Final Report - Belgian Symposium on Tissue Engineering (BSTE) 2012

(A) SUMMARY

Date : 17th - 18th September 2012

Venue : Auditorium BMW 6, Building O&N2, Fac. of Medicine, KU Leuven. Partner universities : Ghent University, Vrije Universiteit Brussel, University of Liège

Description :

The first ever, two-day national symposium on tissue engineering was successfully organised by "**Prometheus** - the Leuven Research & Development Division of Skeletal Tissue Engineering of the **KU** Leuven (http://www.kuleuven.be/prometheus". It represented an interuniversity initiative that was coorganised by tissue engineering oriented research groups from partner universities across Belgium, namely:

- (a) the Polymer Chemistry and Biomaterials Group, headed by Prof. dr. Peter Dubruel, Ghent University.
- (b) the Tissue Engineering Group, headed by Prof. dr. Maria Cornelissen, Ghent Unviersity.
- (c) the Liver Tissue Engineering Group, headed by Prof. dr. Leo van Grunsven, Vrije Universiteit Brussels.
- (d) the Biomechanics Research Unit, headed by Prof. dr. Liesbet Geris, University of Liege.

This symposium attracted a significant number of young scientists nationwide (97 peoples out of 125 in total) as well as internationally (20 peoples from Germany, United Kingdom, United State of America, Canada, The Netherlands, France, Poland, Switzerland and Australia). Together they contributed to nearly 60 accepted abstracts (after stringent review by a scientific committee). Among these, 24 outstanding abstracts were selected by the scientific committee for oral presentation in six "young scientist forum (YSF)" sessions that were distributed over the two days. All other accepted abstracts were presented in the poster session.

In addition, the symposium was streamlined with **8 invited lectures** by world renowned scientists on a series of scientific questions formulated based on a thorough study by Prometheus on the state-of-the art of tissue engineering and its' limitations, specifically for bone engineering. These included:

- (1) Novel approach to engineer large quantities of human mature bone for autologous transplantation.
- (2) The state-of-the art on the fabrication of "designed" tissue engineered products, including automation for robust stem cell bioprocessing, microengineering and 3D tissue assembly & tissue formation.
- (3) Vascularization strategies for TE Constructs, focusing on angiogenesis versus inosculation.
- (4) The advance of pluripotent stem cells (iPS) technology to produce alternative stem cells population for cartilage and bone tissue engineering based on the developmental biology approach.

List of Invited Speakers:

- (a) Prof. dr. Molly Stevens (Imperial College London, UK). Topic: Bioinspired Materials for Regenerative Medicine.
- (b) **Prof. dr. Athanasios Mantalaris** (Imperial College London, UK). Topic: *Are We Culturing Cells in A "Natural" or "Engineered" Manner? Implications for Tissue Engineering & Stem Cell Therapy Approaches*
- (c) Dr. Farlan Veraitch (University College London, UK). Topic: Engineering Robust, Reproducible and Efficient Stem Cell Bioprocesses
- (d) **Dr. Mehmet Dokmeci** (Harvard Medical School, USA). Topic: Microengineered Tissue Engineering Constructs for 3D Tissue Assembly & Tissue Formation
- (e) **Dr. Matthias W. Laschke** (University of Saarland, Germany). Topic: *Vascularization Strategies for Tissue Engineering Constructs: Angiogenesis versus Inosculation*
- (f) Dr. April Craft (University Health Network, Canada). Topic: Pluripotent Stem Cells: A Developmental Approach for Cartilage and Bone Tissue Engineering
- (g) **Dr. Martin Stoddart** (AO Research Institute Davos, Switzerland). Topic: *Mechanically Induced Chondrogenesis Mimicking the In Vivo Enviroment In Vitro*
- (h) **Dr. Peter Peumans** (IMEC, Belgium). Topic: Semiconductor Technologies and Methodologies for Bio-manufacturing Process Control

(B) DESCRIPTION OF THE SCIENTIFIC CONTENT OF & DISCUSSION AT THE EVENT

This symposium consisted of 4 main topics which were addressed in 4 sessions over the two days. Each session was primed with one or two invited lectures by international experts presenting the state-of-the art and their latest research technologies/findings, to initiate discussion on that specific topic. The sessions were then followed by a "young scientist forum (YSF)" where outstanding research findings relevant to the topic by young researchers were presented.

The first session was focused on "Vascularisation strategies for tissue engineering constructs", combined with "Bone developmental strategies to promote ossification via chondrogenesis and hypertrophy events". Dr. M.W. Laschke, from the University of Saarland, Germany, introduced the use of a skinfold chamber to study angiogenesis and inosculation of implanted 3D scaffolds (that were prevascularised *in vivo*) via intravital fluorescence microscopy, and have shown the acceleration of blood perfusion in prevascularised constructs after implantation as compared to non-prevascularised controls. Inosculation was further optimised by short-term precultivation or by embedding constructs in a pro-angiogenic extracellular matrix. Spectacularly, the used of microvascular fragments (that were derived from adipose tissue) within the constructs was shown to rapidly formed new microvasculature networks which inosculated with the host blood vessels upon implantation. This represents a simple prevascularisation strategy that may play a significant contribution to the success of tissue engineering applications in the future. Besides that, distinctive studies on the interactions between MSC-like periosteal cells and blood vessels during bone autograft healing, and the used of dental stem cells as alternative source for angiogenesis were brought to discussions in the first YSF session. Regarding the developmental approach for bone formation, Dr. A.M. Craft, from the McEwen Centre for Regenerative Medicine, Canada, presented her fascinating findings on the generation of highly enriched population of growth plate-like (GPC) and articular chondrocytes (AC) through BMP4 and GDF5 treatments on mouse embryonic stem cell (mESC)-derived somatic populations respectively, where implantation of such tissue construct by co-culturing both cell types resulted in the development of cartilage tissue that became ossified within eight weeks without teratoma formation. This study demonstrated a robust technique to produce distinct populations of m

signalling pathways, which may lead to the development of novel therapies for skeletal defect repair. From a YSF point of view, co-culturing mesenchymal stem cells at different stages of chondrogenic differentiation within tissue engineering constructs, presented by a PhD student from the AO Research Institute, Switzerland, and the development of a semi-autonomous model of endochondral ossification, presented by Dr. Scott Robert (from Prometheus), were the selected outstanding studies in the first YSF to further evidence this strategy on developmental bone tissue engineering.

The second session highlighted the latest development in technological tools for "3D tissues assembly and formation" and for "In vitro mimicking of in vivo microenvironment to enhance biological parameters of tissue engineering constructs". At first, Dr. Mehmet R. Dokmeci, a senior microelectronic engineer and instructor at the Harvard medical School, USA, talked on their "top-down" and "bottom-up" micro-fabrication techniques for patterning 3D microgels and the assembly into 3D macro-tissues. This included the use of photopatterning to create microchannels to enhance cell viability inside thicker tissue constructs, and the incorporation of nanomaterials such as carbon nanotubes and grapheme oxide particles into hydrogels to create electrically conductive hydrogels with tunable mechanical properties. Then, it was our pleasure to have Prof. M. Stevens, from the imperial College London, U.K., talk on their recent development in bioinspired nanomaterials for tissue regeneration. They focused on the design of bio-responsive nanomaterials, and the control of nanoscale topography and chemistry of nanostructured scaffolds that mimic the nanostructure of the tissues in the body. The session then continued with contributions from selected young researchers on the production of controlled tissue constructs via high-throughput platform, manipulation of hydrogel properties to create controlled porosity, mechanical stimulation of in vitro engineered 3D bone tissue, and the modulation of cell differentiation with microenviroment mimicking the in vivo conditions.

The third session emphasised on the quality of routine *in vitro* cell culture technology and the influence of culture parameters on the *in vivo* outcomes, as well as latest technologies that are applicable for non-invasive, online cell culture quality assessment and monitoring. We first had Prof. A. Mantalaris, from the Imperial College London, UK, and Dr. Farlan Veraitch, from the University College London, UK, to talk on the implications of current cell culture technologies for tissue engineering and stem cell therapy approaches, and the engineering of robust, reproducible and efficient stem cell bioprocesses. Hereby, microsensors were implemented and cellular metabolites were monitored and used as markers for the assessment of the specific stages of cell differentiation or tissue development. Then, Dr. Peter Peumans, from IMEC, Belgium, introduced semiconductor technologies and methodologies as novel tools for bio-manufacturing process control, where chip sensors can be incorporated into the bioreactor for high-throughput screening and assessment of the culture parameters. In the respective YSF sessions, novels technologies for multi-parameter control of *in vitro* cell cultures based on standard silicon fabrication methods were presented, including a new technique based on lens-free imagers that offer ultra-compact imaging solution and 3D reconstruction. In addition, computational modelling based on dynamic graph model to assess the importance of biological actors in cell differentiation, generation of functional human hepatocytes using a micro-liver device, non-invasive 3D quantitation of cartilage subarchitecture using high resolution nano-computed tomography, and the engineering of skeletal muscle with autologous deposited extracellular matrix, are among the others interesting research methodologies that were presented in the YSF sessions.

The last session was headed by the lecture of Dr. Martin Stoddart, a senior researcher from AO Research Institute Davos, Switzerland, who talked on the use of a custom built loading device (combining compression and shear stimulations) to mimic the mechanics of *in vivo* joint environment *in vitro*, in order to

induce chondrogenesis for cartilage regeneration. This strategy may represent a novel cartilage repair therapy which utilise rehabilitation protocols to optimise cartilaginous differentiation of MSCs. This session was concluded with a selection of outstanding studies by young scientists, on topics about novel biomaterials as 3D scaffolds for cell encapsulation and tissue engineering, as well as growth factors incorporation and control-release.

Two awards were awarded to the best oral presenter and the best poster presenter selected from the YSF and poster sessions based on the scoring system below:

- For oral award, each presentation will be evaluated by three judges (i.e. the chairs of a session) based on a score system (0 10 points), and the top scorers of every sessions will then be selected as finalists for the award. Final decision will then be made by only the invited speakers for the best oral presentation award to ensure fairness of the competition.
- For poster award, only the non-oral presenter can compete for this award. During the poster session, each invited speakers and principle investigators (PIs) of the organiser and co-organisers will nominate two poster presentation together with the score, and the best scorer will then be selected for the best poster award. In the case of equal scoring, final decision will then be made by only the invited speakers for the award.

(C) ASSESSMENT OF THE RESULTS AND IMPACT OF THE EVENT ON THE FUTURE DIRECTION OF THE FIELD

This symposium was the first ever event on tissue engineering in Belgium, which has gathered the respective scientific communities within the country and also international experts and young researchers to share and discuss the state-of-the art and latest findings on such an interdisciplinary field of research. Through this meeting, individual local research groups that are active in tissue engineering, stem cell, biomaterials, and computational modelling researches were recognised by the local and international scientific communities and the research networking was thus nurtured. Specifically, this event has resulted in an positive impact on the following:

- (1) Promoted scientific networking and potential collaborations within the related research communities in Belgium and at international level.
- (2) Encouraged young scientists to participate actively in research publications, soft skills development, networking and direct interaction with PIs.
- (3) Gained further insights on both the state-of-the art and bottlenecks exists in the research field of tissue engineering through the keynote lectures, which are beneficial for re-positioning of current research tracks towards better outcomes.

Analysis of participants:

PhD student : 38 peoples
Postdoc researchers : 27 peoples
KU Leuven participants : 49 peoples
Others (faculty/Industrial/research staff) : 33 peoples

: 20 peoples

(D) FINAL PROGRAMME

Scientific Program Monday, 17th September 2012

8:15 – 9:00	Registration					
9:00 – 9:15	Welcome Prof. Dr. Frank P. Luyten (Chairman, Prometheus, KU Leuven, Belgium)					
9:15 – 10:00	Invited Lecture 1: (Chair: FP. Luyten) Vascularization Strategies for Tissue Engineering Constructs: Angiogenesis Versus Inosculation PD Dr. Matthias W. Laschke (Univ. of Saarland, Germany)					
10:00 – 10:20	Coffee Break					
10:20 – 11:05	Invited Lecture 2: (Chair: J. Schrooten) Pluripotent Stem Cells: A Developmental Approach for Cartilage and Bone Tissue Engineering Dr. April M. Craft (Univ. Health Network, Canada)					
Young Scientist Forum (YSF) 1 Chairs: J. Schrooten, MW. Laschke, R. Cornelissen						
11:05 – 11:20	Interactions between Periosteal Cells and Blood Vessels during Bone Autograft Healing: Implications for Tissue Engineering Strategies Nick van Gastel (KU Leuven, Belgium)					

11:20 – 11:35	Dental Stem Cells: Leading the Way Towards Angiogenesis Petra Hilkens (Univ. Hasselt, Belgium)						
11:35 – 11:50	Co-Culture of Mesenchymal Stem Cells at Different Stages of Chondrogenic Differentiation within a Tissue Engineering Construct: Effects on Chondrogenesis and Hypertrophy Oliver F.W. Gardner (AO Research Institute, Switzerland)						
11:50 – 12:05	A Semi-Autonomous Model of Endochondral Ossification for Developmental Tissue Engineering Scott J. Roberts (KU Leuven, Belgium)						
12:05 – 13:30	Lunch						
13:30 – 14:15	Invited Lecture 3: (Chair: L. van Grunsven) Microengineered Tissue Engineering Constructs for 3D Tissue Assembly & Tissue Formation Dr. Mehmet R. Dokmeci (Harvard Medical School, USA)						
	Young Scientist Forum (YSF) 2 Chairs: L. van Grunsven, MR. Dokmeci, Y.C. Chai						
14:15 – 14:30	Improved Neo-cartilage Formation in Dex-TA Hydrogels by Seeding Cell Micro-aggregates Produced in a Novel Controllable High-Throughput Platform Liliana S. Moreira Teixeira (Univ. Twente, The Netherlands/KU Leuven)						
14:30 – 14:45	Design and Development of Porous Pluronic-based Scaffolds for Tissue Engineering Mieke Vandenhaute (UGhent, Belgium)						

14:45 – 15:00	Development and Validation of A Bioreactor for Mechanical Stimulation of In Vitro Engineered 3D Bone Tissue Guenaelle Bouet (Université Jean Monnet, France)					
15:00 – 15:15	Generation of a Cell-Gelatin Scaffold for Hepatic Tissue Engineering Elien Gevaert (UGhent, Belgium)					
15:15 – 15:45	Coffee Break					
15:45 – 16:30	Invited Lecture 4: (Chair: S. Van Vlierberghe) Bioinspired Materials for Regenerative Medicine Prof. Dr. Molly Stevens (Imperial College London, UK)					
	Young Scientist Forum (YSF) 3 Chairs: M. Stevens, J.M. Aerts, S. Van Vlierberghe					
16:30 – 16:45	Dynamic Culture Conditions Modulate not only Osteoblastic Differentiation but also IL-11 and VEGF Secretion by hMSCs on 3D Coral Scaffolds Katleen Vandamme (KU Leuven, Belgium)					
16:45 – 17:00	Preconditioning Mouse Periosteal Cells to Hypoxia by Inactivation of the Phd2 Oxygen Sensor Improves In Vivo Ectopic Bone Formation Steve Stegen (KU Leuven, Belgium)					
17:00 – 17:15	Dynamic Control over the Mechanical Microenvironment During The Neuronal Differentiation of Mouse Embryonic Stem Cells Shahzad Ali (Univ. College London, UK)					
17:15 – 17:30	Sox9 Reprogrammed Dermal Fibroblasts Undergo Chondrogenic Differentiation In Vitro and In Vivo Wai Long Tam (KU Leuven, Belgium)					

17:30 – 18:45	Poster Presentation & Networking (with reception)
20:00	Dinner @ Faculty Club, Leuven

Scientific Program Tuesday, 18th September 2012

8:15 – 9:00	Registration
9:00 – 9:45	Invited Lecture 5: (Chair: J.M. Aerts) Are We Culturing Cells in A "Natural" or "Engineered" Manner? Implications for Tissue Engineering & Stem Cell Therapy Approaches Prof. Dr. Athanasios Mantalaris (Imperial College London, UK)
9:45 – 10:30	Invited Lecture 6: (Chair: G. Carmeliet) Semiconductor Technologies and Methodologies for Bio-manufacturing Process Control Dr. Peter Peumans (Imec, Belgium)
10:30 – 11.00	Coffee Break
	Young Scientist Forum (YSF) 4 Chairs: A. Mantalaris, G. Carmeliet, P. Dubruel
11:00 – 11:15	Detection of Changes in Membrane Properties and Morphology in Single Cells for Tomorrow's Bioreactors Dries Braeken (Imec, Belgium)
11:15 – 11:30	A Dynamic Graph Model of Endochondral Ossification can Assess the Importance of Biological Actors in Differentiation Johan Kerkhofs

	(KU Leuven)					
11:30 – 11:45	Building a Microliver Device Sofia. B. Leite (VUB)					
11:45 – 12:00	High-Resolution Non-Destructive 3D Quantitative Imaging of the Cartilage Subarchitecture Greet Kerckhofs (KU Leuven)					
12:00 – 14:00	Lunch Break					
14:00 – 14:45	Invited Lecture 7: (Chair: H. Van Oosterwyck) Engineering Robust, Reproducible and Efficient Stem Cell Bioprocesses Dr. Farlan Veraitch (Univ. College London, UK)					
	Young Scientist Forum (YSF) 5 Chairs: H. Van Oosterwyck, P. Peumans, M. Stoddart					
14:45 – 15:00						
14:45 – 15:00 15:00 – 15:15	Chairs: H. Van Oosterwyck, P. Peumans, M. Stoddart Mapping Osteogenic Gene Networks to Target Osteoinduction by Human Periosteum Derived Cells In Vivo Jeroen Eyckmans					
	Chairs: H. Van Oosterwyck, P. Peumans, M. Stoddart Mapping Osteogenic Gene Networks to Target Osteoinduction by Human Periosteum Derived Cells In Vivo Jeroen Eyckmans (KU Leuven/UPennsylvania) Engineering of Skeletal Muscle with an Autologous Deposited Extracellular Matrix Lieven Thorrez					

16:00 – 16:45	Invited Lecture 8: (Chair: J. Patterson) Mechanically Induced Chondrogenesis — Mimicking the In Vivo Environment In Vitro Dr. Martin Stoddart (AO Research Institute Davos, Switzerland)
	Young Scientist Forum (YSF) 6 Chairs: J. Patterson, F. Veraitch, H. Declercq
16:45 – 17:00	Fabrication of 3D Porous Hydrogel Scaffolds for Cell Encapsulation Purposes Thomas Billiet (Univ. Ghent, Belgium)
17:00 – 17:15	Injectable 3D Implants Delivering GDNF for Spinal Cord Regeneration Anne des Rieux (Université Catholique de Louvain, Belgium)
17:15 – 17:30	Electrospun PCL/Gelatine Nanofibrous Membrane with Stromal Cell Derived Factor-1α (SDF-1 α) Release for Guided Bone Regeneration (GBR) Wei Ji (Univ. Nijmegen Medical Ctr., The Netherlands)
17:30 – 17:45	Development of a Dual Layer Electrospun Scaffold for Corneal Stroma Tissue Engineering Siobhán Dunphy (Univ. of Nottingham, UK)
17:45 – 18:00	Chitosan as Scaffold Material for Esophageal Defect Repair Very Coulic ('Université Libre de Bruxelles, Belgium)
18:00 – 18:30	Awards & Closing (YSF Oral & Poster Awards)

List of Participants

No.	Name	FirstName	Salutation	Position	Institution	Email
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