Stem Cells and BioProcessing

Tuesday, 03 June 2014
Cineworld: The O2, London, SE10 0DX, UK
www.regonline.co.uk/StemBio2014

Harnessing the immense therapeutic and research potential of stem cells requires extensive quality control to ensure the identity, quality, and safety of the cell. Stem cells of different origin and their capability to differentiate towards a specific phenotype as well as tissue engineered constructs are dependent of all kinds of bioprocesses including cultivation media, biomechanical conditions and purification techniques. All topics dealing with the optimization and analysis of processes leading to defined in vitro cultivated cell lines and engineered tissues - with a special focus on bioreactors - will be discussed in this session. This event has **CPD accreditation.**

This event is part of The 2014 **Tissue Engineering Congress**

Meeting Chair: *Dr Johanna Buschmann,* Head of Research Laboratories, University Hospital Zurich, Plastic Surgery, Switzerland

Who Should Attend: All those interested in the use of stem cells for tissue engineered constructs should find this meeting extremely valuable.

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 Johanna Buschmann,* Head of Research Laboratories, University Hospital Zurich, Plastic Surgery, Switzerland

10:30 – 10:55 **Proliferation of ASC-derived endothelial cells in a 3D electrospun mesh: Impact of bone-biomimetic nanocomposite and co-culture with ASC-derived osteoblasts.**
Dr Johanna Buschmann, Head of Research Laboratories, University Hospital Zurich, Plastic Surgery, Switzerland
With the background in mind that (i) a scaffold with a mineral component, (ii) an in vitro pre-differentiation of stem cells and (iii) a co-culture system will provide a beneficial starting point for a functional bone graft, we chose an electrospun 3D nanocomposite and human adipose-derived stem cells (ASCs) for differentiation towards the osteoblastic as well as the endothelial cell type. The objectives are: (i) what impact do ASC-derived osteoblasts have on ASC-derived endothelial cells when seeded in co-culture of and (ii) what effect do 40 wt % of an inorganic component have on ASC-derived ECs when present in PLGA?

10:55 - 11:20 **Development of a Bio-Inspired Blood Factory for Personalised Healthcare**
Professor Athanasios Mantalaris, Imperial College London, UK
Personalized medicine is a medical model that proposes the customization of healthcare, with decisions and practices being tailored to the individual patient by use of patient-specific information (initially genetics information) and/or the application of patient-specific cell-based therapies. The BioBlood proposal aims to deliver personalised healthcare through a “step change” in the clinical field of haemato-oncology. BioBlood represents an engineered bio-inspired integrated experimental/modelling platform for normal and abnormal haematopoiesis that receives disease & patient input (patient primary cells & patient/disease-specific data) and will produce cellular (red blood cell product) and drug (optimal drug treatment) therapies as its output.

11:20 - 11:45 **Speakers’ photo then mid-morning break and poster exhibition and trade show**
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11:45 - 12:10 **Oxygen controlled whole-bioprocessing of pluripotent stem cells**

Dr Farlan Veraitch, Department of Biochemical Engineering, University College London, UK

Oxygen is a key element of the microenvironment which can yield step-changes in the efficiency of pluripotent stem cell production processes. This talk will highlight key findings from the Veraitch laborotory starting with the first discovery that low oxygen tensions could be used to radically enhance the yield of neuronal differentiations processes. Using a whole-bioprocessing approach recent studies have investigated how lowering oxygen tension during the expansion phase can have a significant knock effect on subsequent differenetiation bias. These results also highlight fundamental differences between the behaviour of mouse and human pluripotent stem cells in repsonse to hypoxic conditions.

12:10 – 12:40 ORAL PRESENTATIONS

12:10 - 12: 25 **A THERMOSENSITIVE MICROGEL-BASED STEM CELL CULTURE PLATFORM**

Hu Zhang, School of Chemical Engineering, The University of Adelaide, SA, 5005, Australia

12:25 - 12:40 **INTEGRATED 3D BIOPROCESSING FOR THE EXPANSION AND RECOVERY OF A FUNCTIONAL PROGENITOR CELL POPULATION WITH UNCOMPROMISED OSTEOGENIC REGENERATION POTENTIAL**

Maarten Sonnaert[1, 2], Ioannis Papantoniou[1,3], Frank P. Luyten[1,3], Jan Schrooten[1,2] *[1]Prometheus, Division of Skeletal Tissue Engineering, KU Leuven, Onderwijs en Navorsing 1, +8 Herestraat 49, box 813, B-3000 Leuven, Belgium; [2]Department of Metallurgy and Materials Engineering, KU Leuven, Heverlee, Belgium; [3]Skeletal Biology and Engineering Research Centre, KU Leuven, Leuven, Belgium*

12:40 - 13:30 **Lunch, poster exhibition and trade show**

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13:30 – 14:00 **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

14:00 – 14:45 ORAL PRESENTATIONS

14:00 - 14:15 EFFECT OF COMPRESSION ON hMSCs SEEDED IN A POROUS PCL SCAFFOLD EMBEDDED WITH COLLAGEN GEL

M. Brunelli, C. M. Perrault, D. Lacroix, *INSIGNEO Institute for in silico Medicine, Department of Mechanical Engineering, Mappin Street, S1 3JD, Sheffield, UK*

14:15 - 14:30 ***DOES ENDOTHELIAL DIFFERENTIATION OF WHARTON'S JELLY MESENCHYMAL STEM CELLS AFFECT THEIR IMMUNOSUPPRESSIVE EFFECTS?***

R. EL OMAR[1], E. Velot, P. Menu, J.-F. Stoltz, V. Decot

[1]CNRS-UMR 7365, IMoPA laboratory, Faculty of Medicine, Lorraine University, 9 avenue de la Forêt de Haye, 54505- Nancy, FRANCE

14:30 - 14:45 ***DEFINED THREE DIMENSIONAL MICROFIBROUS SYSTEM FOR PATIENT-SPECIFIC IPSC GENERATION AND DIRECT DIFFERENTIATION***

H. F. Lu, M. F. Leong, K. Narayanan, S. Gao, and A. C. A. Wan
Institute of Bioengineering and Nanotechnology, 31 Biopolis Way, Singapore

14: 45 - 15:10 **Bioreactors for tissue engineering**

Dr Marianne Ellis, University of Bath, UK

If tissue engineering is to provide viable solutions for the emerging cell-based therapies and cultured meat industries it is necessary to scale up the culture processes in a way that replicates the physiological environment while being cost effective and meet regulatory requirements, a key part of which is the bioreactor design. This talk will describe the fundamental design of bioreactor configurations to demonstrate an approach to addressing the need for a physiological environment and a cost effectiveness bioprocess with examples from bone and heart regeneration, in vitro to in vivo extrapolation of toxicity data for the liver, and cultured meat.

15:10 - 15:40 **Afternoon Tea, last poster session and trade show**

15:40 - 16:05 **Robust Generation and Maintenance of Human Induced Pluripotent Stem Cells under Defined and Xeno-Free Conditions**

Dr Gerhard Muster, Lonza, Germany

The process to generate hiPSCs is inefficient and technically challenging, even when utilizing viral methods and mouse embryonic fibroblast feeder layers. Efficiencies fall even further when generating iPSCs using non-integrating technologies under defined conditions. These realities lead Lonza to focus on developing a robust system, named L7 hPSC Reprogramming and Culture System. L 7 is comprised of a culture platform supporting every-other-day feeding of human PSCs. In combination with an enhanced episomal reprogramming method, the resulting hiPSCs share characteristics with human ESCs, including the expression of ESC-associated markers. In addition, these hiPSCs can efficiently differentiate and have a normal karyotype.

16:05 - 16:30 **Developing processes and release assays for cell therapy products**

Dr Ivan Wall, Lecturer in Regenerative Medicine Bioprocessing, University College London, UK

There is a clear need to translate current cell culture methods to sustainable biomanufacture platforms to meet clinical demand. Moreover, adoption of biofunctionalisation and bioactivation strategies that improve the survival, growth and differentiation of progenitor cells will be important for optimised tissue production and cell product performance. Our group are interested in assessing a range of platforms for scale up and optimisation and this talk will present some of our current work, notably the development and testing of microcarriers made from implantable materials. Data regarding functional identity of cell therapy products will then be presented.

16:30 - 16:55 **Immune Regulation by Mesenchymal Stromal Cells from Umbilical Cord**

Dr John Girdlestone, NHS Blood and Transplant, UK

Mesenchymal stromal cells (MSC) are connective tissue progenitors, but the majority of clinical trials investigating their therapeutic potential are directed at exploiting their ability to suppress immune reactions. MSC from the umbilical cord are an alternative to those derived from bone marrow, and their immunoregulatory properties and potential for therapeutic use will be discussed.

16:55 - 17:00 **Chairman's summing up**

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

Registration Website: www.regonline.co.uk/StemBio2014

About the Chair

Johanna Buschmann studied Chemistry at the ETH Zurich, Switzerland (1988-1992). In 1998, she finished her PhD Thesis in Environmental Organic Chemistry at ETH Zurich and performed several Post-Doc projects dealing with environmental pollution and health aspects - primarily evoked by water pollution. Dr Buschmann then turned her interests towards material-cell interactions and focussed her

research interests to tendon and bone reconstruction. Using human adipose-derived stem cells, she applies different bio-mimetic materials for fabricating artifical bone grafts. Currently, she works at the University Hospital in Zurich and is the Head of Research Laboratories in the Clinic for Plastic Surgery.

About the Speakers

Athanasios Mantalaris is Professor in Biosystems Engineering at Imperial College London. He has research interests in the areas of stem cell bioprocessing, tissue engineering and mammalian cell bioprocessing.

Marianne Ellis is a Senior Lecturer in Biochemical Engineering in the Department of Chemical Enginering at the University of Bath. She was awarded a BEng in Chemical & Bioprocess Engineering in 2001 and a PhD in 2005 from the same department. After a year as a postdoctoral researcher she took up an academic position in 2005. Her research interests are focused on bioreactor and bioprocess design for the scale up of cell therapies and cultured meat, and to produce physiologically-relevant in vitro models for toxicology and bioartificial organs.

Ivan Wall is a Lecturer in the Department of Biochemical Engineering at UCL. A cell and molecular biologist by training, his focus is the development of new bioprocess solutions for stem cell and tissue engineering applications for a range of different tissues. His core research themes include: defining critical quality attributes for cell therapy products; improving cell retention for improved functional outcomes; and scalable process solutions for tissue engineering. He is a visiting professor at Dankook University in South Korea.

John Girdlestone has over 30 years of research experience in molecular and cellular biology, gained as a senior scientist in university, MRC, biotech start-up and NHS laboratories. He currently is the senior research fellow and programme manager of the H&I Research group at NHS Blood and Transplant Colindale, which is responsible for the development of immunobiological and immunogenetic projects relevant to the R&D and service needs of NHSBT. Current projects funded by NHSBT and external agencies include: Immune Reconstitution Following Umbilical Cord Blood Transplantation (NHSBT), and Umbilical Cord Mesenchymal Stromal Cells for treating Graft-versus-Host Disease (LLR).

Athanasios (Sakis) Mantalaris is Professor of BioSystems Engineering in the Department of Chemical Engineering at Imperial College London. He received his PhD (2000) in Chemical Engineering from the University of Rochester. His expertise is in modelling of biological systems and bioprocesses with a focus on mammalian cell culture systems, stem cell bioprocessing, and tissue engineering. He has published over 150 original manuscripts, co-edited one book, and holds several patents with several more pending. He has received several awards including the Junior Moulton Award for best paper by the Institute of Chemical Engineers (IChemE) in 2004. In 2012, he was elected Fellow of the American Institute for Medical & Biological Engineering and in 2013 he was awarded a European Research Council (ERC) Advanced Award.

Farlan Veraitch'S research focuses on the development of robust, reproducible and cost effective production processes in the emerging field of cell therapy. His team are establishing novel processing technologies which will underpin the commercialisation of these types of products. Their work uses a whole bioprocessing methodology pioneered at UCL to ensure that new production process are considered as whole rather than individual operations in isolation. Using pluripotent stem cells as a model system Farlan's group are developing new methods for the majority of steps involved in the production of cellular therapies. Current projects include the application of bioprocessing methodologies to (i) the expansion of pluripotent stem cells, (ii) their directed differentiation into regenerative populations, (iii) the non-destructive dissociation of differentiated cellular aggregates into single cell suspensions, (iv) purification techniques for positive selection and (v) point-of-care processing which includes cryopreservation, shipping, thawing, washing and presentation of the final therapy ready for administration. The overall goal of this program of work is to develop platform technologies for the manufacture of stem cell therapi**es.**

ORAL PRESENTATIONS

A THERMOSENSITIVE MICROGEL-BASED STEM CELL CULTURE PLATFORM

Hu Zhan,School of Chemical Engineering, The University of Adelaide, SA, 5005, Australia

Cell therapy has been demonstrated as a very promising approach for diseases which traditional therapeutics have little efficacy. The proliferation of desired cells remains a challenge for clinical applications: to obtain a large number of viable cells under controlled microenvironments in a very short time at a low cost. We have developed a thermosensitive microgel-based cell culture platform to embed stem cells in a 3D hydrogel network, so that nutrient entry into the pore network and a 3D support facilitate stem cell proliferation. When cells are harvested, no trypsin is required. By simply reducing the temperature to room temperature, cells are released into the liquid solution, so that no damage is done to the extracellular matricies of the stem cells. The microgel synthesis and characterization will be briefly mentioned and then stem cell proliferation inside the microgel-based system will be explained. The initial research outcomes are very promising and it may become a novel 3D cell culture platform for some primary cells which are not able to survive on the 2D rigid surfaces.

INTEGRATED 3D BIOPROCESSING FOR THE EXPANSION AND RECOVERY OF A FUNCTIONAL PROGENITOR CELL POPULATION WITH UNCOMPROMISED OSTEOGENIC REGENERATION POTENTIAL

Maarten Sonnaert[1, 2], Ioannis Papantoniou[1,3], Frank P. Luyten[1,3], Jan Schrooten[1,2]

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As the field of tissue engineering matures towards clinical applications, the development of bioprocesses that can address the growing need for consistent production of advanced therapy medicinal products, becomes crucial. In this regard, the use of bioreactor systems is considered to be indispensable. Although methods for both cell expansion and construct development are available, an integrate process development approach with *in vivo* tests as quality control is often lacking. To enable stem cell expansion bioprocess strategies, harvest methodologies resulting in both a qualitative and quantitative high stem cell yield are required, but still remain a step that is usually subsided in literature.
Therefore, we used a Design of Experiment (DoE) approach to gain understanding and optimise a harvest process for cells expanded in a 3D perfusion bioreactor in terms of recovered cell yield and viability. Finally we evaluated the osteogenic regenerative potential of the processed hPDCs by ectopically implanting them in nude mice.
Human periosteal derived stem cells were seeded on regular 3D Ti6Al4V scaffolds and cultured in a perfusion bioreactor at a flow rate of 0.04ml/min in cell growth medium. Proliferation was monitored using the Presto Blue metabolic activity assay which showed a stagnation of proliferation after two weeks, caused by the filling of the scaffold surface and void as confirmed with live/ dead staining and contrast enhanced nanoCT. At that time-point cells were harvested from the scaffolds using an oscillatory perfusion regime. An initial screening experiment exploring the use of different enzymatic reagents showed collagenase IV to be the most effective. Subsequently a DoE approach was used to assess the influence of reagent concentration, incubation time and flow rate on the efficiency of the harvest process and the viability of the resulting cell population. Results showed no influence of the three evaluated parameters on the viability of the resulting cell population, while an increase in both incubation time and concentration of the reagent resulted in significantly higher harvest yields. Subsequently, the *in vivo* bone forming capacity of the perfusion bioreactor expanded and harvested cell population was compared with cells expanded in standard 2D conditions using an established ectopic *in vivo* bone formation assay in nude mice. Cell seeded CaP-collagen based constructs were analysed after 6 weeks implantation using µCT and showed that 3D processed cells retained their bone forming potential.
In conclusion, the proposed methodology allowed recovering a progenitor cell population after bioreactor expansion while maintaining their *in vivo* osteogenic differentiation potential, thereby enabling the further translation of current manual 2D cell culture protocols to 3D, monitored, scalable and industrially applicable bioprocesses.

EFFECT OF COMPRESSION ON hMSCs SEEDED IN A POROUS PCL SCAFFOLD EMBEDDED WITH COLLAGEN GEL

M. Brunelli, C. M. Perrault, D. Lacroix

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INTRODUCTION

Cell commitment toward a defined phenotype is regulated by the surrounding environment and the sensed mechanical stimuli [1]. The role of compression on cellular differentiation is still unclear and can vary depending on the strain applied [2]. In this study, compression is applied to a porous Poly-(caprolactone) (PCL) scaffolds embedded with collagen gel. The PCL scaffold provides a geometrically regular environment for the investigation of the effect of different compression protocols on differentiation of human mesenchymal stem cells (hMSCs). The aim of this study consists in applying 8% of compression strain at 0.5 Hz for 1 hour a day and in observing the effect on hMSCs growth over 5 days by performing viability assay. Further studies need to be carried out in order to confirm the results obtained and to define which differentiation pathway is followed by cells during the stimulation protocol mentioned above.

MATERIALS AND METHODS

PCL mechanical properties. The PCL scaffold (3D Biotek, U.S.A.) is 5mm in diameter and 1.5 mm thick. The porosity and the apparent elastic modulus are 40.4±0.3% and 22.1±1.8 MPa respectively.

hMSCs culture. Cells were cultured and supplemented with complete media (α-MEM (Lonza), 10% FBS, 1% pen/strep) and FGF (2 ng/ml) until 90% confluence was reached. Passage 8 hMSCs were harvested and diluted in collagen solution in order to obtain an overall density of 2000 cells/cm^2 per each sample.

Sample preparation. 50 µl of bovine collagen type 1 (Gibco) solution at a concentration of 2 mg/ml embedded with hMSCs was placed on the top of the 7 scaffolds. Samples underwent 10 minutes vacuum and incubation at 37°C for 40 minutes before adding 1 ml of complete media. A control was defined, consisting in 3000 cells seeded in a 24-well plate.

Compression protocol. 4 samples were placed in the BOSE Biodynamic Chamber. A preload of 0.4 N was applied, followed by a 10% compressive strain ramp and a sinusoidal wave of additional 2% compressive strain for 1800 cycles. The stimulation was performed once a day for 5 days.

Viability of cells. Presto Blue assay (Invitrogen) was performed at day 1 and 1 hour after each stimulation. All the results were normalized over the signal obtained by the control after day 1.

RESULTS

Consistency among the samples is clearly observable after 1 day from the seeding as all of them show an average viability of 79% compared to the control. At day 2, an increase in cellular viability up to 15% occurs in both loaded and unloaded samples. Comparing loaded samples with unloaded samples at any timepoint, no significant differences can be noticed as all the samples presented similar cell response.

DISCUSSIONS AND CONCLUSIONS

The results of viability assay after 1 day confirm the repeatability of the method applied for sample preparation and the homogeneous distribution of cells inside the collagen. hMSCs are healthy and alive suggesting the suitability of our construct acting as environment for cellular growth and differentiation. An increment in cell number is notified by the significant increase in viability observed at day 2 ($p<0.01$). Despite of this, a stimulation of 8% strain does not provide any significant difference in terms of proliferation between tested samples and controls. Future plans will involve the investigation of the role of various mechanical compression stimuli on cellular differentiation, involving PCL scaffolds embedded with collagen. Particular attention will be placed on collagen and mineralized content quantification and on osteogenic markers expression though RT-PCR.

REFERENCES

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ACKNOWLEDGEMENTS

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DOES ENDOTHELIAL DIFFERENTIATION OF WHARTON'S JELLY MESENCHYMAL STEM CELLS AFFECT THEIR IMMUNOSUPPRESSIVE EFFECTS?

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Objective: Based on their two main features, immunosuppression and immunoprivilege, mesenchymal stem cells (MSCs) are a promising tool in immunomodulatory therapy. Umbilical cord Wharton's Jelly MSCs (WJ-MSCs) derive from a neo-natal tissue and are naturally immune-privileged. Reported studies on MSC's hypoimmunogenicity are mostly based on *in vitro* or *in vivo* experiments using undifferentiated cells. One of the most interesting questions in regenerative medicine is, whether these cells, upon differentiation, maintain their immunomodulatory properties. In this study, we evaluated the immunosuppressive capacities of WJ-MSCs on immune cells after differentiation towards an endothelial phenotype.
Material and methods: WJ-MSCs were cultivated at third passage on appropriate culture surface. Their phenotype was checked by flow cytometry before seeding. The endothelial phenotype was induced by adding angiogenic growth factors cocktail (EGM-2, Lonza®). We evaluated the kinetics of cell surface immune markers expression such as HLA-DR and CD86 during the differentiation culture period. Endothelial phenotype was verified by western blot through the expression of specific endothelial markers (CD31, VE-Cadherin and VEGFR2). Endothelial functionality was confirmed by the expression of von Willebrand (vWF) marker using immunofluorescence staining and the capacity of differentiated cells to incorporate acetylated LDL (Ac-LDL). To assess their immunosuppressive effects, WJ-MSCs and ELCs were cultured with stimulated peripheral blood mononuclear cells (PBMC), then with Phytohematoglutinin (PHA) blasts or natural killer (NK) cells in a direct contact or separated by a transwell membrane. After 3 days of co-culture, lymphocytes, adherent cells and the supernatant were collected for, respectively, the measure of lymphocyte proliferation (Hoechst assay) and cyototoxicity (DELFIA EuTDA cytotoxicity assay), the analysis of immunosuppressive factors expressed by WJ-MSCs and ELCs (quantitative PCR) and the dosage of secreted factors in the medium by BD™ Cytometric Bead Array (CBA).

Results: Before differentiation**,** WJ-MSCs were positive for MSC markers (CD73, CD90, and CD105) and negative for hematopoietic (CD34 and CD45) and immune (CD86 and HLA-DR) markers. During the differentiation process, no expression of HLA-DR and CD86 was detected. After differentiation, endothelial phenotype was confirmed by the expression of CD31, VE-Cadherin and VEGFR2. ELCs showed a positive expression of vWF and were able to uptake Ac-LDL. DNA quantification of stimulated PHA blasts and NK cells showed that ELCs, like WJ-MSCs, significantly inhibited their proliferation by a mechanism probably associated to a direct cellular contact between receptors and their ligands expressed on the surface of cells from both populations in co-cultures. ELCs also partially inhibited the cytotoxicity of NK cells against target cells (K562). IL-12p70, IL-8 and TNF-α concentrations were decreased while IL-6 concentration was increased in the supernatant of cultures with ELCs compared to stimulated lymphocytes alone. Among the immunosuppressive factors expressed by ELCs, indoleamine-2.3-oxygenase (IDO), TGF-β, MMP-2 and MMP-9 may be involved.

Conclusion: Endothelial differentiation of WJ-MSCs seems not to influence their immunosuppressive functions, suggesting their possible use in vascular tissue engineering.

DEFINED THREE DIMENSIONAL MICROFIBROUS SYSTEM FOR PATIENT-SPECIFIC IPSC GENERATION AND DIRECT DIFFERENTIATION

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Directed differentiation of specific lineages from patient induced pluripotent stem cells (iPSCs) holds great promise for constructing development or disease models, drug screening tools or cellular therapies. The current challenge in realizing these potential applications is to develop scalable culture systems to control iPSC self-renewal and tissue-specific differentiation. A wide spectrum of materials, including natural proteins, synthetic polymers and nanomaterials has been used for stem cell culture. However, these involve 2D culture systems which lack scalability and the appropriate three-dimensional microenvironmental cues for stem cell physiological control, imposing a major limitation in their biomedical application. We report herein an interfacial polyelectrolyte complexation (IPC) fibrous system for patient-specific iPSC generation, long-term self-renewal and tissue-specific differentiation under chemically defined conditions. The complexation between two oppositely charged polyelectrolytes leads to the formation of an insoluble complex, which can be drawn from the solution interface to form nano- to micro- scale IPC fibers. The mild processing conditions of IPC, including the use of aqueous solutions at room temperature, enable the incorporation of cells and protein, resulting in a highly tunable biomaterial for cell culture application. A floating culture format of cell-fiber constructs enables uniform high cell loading density and cell growth while an enzyme decapsulation method allows quick recovery of encapsulated cells with full preservation of cell viability and 3D organoidal structure. By manipulating the defined culture conditions, we efficiently achieved i) generation of viral-free transgene-free patient-specific iPSCs; ii) maintenance of long-term self-renewal of the derived iPSCs; iii) directed differentiation of these iPSCs into tissue-specific cells (> 90%), which were non-tumorigenic when transplanted into severe combined immunodeficient (SCID) mice. These results bring us one step closer towards realizing large-scale production of patient-specific iPSCs and their derivatives for clinical and translational application.

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