Evolution of iPS Technologies and Epigenetic Patterns Governing iPS Cell Fate**
Dr. Rachel Craddock
*Stem and Specialty Cell Culture Specialist
 Merck Millipore*
 In 2006, Takahashi and Yamanaka published their seminal work in Cell, demonstrating four factors could be used to induce pluripotency in mouse fibroblasts. The potential for induced pluripotent stem (iPS) cells in research and therapy was seemingly limitless; a renewable resource for studying complex mechanisms of pluripotency and differentiation and perhaps more strikingly, the beginnings of a therapeutic solution to transplant rejection by using autologous tissue, reprogrammed to regenerate diseased tissue.
 Five years later, an overwhelming amount of work has been published using this evolving technology, which strives to produce ever more faithful pluripotent cells from somatic tissue by reducing viral gene integration sites, or by use of proteins, small molecules and most recently miRNA to substitute reprogramming genes.
 The underlying challenge is to generate iPS lines as faithful to physiological ES cells as possible. Currently, differences between iPS and ES are identified through comparison of transcriptomes, proteomes and methylomes as well as phenotypic surface and intracellular marker expression. Discussion has recently emerged as to whether differentiated iPS cells can reach the same functional maturity as physiological cells and epigenetic patterns have been implicated in developmental issues.
 This session is intended to open discussion into improvement of iPS models and how we can achieve functionally mature cells through differentiation of iPS cells.
- 12: 15 **Working Lunch**
 Please collect your lunch and take it to your discussion table (session 1)
- 12:30 – 13:45 **Discussion Groups (Sessions 1, 2, 3 & 4)**
- Round table discussion groups (15 minutes each) will be held throughout the afternoon
 - Delegates will rotate so that they may participate in all the discussion tables
 - All delegates will also be allocated a session for visiting the exhibition stands
 - Where appropriate delegates will be able to bring their samples to the discussions
 - See end of agenda for description of discussion tables
- 13:45 – 14:05 **Talk TBC**
Mr Julian Hitchcock
Life Science lawyer
- 14:05– 14:25 **Practical Problems in the Production of iPS Lines and their Selection**
Dr Ludovic Vallier
*MRC Senior Non-Clinical Fellow
 Cambridge University, UK*
 Human pluripotent stem cells derived from reprogrammed somatic cells by overexpression of pluripotency factors (human Induced Pluripotent Stem Cells or hiPSCs) offer unmatched prospect for autologous cell based therapy and disease modelling in vitro. Indeed, they can be generated using cells obtained from patients with specific disease and then used to develop in vitro models allowing large scale studies impossible with primary cell cultures or with biopsy material. Here, we will discuss the practical aspects and challenges associated with hiPSCs derivation using the experience accumulated through the derivation of 300 hiPSC lines from 50 patients
- 14:25 – 15:40 **Discussion Groups (Sessions 5, 6, 7 and 8)**

15:40 – 16:00 **Stem Cell Growth, Adhesion and Differentiation**

Dr Erik Miljan

*Product Specialist, Stem Cells and Regenerative Medicine
AMS Biotechnology, UK*

Stem cells are unspecialized cells that are capable of dividing and renewing themselves for long periods of time and can differentiate into many specialised cell types. When culturing stem cells, the optimisation of growth conditions is important in order to retain and maintain phenotypic and biological activity. The medium composition and extracellular matrix on which stem cells are maintained are crucial to most closely resemble their in vivo niche. Differentiation of stem cells into the desired derivative represents a significant challenge. Ultimately, the goal is to produce robust and reliable stem cell differentiation processes that can be controlled within the laboratory. Principles and reagents to best support stem cell research will be discussed.

16:00 – 17:00 **Question and Answer Session**

This session will include:

- Summing up of the discussion tables
- Questions submitted prior to the meeting and throughout the day

17:00 **Chairman's Summing Up**

Discussion Table Sessions:

Table A: Sourcing Stem Cell Lines: Points to Consider

Hosted by Glyn Stacey, Head of the Division of Cell Biology and Imaging at NIBSC and Director for the UK Stem Cell Bank. His scientific background has been in microbiology and cancer research. From 1989-1998 he worked at Porton Down, UK, where he developed cell banking procedures and the development of cells for manufacture of medical products and cell-based diagnostic assays. At NIBSC he has developed a broad remit relating to the quality and safety of new biological medicines and therapies based on the use of human and animal cells. He has also acted as an advisor to the UK Department of Health and the World Health Organization. He coordinates the International Stem Cell Banking Initiative funded by a consortium of funding agencies from 20 countries. He has recently overseen the establishment of a new and expanded GMP facility for banking stem cell lines. He has published numerous scientific papers and books on cell banking and quality control.

Table B: Culture and Differentiation of Human Pluripotent Stem Cells

Hosted by Chris Denning, PhD in Cancer Gene Therapy at Beatson Institute for Cancer Research, University of Glasgow, 1997; Postdoctoral Research Fellow - gene targeting in mouse ES cells, Institute for Stem Cell Research, University of Edinburgh, 1997-1998; Postdoctoral Research Fellow - gene targeting in somatic cells; first targeted gene disruption in animals other than mouse, Roslin Institute 1998-2001; Principal Investigator, University of Nottingham, 2001-2003; Medical Research Council Fellow in Stem Cell Biology, University of Nottingham, 2003-2006; Lecturer in Stem Cell Biology, University of Nottingham, 2006-2008; Associate Professor & Reader in Stem Cell Biology, University of Nottingham 2008-

Table C: Challenges in the Generation of Cardiomyocytes from hESC and hiPSC - What is Being Done to Overcome the Hurdles

Hosted by Nadire Ali, a Senior Research Fellow and Head of Embryonic Stem Cell Team at the NHLI, Imperial College London. She is also a member of BHF Centre of Research Excellence and serves on Editorial Board of Stem Cells International. After her PhD (Biochemistry, London, 1983) she continued her studies with bone cells at UCL, RVC, ICRF at Lincoln Inn Fields and QMW. In 2000, she joined TERM Centre at Imperial and established the ESC Laboratory at NHLI (2003). Interested in optimising cardiomyocyte-generation from ESC/iPSC and studying their characteristics; purification of ESC-CM by non-genetic means; generate & study patient-specific-iPSC.

Table D: Characterisation of Human Pluripotent Stem Cells

Hosted by Dr Paul Gokhale, PhD, Tumour Cell Biology, 1999. Postdoctoral researcher with Prof. PW Andrews, University of Sheffield (1999-2005). International Stem Cell Initiative (2005-present). ISCI-1 (2005-2008): Characterisation of Human embryonic stem cells and ISCI-2 (2008-2011): Identification of common genetic changes in Human embryonic stem cells.

Table E: Problems in Cryopreservation of Stem Cells

Hosted by Dr Charlie Hunt, whose background has been in the fields of cryobiology and tissue banking. In 1978, he joined the MRC Medical Cryobiology Group at the University of Cambridge where his research involved the cryopreservation of cornea, pancreatic islets, and arteries. In 1992, he and colleagues founded the East Anglia Tissue Bank; where he was responsible for the heart valve and autologous stem cell banking programs and developing skin and amniotic membrane banking. In 2003, he took charge of the newly founded UK Stem Cell Bank at the National Institute for Biological Standards and Control, where he is currently the Operations Manager.

Table F: Refining & Redefining Stem Cell Culture

Hosted by Dr Paul Bello, Site Head, Director of Technology Transfer and Head of Stem Cells & Media Systems at Stem Cell Sciences (UK), a wholly owned subsidiary of StemCells Inc. (USA). Prior to SCS, Dr Bello was BresaGen's Human Stem Cell Studies Group Leader investigating ES cell pluripotency and differentiation protein networks, and also involved in human ES cell-based for Parkinsons' therapy research, then became BresaGen's Protein Pharmaceutical Division (ProtEcoITM Contract Manager for novel cGMP APIs in clinical trials. Dr Bello was head of SCS' Research Centre (Australia), and since acquisition by StemCells Inc. (USA) in 2009, he is now Site Head, Director of Technology Transfer and Head of Stem Cells Systems responsible for stem cell technologies and products, while also contributing to the Company's international research, collaborative and business efforts.

Table G: How to Improve Characterisation of IPS Cell Lines and Can Epigenetic Elements Improve the Fidelity of iPS Lines.

Hosted by Dr. Rachel Craddock, a Stem and Specialty Cell Culture Specialist with Merck Millipore since 2008. She gained her PhD (2003) in ceramide/lipid raft signalling through death receptor complexes in unresolving inflammation at the Division of Immunity and Infection, University of Birmingham. She then worked as a Post Doctoral Research Fellow at The Babraham Institute, Cambridge (2003 – 2005) – identifying mechanisms of oxidative stress in neuropsychiatric diseases and the development of a surrogate cell model for identifying signaling abnormalities in schizophrenia and at the Cambridge Centre for Neuro-psychiatric Research, Institute of biotechnology, University of Cambridge (2005 – 2007) – Identifying biomarkers in schizophrenia for development of diagnostic biosensors, using surrogate cell model system.

About our Invited Speakers:

Ludovic Vallier is a MRC senior non-clinical fellow and a principal investigator in the Anne McLaren Laboratory for Regenerative Medicine (Cambridge University). He has developed a strong expertise on human Pluripotent Stem cells by discovering key mechanisms controlling their differentiation and pluripotency. His laboratory studies mechanisms controlling differentiation of pluripotent cells into endoderm from which the pancreas and liver originate. His overall objective is not only to acquire the knowledge necessary to control differentiation of pluripotent stem cells into endodermal cells but also to generate cell types for cell based therapy against diabetes and inherited metabolic diseases of the liver.

Erik Miljan has over 9 years experience in the Stem Cell Biotech sector, from intellectual property (IP) portfolio management through product development to regulatory approval. Initiated, implemented and delivered the operational and management strategy leading to the first ever stem cell based product approved for clinical trial in the UK in addition to delivering non-therapeutic stem cell products to market. He has experience in International settings across both academia and industry in the US, Japan, Australia and the European Union.

Key words:

automation, human pluripotent stem cells, disease modelling, cardiomyocytes, genetic modification, hES cells (hESC), iPS cells (iPSC), freezing, vitrification, cryopreservation, stem cells, culture, defined media, cardiomyogenesis, hESC-CM, iPSC-CM, extracellular matrix, 3D culture, pluripotency assays, hIPSCs, reprogramming, differentiation, epigenetics, DNA methylation, cell therapies

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This meeting was organised by Euroscicon (www.euroscicon.com), a team of dedicated professionals working for the continuous improvement of technical knowledge transfer to all scientists. Euroscicon believe that they can make a positive difference to the quality of science by providing cutting edge information on new technological advancements to the scientific community. This is provided via our exceptional services to individual scientists, research institutions and industry.

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