The 2014 Regenerative Medicine Event: Stem Cell Reprogramming

www.regonline.co.uk/Regen2014
Monday, 02 June 2014
Cineworld: The O2, London, SE10 0DX, UK

This event will highlight and discuss recent advances in strategies for controlling stem cell fate and reprogramming. Progress towards therapeutic applications, and new insights into the molecular basis of pluripotency, differentiation, and transdifferentiation will be discussed in an informal setting with plenty of opportunity for networking. This event has **CPD accreditation**. This event is part of **The 2014 Tissue Engineering Congress.**

Who Should Attend
Biotech and Pharma Industry: CEOs, Chief Scientists, Group Heads, Senior and Junior Scientists, Research Managers
Academic and Research Institutes: Group and Lab Heads, Postdoctoral Scientists and Research Students

Meeting Chair: *Dr Christopher Ward*, Senior Lecturer in Stem Cell Biology, The University of Manchester, UK

Abstracts for *poster presentation only* can be submitted up to two weeks before the event. You can download the instructions for authors at: **www.euroscicon.com/AbstractsForOralAndPosterPresentation.pdf**

Talk times include 5 – 10 minutes for questions

9:30 - 10:15 **Registration**

10:15 - 10:30 **Introduction by the Chair:**
Dr Christopher Ward, Senior Lecturer in Stem Cell Biology, The University of Manchester, UK

10:30 - 11:00 **Manipulation of E-cadherin for the culture and differentiation of pluripotent stem cells**
Dr Christopher Ward, Senior Lecturer in Stem Cell Biology, The University of Manchester, UK
E-cadherin is a cell-cell adhesion protein that has several functions in pluripotent stem cells. In mouse ES cells, E-cadherin is required for LIF-dependent pluripotency and inhibition of self-renewal by Activin/Nodal. In human ES cells, E-cadherin expression appears to be required for optimal proliferation and single cell cloning. In this talk I will present data on several small peptides that target E-cadherin and show that these can be used for both propagation of human ES and iPS cells in an undifferentiated state and for differentiation to neural lineages.

11:00 - 11:30 **Cell Sex Matters. It Could Affect Findings**
Dr Elizabeth Pollitzer, Portia, London, UK
The fact that sex and gender do matter has been recognised for years in clinical research, a field in which researchers have often disproportionally sampled men. Studies using male subjects also dominate basic research. Most cell biologists do not note whether the cells they are using come from males or females. But, evidence is mounting that cells differ according to sex, e.g. in response to stress, irrespective of their history of exposure to sex hormones. Discoveries of sexual dimorphism in metabolic pathways, and in regenerative properties of muscle-derived stem cells show cell sex matters.

11:30 - 12:00 **Heterogeneity in pluripotent stem cell populations**
Dr Kirsten Mcewen, MRC Clinical Sciences Centre, UK
Pluripotent stem cells (PSCs) are a unique resource for regenerative medicine. These cell populations exist in two predominant states: naïve, as in the case of mouse embryonic stem cells (ESCs) or induced PSCs, and primed, such as traditional human

PSCs and mouse epiblast stem cells. We and others have previously shown that the molecular setup of mouse naïve PSCs is dependent on the culture condition the cells are grown in, with 2i conditions thought to more closely resemble their in vivo counterpart. Characterisation of these molecular states will aid the process of controlling reprogramming to and differentiation from PSCs, in addition to maintaining these cells in the steady state. Heterogeneity of PSCs can affect these properties and we are currently investigating this process in further detail.

12:00 - 12:30 **Speakers' photo then mid-morning break and poster exhibition and trade show**

Please try to visit all the exhibition stands during your day at this event. Not only do our sponsors enable Euroscicon to keep the registration fees competitive, but they are also here specifically to talk to you.

12:30 - 13:00 **Progressing human pluripotent stem cell technologies for drug discovery and regenerative medicine by genome engineering**

Dr Peter Sartipy, Cellectis AB, Göteborg, Sweden

Culturing and differentiation of human pluripotent stem cells are today activities performed in many laboratories world-wide. We have witnessed many breakthroughs in recent years which allows the generation of induced pluripotent stem cells from a wide range of somatic cells, and their subsequent controlled differentiation into specific cell types. Nevertheless, challenges still exist to generate fully mature cell phenotypes from human pluripotent stem cells. Through the application of site specific genome engineering, it is possible to improve the functional phenotypes by targeting the genome of the cells in order to express or repress key elements. These advancements are critical in order to create improved in vitro testing systems for drug discovery and safety assessment and also to pave the way for future regenerative medicine applications based on human pluripotent stem cells.

13:00 - 14:00 **Lunch, poster exhibition and trade show**

Please try to visit all the exhibition stands during your day at this event. Not only do our sponsors enable Euroscicon to keep the registration fees competitive, but they are also here specifically to talk to you.

14:00 - 15:00 **Discussion session**

This discussion session is an informal question and answer session. This is an ideal opportunity to get advice and opinion from experts in this area. This session is not for questions about specific talks, which can be asked after the speakers session, but for discussing either general topics or specific issues.

There are three ways you can ask questions:

1. Before the session you can *submit your question to Euroscicon staff* at the registration desk,
2. Before and during the session you can *submit a question or comments, by email*, which will be provided on the day of the event
3. During the session you can *put your hand up* and join in

15:00 -15:30 **Chemical Reprogramming of Human Amniotic FLuid Stem Cells to Pluripotency**

Dr Pascale V Guillot, Senior Lecturer, University College London, UK

The conversion of somatic cells to pluripotency (iPSC) via ectopic expression of a combination of transcription factors provided proof of concept that cell fate could be reset, but a number of hurdles limit the application of iPSC in regenerative medicine. We use small compounds to mimic the effects of the transcription factors. Human c-KIT+ amniotic fluid stem cells (AFSC) show an intermediate phenotype between embryonic and adult stem cells, endogenously expressing oct4. We derived chemically-induced iPSC from AFSC by exposure to the histone deacetylase inhibitor valproic acid. This resulted in the derivation of a bona fide factor-free pluripotent cell type.

15:30 - 16:00 **Afternoon Tea, last poster session and trade show**

16:00 - 16:30 **Disease modelling in a dish: use of cardiovascular derivatives of human pluripotent stem cells**
Dr Gabor Foldes, Imperial College London, UK
The potential of stem cell-based disease modelling is enhanced by the realisation that cardiomyocytes from human embryonic stem cells and induced pluripotent stem cells can be obtained with disease-specificity. One of the high priority disease targets is hypertrophy because of its central role in the transition to heart failure. However, superficial similarities between human embryonic/induced pluripotent stem cell-derived cardiomyocytes and adult cardiomyocytes may mask complex differences in signalling. This talk raises questions regarding the use of stem cell-derived cardiomyocytes as a valid model system for certain aspects of cardiac disease.

16:30 - 17:00 **Regulation of human neural stem cell differentiation by noncanonical Wnt signaling**
Dr Robert Kypta, Group Leader, Center for Cooperative Research in Biosciences (CIC bioGUNE) and Imperial College London, UK
Neural stem cells (NSC) hold great promise for neural repair after injury or disease and as a renewable source for drug screening. A deeper understanding of the signals that control NSC differentiation is expected to improve neuron yield for these applications and may also provide new insight into neurodegenerative disease mechanisms. We study Wnt signalling, which is implicated in neurodegenerative and neuropsychiatric diseases and plays complex roles in NSC proliferation and differentiation. I will present our recent results highlighting a switch from Wnt/β-catenin (canonical) to noncanonical Wnt signalling that takes place during early NSC differentiation.

17:00 **Chairman's summing up and Close of Meeting**

Registration Website: www.regonline.co.uk/Regen2014

Meeting reports from this event will be published in Regenerative Medicine and by HONNAO publishing as a Kindle ebook

About the Chair

Chris Ward is a Senior Lecturer in Stem Cell Biology at The University of Manchester and head of the Stem Cell Biology Research Group. Chris is a recognized expert in stem cell biology and his research focuses on the role of the cell adhesion protein E-cadherin in ES cell pluripotency and differentiation.

About the Speakers

Peter Sartipy received his M.Sc. in Chemical Engineering in 1994 from Chalmers University of Technology (Göteborg, Sweden). He then went on to earn his Ph.D. in 2000 from the Faculty of Medicine at Göteborg University. After working as a post-doc at the Department of Cell Biology at The Scripps Research Institute (La Jolla, CA, USA) he returned to Göteborg and joined the start-up company Cellartis AB in 2002. Cellartis AB was acquired by Cellectis SA in November 2011, and Dr Sartipy is currently holding a position as Vice President Stem Cell Discovery and Senior Principal Scientist in the company. His previous research experiences were focused on cardiovascular disease prevention and diseases associated with the metabolic syndrome. His current research is mainly directed at exploring human pluripotent stem cell differentiation towards functional cell types and development of novel drug discovery applications based on these cells. He is the author of 60+ research papers including book chapters and reviews, and is the inventor of several patents/patent applications.

Pascale V Guillot is a Senior Lecturer in Fetal and Maternal Health at University College London. Her group studies fetal stem cell biology and development, and is interested in applying a chemical approach to cellular reprogramming and differentiation, to develop new approaches for the treatment of a number of diseases They combine whole genome and single-cell gene expression analysis to try and understand the molecular mechanisms underlying pluripotency and nuclear reprogramming.

Gábor Földes, MD PhD is an associate Professor at Heart and Vascular Center, Semmelweis University, Hungary and runs stem cell lab at the National Heart and Lung Institute, Imperial College London. Dr Foldes specialised in Internal Medicine and in Cardiology. His research interests are in particular the cellular and molecular mechanisms of cardiac remodelling and heart failure. In addition he has a long-standing interest in cardiac regeneration and continues to be involved with pluripotent stem cell characterisation projects.

Elizabeth Pollitzer has background in biophysics and computing. More recently, she established the Gender Summit (www.gender-summit.com) as a platform for scientists, policy makers and gender scholars to evaluate research evidence showing where, why and how females and males are different or similar and when this matters to quality of research and innovation. Now in 4th year, the Summit developed into four regional events: Europe, North Americal, Asia-Pacific, and Africa. The European summit is strongly linked to integrating gender dimension in Horizon 2020 .

Robert Kypta did his PhD at the European Molecular Biology Laboratory (EMBL) in Heidelberg and postdoctoral work at the University of California San Francisco, where he studied neuronal cell adhesion proteins. After four years at the MRC LMCB on a Wellcome Trust Career Development Fellowship, he took a Lectureship at Imperial College. In 2005 he set up a lab in the Cell Biology and Stem Cells Unit at CIC bioGUNE, an institute near Bilbao funded by the a local government. His groups study how Wnt and GSK-3 signals regulate cancer and stem cell growth and differentiation.

Kirsten McEwen completed a Biomedical Science Honours degree in New Zealand before undertaking a PhD in genomic imprinting at the University of Cambridge, UK with Anne Ferguson-Smith. Kirsten has continued her academic career as a post-doctoral fellow at the MRC Clinical Sciences Centre, joint with Imperial College London and is working with Petra Hajkova in the Reprogramming and Chromatin group. Kirsten's focus is on basic reseach of transcriptional and epigenetic processes in murine pluripotent stem cells.

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.

Frequently asked questions about our events

Is the delegate list available?

Yes this is available to everyone who attends the event and our sponsors. It is available in real time. To access the list please just log into your registration details or use the QR code on right of the agenda card which is provided on the day of the event. You will not be included in this list if you have opted out and you can do this by logging into your registration details. This list will not be sold or ever give out to third parties.

Can I have the speakers slides?
We cannot give out the slides from our speaker's presentations as they are deleted immediately after each event. If you require a particular set of slides please approach the speaker. We will however have a meeting report and you will be emailed when this report is published.

Can I have a notepad?
Notepads and pens are provided in the delegate bags and at the registration desk.

How can I keep up to date with Euroscicon Events?
To keep updated on our events and other Life Science News, please sign up for our newsletter at www.eurosciconnews.com

I don't want my photograph on any Euroscicon promotional material
Please let our tech person know.

Is there WIFI?
Yes, please ask registration for log in details
.
Can I have a CPD certificate?
Please leave your name with registration before the end of lunch a certificate will be created for you and available in the afternoon.

POSTERS

The therapeutic effects of bone marrow-derived mesenchymal stem cells and simvastatin in a rat model of liver fibrosis

Tarek M.K. Motawi[1], Hazem M Atta[2], Nermin A.H. Sadik[1]*, May Azzam[1]
[1]Biochemistry Department, Faculty of Pharmacy, Cairo University, Cairo, Egypt
[2]Department of Medical Biochemistry, Unit of Biochemistry and Molecular Biology, Faculty of Medicine, Cairo University, Cairo, Eqypt

Liver fibrosis is the excessive accumulation of extracellular matrix (ECM) proteins including collagen that occurs in most types of chronic liver diseases. Studies concerning the capacity of mesenchymal stem cells (MSCs) and simvasatain (SIMV) to repair fibrotic tissues through reducing inflammation, collagen deposition are still controversial. This study aimed to investigate the effect of infusion of bone marrow (BM)-derived MSCs and SIMV on carbon tetrachloride (CCl4) -induced liver fibrosis in rats. Rats were divided into: normal, CCl4, CCl4/MSCs, CCl4/SIMV, CCl4/MSCs/SIMV and SIMV groups. BM-derived MSCs were detected by RT-PCR of CD29 and were then infused into the tail vein of female rats that received CCl4 injection to induce liver fibrosis. Sex-determining region Y gene (sry) on Y-chromosome gene was assessed by PCR to confirm homing of the male stem cells in liver tissue of the female recipients. Serum liver function tests, liver procollagen-

I &III, tissue inhibitors of metalloproteinase-1(TIMP-1), endoglin, matrix metalloproteinase-1(MMP-1) gene expressions, transforming growth factor-beta (TGF-β1) immunostaining and histopathologicl examination were performed. MSCs and SIMV decreased liver procollagen-I &III, TIMP-1 and endoglin gene expressions, TGF-β1 immunostaining and serum liver function tests compared with the CCl_4 group. MMP-1 expression was increased in CCl_4/MSCs group. Histopathological examination as well as fibrosis score support the biochemical and molecular findings. It can be concluded that MSCs and SIMV were effective in the treatment of hepatic CCl_4-induced fibrosis-rat model. Treatment with MSCs was superior to SIMV. This antifibrotic effect can be attributed to their effect on the MMPs/TIMPs balance which is central in fibrogenesis.

Integrins ITGAV and ITGA11 regulate adipogenesis

E.Morandi, R.Verstappen, S.Lobenwein, S.Geley, G.Pierer, C.Ploner[1]
[1]Department for Plastic, Reconstructive & Aesthetic Surgery
Medical University Innsbruck
Anichstraße 35, 6020 Innsbruck, Austria

Background

The white adipose tissue remains a readily accessible and abundant source for human adipose derived stem cells (ASC). The regulation of stem cell fate is largely determined by biochemical and mechanical signals derived from the extracellular matrix (ECM), which are transmitted by integrins, a family of transmembraneous proteins that connect the ECM to intracellular anchorage and signaling pathways. The aim of this study is to investigate the expression and functions of integrins in ASC and their differentiated derivatives, i.e., adipocytes, chondrocytes and osteoblasts, in order to optimize conditions for expanding cells suitable for reconstructive surgery applications.

Methods

Primary $CD34^+$-ASC were isolated from fat tissue of informed consent patients undergoing plastic surgery. Gene expression profiling was performed by quantitative RT-PCR of all known alpha integrins. Integrin gene functions were investigated by knock-down experiments using lentivirally transduced RNAi. Cell behavior and downstream pathways were analyzed both on RNA and protein level, by functional assays and microscopy.

Results

Using comparative integrin expression profiling in human CD34+ASC and differentiated chondrocytes, osteoblasts and adipocytes we identified ITGAV, ITGA7 and ITGA11 to be regulated during differentiation of adipocytes. While ITGAV and ITGA11 were highly expressed in ASC, ITGA7 mRNA levels were high in adipocytes. We performed lentivirally transduced knock-down (KD) experiments to elucidate integrin functions in ASC viability and differentiation capacity. Knockdown of ITGAV reduced ASC proliferation and viability, which resulted in decreased differentiation capability. Moreover, loss of ITGAV decreased ASC attachment and spreading, which was associated with the induction of potential cell death genes, such as the pro-apoptotic BCL2 protein Bad. Interestingly, surviving ITGAV-KD cells efficiently differentiated into adipocytes. Similar to ITGAV KD, loss of ITGA11 reduced proliferation but cells retained their morphology and viability as assessed by microscopy and FACS analysis. In ITGA11 KD cells, adipogenesis was slightly increased. Contrary to ITGAV and ITGA11-KD, loss of ITGA7, which was induced in differentiated cells, did not interfere with differentiation, proliferation or viability.

Conclusion

The ASC expressed integrins ITGAV and ITGA11 are essential for the regulation of ASC viability and differentiation potential, whereas ITGA7 plays only a minor role.

THE EFFECT OF 2i INHIBITOR SYSTEM ON PLURIPOTENCY MARKER GENES EXPRESSION IN BOVINE BLASTOCYSTS.

Hryniewicz K, Madeja ZE, Lechniak-Cieslak D.

Poznan University of Life Sciences, Department of Genetics and Animal Breeding. Poland
kamilapl@up.poznan.pl

The derivation of true embryonic stem cells from farm animal species is still an unresolved issue. Published evidence shows that the classical system relying on LIF/FGF supplementation is not optimal, thus the efforts concentrate on supporting self-renewal by specific inhibition of differentiation-inducing signalling. Signalling pathway inhibitors have proven successful in derivation of rat ESC [Buehr et al., 2008]. The applied 2i system sustained Wnt/β-catenin signalling (inner cell mass maintenance) and inhibited MEK/ERK pathway, thus preventing ESC from commitment.

In order to understand the plausible role of signalling pathway inhibitors in bovine ESC derivation, we have aimed to evaluate the influence of the 2i system on pluripotency marker expression in bovine preimplantation embryos - inner cell mass (ICM) versus trophoblast (TE).

Bovine embryos were obtained *in vitro* and cultured until blastocyst hatching (9 days post insemination). The medium was supplemented with GSK-3 inhibitor [3μM, CHIR99021] and MEK/ERK inhibitor [1μM, PD0325901]. Blastocysts were microsurgically dissected into ICM and TE samples, which were subjected to gene expression analysis. Relying on previous findings of our group [Madeja et al., 2013] we have selected a set of 4 pluripotency markers, which similarly to the classical mouse model, label the ICM (OCT4, NANOG) and the TE (CDX2, KRT-18) lineages.

The results of quantitative gene expression analysis (real-time PCR) indicate that the 2i system up-regulates transcript abundance of the ICM specific genes *OCT4* and *NANOG* within bovine ICM cells. Moreover, a significantly higher mRNA level of *NANOG* gene was noted in the trophoblast. It may be therefore concluded, that developmentally important signalling pathways described in rodents, may also prove to be important in supporting bovine ESC derivation.