

Compiled and Edited by
Felicity Rose (Nottm) & Vivek Mudera (UCL)

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From the editors.....

If you wish to contribute to the TCES newsletter (next edition out Summer 2008) then please email us at....

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We are looking for articles of interest to the TCES community which may include conference reviews, research, or hot topics. We look forward to hearing from you!

Keep up to date with the latest on the TCES conference this year by checking out our website www.tces.org

Felicity & Vivek

TERMIS-EU 2007 - London

The 2nd Annual TERMIS-EU meeting was held at Regents College, London, from the 4th - 7th September 2007. The welcome reception was preceded by an Open Forum focussing on the drivers and inhibitors of stem cell research in the UK, with the panel consisting of eminent speakers including Baroness Warnock (Author of the Warnock 1984 report into human fertilisation and embryology) and Geoff Watts (BBC Journalist and Broadcaster). This was all kick-started by the Provost of UCL, Professor Malcolm Grant, and resulted in some interesting questions from the audience on changes to stem cell regulations, especially as it was only announced that very week that UK regulators would allow the use and production of human-animal hybrid embryos for research purposes, and the effect of emerging EU wide-laws to stem cell research in the UK.

The meeting continued with parallel plenaries on skin and neural regeneration. Of particular interest was a plenary by John Priestley, on the use of silks from silk worms to aid neural cell growth in peripheral nerves and spinal cord during regeneration, as well as Thomas Carlstedt on the surgical treatment of neural injuries.

Pankaj Vadgama gave an insightful lecture into the use of chemical and bio-sensing for Tissue Engineering, which really brought together ideas on how understanding metabolic profiles of cells could be used to non-invasively monitor 3D construct maturation. A lecture by Stephen Minger gave the audience a wonderful overview on controlling differentiation of Human Embryonic Stem cells, with some perspective on regulatory issues surrounding stem cells.

The Plenary on Layer Engineering of Tissues showed some of the commonality in direction of thinking with regards to this method of engineering. Teruo Okano focusing on the production of cell sheets for tissue engineering purposes and Robert A. Brown focusing on the use of acellular and cellular collagen sheets to engineer strong, biomimetic constructs. Other plenary sessions focussed on Cardio-Vascular

Engineering, Bone and its interface, Tissue Vascularisation and Embryonic Stem Cells for Regeneration.

Sessions were varied and topics ranged from Polymer Scaffolds to Tissue modelling, Angiogenesis to Cell Mechanics, and Nanobiotech Strategies for Regeneration to Fibrin and Injectable Scaffolds. The meeting really showed off the vast scope of Tissue Engineering as a field of scientific research, and brought together many experts from diverse backgrounds. Overall it was a great opportunity to explore ideas in a multi-disciplinary setting.

There was also much to do for younger researchers with an organised pub-walk and a hugely successful student-mentor session, which attracted 18 top academics, and well over 50 students. The scientists mentoring were able to offer genuine advice and guidance on career progression in science worldwide, as well as share some insightful tips on helping you get through it!

The meeting drew to a close with a well-attended conference dinner, in the centre of Regents Park, and marked the end of a stimulating opportunity to share knowledge and help in the advancement and understanding of a diverse and growing field. So now we look forward to the next annual meeting to be held in Porto, Portugal!

Umber Cheema & Alison Cambrey
UCL Stanmore

Research Article: Osteogenesis and Angiogenesis – pushing the skeletal envelope

The Bone and Joint Research Group in Southampton has been developing strategies to augment osteogenesis and angiogenesis for orthopaedic applications. Skeletal tissue engineering could offer additional therapeutic avenues to patients suffering from musculoskeletal problems. Angiogenesis plays a pivotal role in the development of the

skeleton and bone fracture repair. For critical-sized defects in particular, the development of an active blood vessel network is an essential pre-requisite for the survival and integration of the engineered tissue with the existing host tissue. In an attempt to mimic the macro- and micro-structure of bones, Shakesheff and Howdle *et al.*, (University of Nottingham) using supercritical CO₂ technology, have constructed novel biodegradable scaffolds from poly (D,L)-lactic acid (PLA) in a multi-channel configuration. Using this method, it is possible to encapsulate growth factors, such as vascular endothelial growth factor (VEGF), within the polymer structure. We have examined the bone regenerative potential of these scaffolds *in vivo*. These studies suggested that human bone marrow stromal cells (HBMSC) seeded on these VEGF-encapsulated PLA scaffolds and implanted in a femur-segmental defect resulted in significant bone regeneration (post 4 weeks) compared to the scaffold alone and scaffold seeded with cells (Figure 1) as analysed by micro-computed tomography (Micro-CT; Kanczler *et al*, *Biomaterials*, 2008 Jan 28; [Epub ahead of print]).

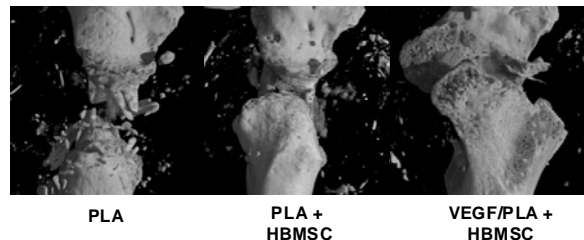


Figure 1. High resolution micro-computed tomography scans of the bone defect regions of interest 28 days post scaffold implantation in a mouse femur segmental defect model.

Understanding the vascular inductivity of tissue engineering scaffolds will provide greater insights for the bio-engineer and aid in the design of constructs and implants with greater compatibility. However, quantification and 3D visualization of new vessel networks within tissue engineered constructs remains a problem. To address this, we have applied a novel technique, utilizing a radio-opaque dye and micro-CT, to study the angiogenic response of osteoprogenitor cells in an impaction bone graft model. Tissue-engineered

constructs consisting of natural bone allograft and synthetic grafts (PLA) seeded with human bone marrow stromal cells, were impacted and implanted subcutaneously into mice for a period of 28 days. Microfil (Carver, USA; a radio-opaque polymer) was perfused through

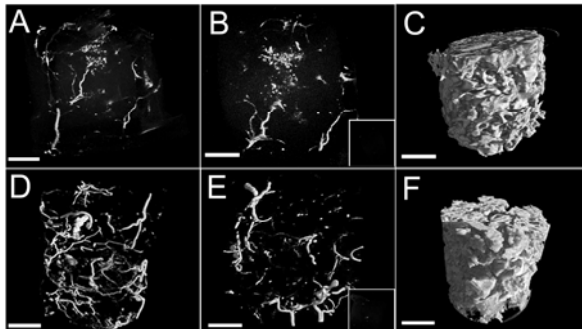


Figure 2 3D micro-CT visualization of vessel networks. micro-CT 3D reconstructions demonstrating new vessel formation outside (A) and inside (B) the impacted allograft/human bone marrow stromal cells capsules compared to allograft alone (B, insert) and outside (D) and inside (E) the impacted PLA/human bone marrow stromal cells samples compared to PLA (E insert) alone. 3D reconstructions of the impacted scaffolds: (C) allograft, (F) PLA.

the mice and scanned. Using this method, we were able to visualise the blood vessels and perform quantitative analysis using the micro-CT associated software. We found a significant increase in blood vessel volume, penetrating vessel number and mean vessel number in the scaffold/stromal cell groups compared to the scaffolds alone group (Figure 2; Bolland et al *Bone In Press* 2008)

Combination therapies of skeletal progenitor cells and polymeric growth factor release scaffolds tailored to promote angiogenesis and osteogenesis are under evaluation and development to actively stimulate bone regeneration. Additionally, data generated from the Microfil/micro-CT 3D vascular networks will undoubtedly prove highly beneficial to future scaffold microstructural design to potentially promote neovascularisation in tissue engineered bone constructs.

Janos Kanczler and Richard OC Oreffo
University of Southampton.

Wolfson Centre for Stem Cells, Tissue Engineering and Modelling (STEM) University of Nottingham

Opening Ceremony September 2007

The Wolfson Centre for Stem Cells, Tissue Engineering and Modelling (STEM) at the University of Nottingham was officially opened last year (September) by Sir Keith O'Nions, Director General Science and Innovation at the Department for Innovation, Universities and Skills. STEM is a new multidisciplinary research centre based within The University of Nottingham's £25m flagship Centre for Biomolecular Sciences (CBS) which opened in May and houses 300 world-leading scientists dedicated to solving the global healthcare challenges of the future.

STEM brings together a unique combination of scientists who are internationally recognised in their field including stem cell biologists from the School of Human Development, tissue engineers from the School of Pharmacy and mathematical modellers from the School of Mathematical Sciences. Their work focuses on producing skeletal, brain, epithelial and heart tissues for treating patients and to increase our understanding of diseases and the drugs that may treat them. In addition, the group is involved in the development of scaffold materials for tissue engineering and controlled release devices for regenerative medicine *in vivo*. The experimentalists are working closely with mathematical modellers to develop models of their research to understand the experimental systems in more detail and to better inform future research.

Sir Keith O'Nions, a British scientist and graduate of The University of Nottingham who is a champion of scientific research and development said: "The UK is a world leader in stem cell research and development. First class scientific research facilities such as STEM and our brilliant researchers are all vital to our continuing success in this area".

A number of guest speakers were invited to contribute to the seminar programme that was held to celebrate the official opening of STEM. Those presenting recent advances in stem cell

biology included Boris Reizis, Assistant Professor Columbia University New York who discussed the role of Zfx in embryonic and haematopoietic stem cell self renewal. Dr Mary Hendrix, Director of the Children's Memorial Research Centre, Chicago spoke about the reprogramming of metastatic tumour cells and Dr Kirsty Spalding, Karolinska Institute presented her research on the analysis of neurogenesis in the adult human brain. The challenges and logistics of translating stem cells into clinical therapies were discussed by Dr Cathy Prescott, Biolatris Ltd and Fiona Fox from The Science Media Centre. Examples of research that is crossing disciplines were highlighted by Professor Richard Oreffo, Southampton with respect to utilizing mathematical modelling and mesenchymal stem cells for bone regeneration. Dr Molly Stevens, Imperial College presented her research on bio-inspired materials for tissue engineering and sensing, and Professor Joel Voldman, MIT, spoke about microtechnology for studying embryonic stem cell self-renewal and differentiation.



Sir Keith O'Nions opens the Wolfson Centre for Stem Cells, Tissue Engineering and Modelling (STEM) at the University of Nottingham. With Sir Keith is Professor Lorraine Young, Director of STEM.

Professor Herb Sewell, Pro Vice Chancellor for Interdisciplinary Research (IDR) at Nottingham said: "STEM is an exciting example of how major challenges in 21st century research needs to be addressed by IDR teams. STEM academics have strong foundations in high quality discipline-based subjects, providing an

excellent model that is reflective of other IDR activities across our University and beyond".

From this October the new centre will run the world's first taught MSc in Stem Cell Technology to train the next generation of scientists required to cope with the world wide expansion of this field. The Schools of Human Development and Pharmacy have joined forces to develop this innovative MSc programme. Its introduction is in response to employers' needs for skills training and interest from graduates wishing to undertake a career in a rapidly developing area of science and biomedicine.

Felicity Rose, Lindsay Brooke & Tim Utton
University of Nottingham

TCES Early Stage Investigator Award 2007

Dr Molly Stevens
Imperial College London

It was an honour to be recognised by the TCES Early Stage Investigator Award in September last year, six years after completing my PhD. A lot has happened in this time and my research has moved in several new and exciting directions. My undergraduate studies were in Pharmaceutical Sciences after which I completed a year working in hospital (a mixture of clinical care, drug information and research) and then took a well earned break travelling around Asia. I decided to do a PhD in single molecule AFM at the University of Nottingham in the Laboratory of Surface Analysis, mainly as a challenge and because it seemed like an exciting multidisciplinary project. The skills gained in biomolecule self-assembly and in a whole range of surface analytical techniques have been useful ever since. I was lucky to have supervisors that were supportive of my desires to explore some quite new investigations into coiled-coil proteins and I was able to set-up a very fruitful collaboration with Professor David Tirrell at Caltech (California, US).

I chose to do a postdoc at MIT with Professor Langer as I found his work very inspirational,

particularly the fact that he was using high quality scientific research to address engineering challenges with a real impact on human quality of life. This work within the field of tissue engineering is now a central research theme in my group. Whilst at MIT I became very interested in bone regeneration and was able to develop new approaches to bone and cartilage tissue engineering which resulted in both high quality publications and a lot of international attention.



Dr Molly Stevens receives the TCES Early Stage Investigator Award 2007 from Prof Alicia El Haj, President of the TCES.

I returned to the UK mainly for personal reasons but chose Imperial College as my base as it has an excellent science foundation and also strong support for entrepreneurial activities and translation of research – very important for clinically relevant areas such as tissue engineering. I took up a lectureship in the Department of Materials in 2004 and was, the following year, promoted to a readership jointly between the Department of Materials and our new Institute for Biomedical Engineering. It has been a really exciting time and I have been directly involved in designing all our new state of the art labs in the Institute into which we moved in 18 months ago. I'm

now Research Director for Biomedical Materials within the Institute. I am blessed with a terrific research group comprising cell biologists, materials scientists, biomedical engineers, chemists, physicists, surgeons and working on bioactive scaffolds for bone and cartilage regeneration as well bio-functionalised nanoparticles for sensing of enzymes and other biologically relevant stimuli. The research in my group covers some very fundamental areas (e.g. trying to understand how cells recognise surfaces or how molecules self-assemble) as well as some more applied areas (e.g. development of nanomaterials for biosensing and scaffolds for tissue engineering).

Last year I co-founded BioCeramic Therapeutics Ltd (with Professor Robert Hill) and am CSO of the company. Setting up this spin-out company is enabling us to further develop and translate our biomaterials so they can find more rapid application in the clinic.

TCES Early Stage Investigator Award 2008 – call for nominations

TCES is calling for nominations for the Early Stage Investigator Award again this year. The award is designed to acknowledge individuals, like Molly Stevens, who have demonstrated research excellence at the start of their career in the field of Tissue and Cell Engineering. The award scheme is open only to those that are members of the TCES. To apply, applicants must have at least 3 but no more than 8 years postdoctoral experience. Those that have taken a career break are still eligible to apply as long as the total number of years at post-doctoral level does not exceed 8 years. Each submission requires a reference to support the application and a second nomination. Referees must also be TCES members and will be emailed to confirm their support for the application. The committee will decide on the winning nomination in May and the Award will be presented at the TCES2008 conference in Nottingham. The winner will be required to present an overview of their research at the conference and write a

short article for the newsletter; they will also win a cash prize.

The closing date for nominations will be 30th April 2008.

Please email completed nomination forms to Professor David Lee (d.a.lee@qmul.ac.uk). Forms are available on the TCES website and on request via email.

TCES Travel Bursary

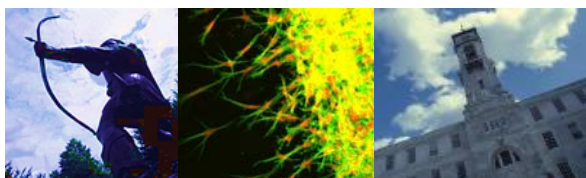
Don't forget that the TCES is providing travel bursaries (maximum £150) to TCES members (post-graduate and post-doctoral researchers) to help promote tissue and cell engineering research. To be eligible to apply, you must have had an abstract accepted for a conference (national or international) which is relevant to the TCES. Only one award will be given per person per academic year and the applicant must provide proof of abstract acceptance from the conference committee & a supporting statement from their supervisor. Applicants who receive an award will have to write a short summary about the conference for the TCES newsletter. Application forms and further details are available on our website.

TCES Annual Society Conference 2-4 July 2008 Nottingham

Abstract Deadline – 7 April 2008

Notification of Acceptance - 25 April 2008
Early Bird Registration - 30 May 2008

Visit the TCES website for abstract template, information and registration forms
Email abstract submissions to tces2008@nottingham.ac.uk



TCES 2008 will be held at Nottingham

Winter 2007/8

Forthcoming Meetings

Regenerative Medicine: Moving to the Next Generation of Therapies
Hilton Head Island, SC USA
12 – 16 March, 2008
www.hiltonhead.gatech.edu

British Society for Matrix Biology Spring 2008 Meeting
York, UK
7-8 April 2008
www.bsmb.ac.uk

World Biomaterials Congress
Amsterdam, The Netherlands
28 May - 1 June 2008
www.wbc2008.com

6th ISSCR Annual Meeting (International Society for Stem Cell Research)
Pennsylvania Convention Center
Philadelphia, PA USA
11 – 14 June 2008
www.isscr.org/meetings

TERMIS-EU Porto, Portugal
Porto Congress Center, Alfândega, Portugal
22 - 26 June 2008
www.termis.org/eu2008

Bone Research Society & British Orthopaedic Research Society
Manchester, UK
23 - 25 June 2008
www.brsoc.org.uk

UK Society for Biomaterials
University of Liverpool, UK
26 – 27 June 2008
www.uksb.org.uk/conference

European Society of Biomechanics
Lucerne, Switzerland
6-9 July 2008
www.esb2008.org/

2nd International Congress on Stem Cells and Tissue Formation
Dresden, Germany
6 – 9 July, 2008
www.stemcellcongress-dresden.de