

Compiled and Edited by
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President's Statement

Congratulations to Dr Matthew Dalby from the University of Glasgow for winning the first TCES Early stage investigator award. He was presented with his prize at the TCES annual conference, Sheffield, in June this year where he presented a keynote on his work entitled 'nanoscale stem cell engineering and topographical mechanotransduction'. I would like to encourage more applications for next year's award which will be presented at the combined TCES/TERMIS meeting in London 2007.

The meeting at Sheffield was well attended and well run in the midst of a UK heatwave! The successful meeting was a good indication of how the Society is growing and I would like to thank the organisers for their efforts. I am particularly pleased to see continuing expanding representation from the postgraduate and postdoctoral community representing many Universities across the UK and Europe. At the AGM we nominated an

industrial representative to the TCES Committee, Dr Stephen Curran from Smith and Nephew and our industrial keynote from Bose EnduraTEC was well received.

New initiatives within the Society are to offer a travel award which is open for members to apply. The conditions are explained within the Newsletter but the aim is to support researchers attending tissue and cell engineering conferences both nationally and internationally. Finally, next year, we aim to run a spring meeting for 'early stage' researchers in Oxford as we did previously in 2004 in Keele. This will be followed by our combined efforts with the European Chapter TERMIS meeting in London in September 2007. We hope you will join us in presenting your work at these meetings!

Alicia El Haj
President
Tissue and Cell Engineering Society

From the editors

If you wish to contribute to the TCES newsletter (next edition out Winter 2006) 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!
Felicity and Vivek

Regenerate World Congress on Tissue Engineering and Regenerative Medicine. April 2006 Pittsburgh, USA.

The Regenerate World Congress / TERMIS meeting held in Pittsburgh, USA (25-27th April 2006) was co-located with the Society for Biomaterials (<http://www.biomaterials.org>) which was held on April 26 – 29th. This international conference attracted over 700

attendees, over 200 of which were students. Student participation and networking in the conference was actively encouraged by events such as student 'meet and greet' and 'student meet mentor'.

The program included a keynote from Dr Gregory Stock, UCLA in which interesting ethical and sociological issues relating to tissue engineering were raised. Delegates also received a copy of one of Dr Stock's books – 'Redesigning humans, choosing our genes, changing our future' to read further on the subject. Dr J.J. Collins from Boston also delivered a keynote describing the interrelationship between the life science and materials science disciplines.

A pre-congress tutorial was held addressing clinical translation of regenerative medicine therapies. This issue was continued during the congress in an interesting debate held in the 'linking pre-clinical and clinical studies' panel session. The session involved panellists from industry, the FDA and academia and the discussion included opinions on issues such as the need for alteration of current standardized ISO / FDA tests in order to distinguish the difference between a medical device and a tissue engineered product.

The scientific sessions were of high quality in both the oral and poster sessions. Presentations in cardiovascular, neural, orthopaedic, embryonic stem cells and bioreactor design areas (to name just a few) were covered.

The cardiovascular sessions included talks that highlighted the following advances: vitrification as a feasible method of storing tissue engineered arteries, temperature-responsive polymers which can be utilised for convenient cultivation of human tissue and the role of HBGM-FGF-1 released at low levels over an 8 day period from calcium alginate gels.

Neural sessions highlighted: The role of FGF-2 for the establishment of the proper number of dopaminergic (DA) neurons in the SNpc (substantia nigra pars compacta (the heterogeneous portion of the mid brain) during regeneration, effect of Schwann cells

prealigned as artificial bands of Bungner on polymer filaments before integration into semi permeable, resorbable nerve tube guides (prior to implantation), 3D patterning using confocal multiphoton laser patterning and effect of chemically modified coumarin agarose hydrogels to guide neural cell growth.

The orthopaedic audience benefited from data on enhanced expansion of stromal cells by perfusing cell seeded porous scaffolds, potential of statins for bone tissue engineering, and a study on tendon to bone interface created using a co-culture on a triphasic scaffold.

Embryonic stem cell researchers were informed of the feasibility of expanding hES cells in 3D using hMSC-encapsulated fibrous scaffold as a support. Results showing a CD146+ subpopulation of hES cells able to differentiate into haematopoietic, myogenic and neurogenic cells were also presented.

Bioreactor design sessions highlighted the following: an *in vivo* bioreactor design for the growth of a new trachea, the demonstration of a multicoaxial bioreactor for liver tissue engineering (metabolically functional for at least 31days) and a novel biohybrid lung prototype utilising a rotating endothelialized microporous hollow fibre bundle.

A special session dedicated to advances in cell culture media was also included. This session addressed issues such as problems with using animal derived sera and the potential of using autologous human sera instead for clinical *in vitro* tissue growth (invited speaker Jan Brinchmann, Oslo, Norway).

After attending this regenerate meeting, it was clear that in comparison, the research presented at our national TCES meeting was in line with quality and direction of research. The next Regenerate conference will be held June 13 – 16th 2007 in Toronto Canada (see <http://www.regenerate-online.com>)

Dr Sarah Cartmell
Keele University

Mathematical modelling in Tissue Engineering

Mathematical modelling has been applied to complex systems for many years, but only to biological systems for about the last 30 years. Tissue engineering, in particular, provides many opportunities for mathematical modelling, for example in cell signalling, cell-substrate interactions, and cell movement and tissue growth.

A mathematical model describes a complex system by a set of equations, which depend on variables specific to that system. The aim of the modeller is to take the information that is already known about the system and formulate a set of governing equations, reducing the complexity of the system and identifying its key features. These equations usually include a conservation equation, for example, it is possible to calculate the rate at which a cell population increases if the number of births and deaths in the population is known. This would give an equation that looked something like:

$$\text{net increase in population} = \text{number of births} \\ - \text{number of deaths.}$$

The skill of modelling comes in reflecting the existing biological knowledge in the individual terms of the mathematical equation. For example, the presence of growth factor might increase the birth rate of cells in the population. We can improve the simple model above by adapting the term for the number of births, making it dependent on the amount of growth factor present. By adding more dependencies, a comprehensive model of the growth of a cell population can be built up.

These systems are solved using a combination of analytical solution methods and computer simulation over the relevant range of physiological parameter values. For example we could solve the population model above for a wide range of growth factor levels, ranging from the very small to the very large. This may generate many model predictions, for example the level of growth factor that ensures a confluent cell population is obtained

within a few days. These predictions can only be tested by comparison with experimental data. A tissue engineer could culture a population of cells and then administer growth factor, testing from just below the predicted level to just above. In a perfect world these results would corroborate each other and a paper published!

The more likely outcome for such a simplified model is that the results will not corroborate each other straight away. The new data generated from this experimental work can be used by the mathematician to tweak terms in the equation. In some cases it may be necessary to add additional physics or dependencies in order to gain corroboration.

There are a number of benefits to trying these ideas on a computer before testing them in a laboratory. Firstly, it is possible to focus on just one aspect of the biology, holding all other variables constant. Secondly, simulations can be run on a computer much faster than experiments can be carried out in the laboratory. By running many simulations it is possible to suggest the most fruitful lines of inquiry to be pursued in the laboratory, thus reducing the cost of experimental work. Finally, predictions from the mathematical model may suggest avenues for experimental investigation that had not previously been considered.

As for most sciences, a comprehensive mathematical model can take years to develop, test and refine. The expectation of such models should be reasonable, but with good collaboration between tissue engineers and mathematicians it is possible for a mathematical model to provide useful and guiding predictions in the world of tissue engineering.

Sarah Eastburn
School of Mathematical Sciences
University of Nottingham

TCES Conference at Sheffield University July 2006

In a break from the usual English summer, it was a bright sunny day on the 3rd of July when over 100 delegates descended upon Ranmoor House at the University of Sheffield for the TCES annual conference. After a sumptuous lunch, the conference swung into full gear with an enthused talk on the role of *in vitro* techniques in tissue engineering by James Kirkpatrick. This was followed by a series of presentations highlighting the role of scaffolds and 3D models in tissue engineering. The second session of the afternoon was opened by Christopher Jacobs from Stanford University. He gave a fascinating presentation on mechanotransduction in bone with insight into the effect of dynamic flow on cells. This keynote lecture then paved the way for several more presentations on mechanobiology. As



Kathryn Lazenby from the Open University receives 1st prize in the 'Best Poster' Competition from Alicia El Haj.

the day wound down, delegates had the opportunity to view a wide range of posters covering recent progress by researchers in a variety of niche areas including stem cells, cell biology and computer modelling.

Later that evening, the conference centre was emptied as the delegates congregated at Hassop Hall for dinner. In the stunning countryside backdrop, the wine flowed and everyone dined surrounded by beautiful artwork and the mellow sounds of a live jazz band. Reluctantly, at midnight, the guests made a return to Ranmoor House to rest for the night.



Second prize in the poster competition went to Umber Cheema, UCL.

The sun did not disappoint on the 4th of July and as its warm rays filtered down, the second day of the conference began in full fervour. Sheila MacNeil gave a keynote lecture on translating tissue engineering research into commercial clinical products and this was a theme echoed by the subsequent set of presenters. After a quick coffee break, the last discussions of the morning centred on bioreactors and advances in imaging. The final session of the conference took place in the afternoon with the poster award presentation which was won by Kathleen Wright. The TCES early stage investigator award recipient, Matthew Dalby, then gave a fascinating talk on cell response to topography and the use of micro arrays to study cell behaviour. A series of speakers then followed, each covering an emerging topic in tissue engineering.

The conference then came to an end but not before one of the main organisers, John



Mark Aherne, Keele University, receives 3rd prize in the 'Best Poster' competition.

Haycock, won a state-of-the-art set of headphones that was donated for a raffle by one of the conference sponsors (BOSE). It was a memorable meeting, not just for the spectacular weather but also because it drew in a large number of prolific researchers based in UK institutions as well as internationally. It was a unique opportunity to exchange ideas and learn about current advances within the fields of tissue engineering and cell biology.

Ruby Majani
Tissue Engineering Group
University of Nottingham

Early Stage Investigator Award – Dr Matthew Dalby.

After completing a degree in Biomedical Chemistry, I started my research career at the IRC in Biomedical Materials, Queen Mary, University of London working towards a PhD with Dr Lucy Di Silvio and Prof Bill Bonfield. During this time, I developed interests in surface effects on osteoblasts; specifically bioactive island and topographical effects. Thus a logical move was to the Centre for Cell Engineering in late 2000 to start a PDRA investigating cellular responses to nanoscale topography with Profs Adam Curtis, Chris



Dr Matthew Dalby received the first TCES Early Stage Investigator Award this year.

Wilkinson and Dr Mathis Riehle. Here, I linked up with molecular biologists in order to move into genomic analysis in addition to the microscopical techniques I was familiar with. In 2003, I was awarded a BBSRC David Phillips Fellowship and have developed an invaluable collaboration with Prof Richard Oreffo (Southampton) in order to investigate stem cell tissue engineering with nanotopography.

Through learning to work in an interdisciplinary environment, I am striving to develop ideas towards product and along with Dr Nikolaj Gadegaard, a Royal Society of Edinburgh Fellow in nanofabrication, I have submitted a patent, been awarded a follow-on grant from the BBSRC and in addition to the usual publication routes, I have been interviewed about these ideas by journalists from the New Scientist and The Big Issue.

However, I strongly feel that as well as trying to get cells to elicit desired effects through the use of scaffold materials, we need to strive to understand what is happening with the cells. We have to be careful not to simply use cells as 'reagents' to understand material properties. We can, in fact, use the materials as non-invasive tools to try and understand more about how cells work, hence my interest in genomics and direct mechanotransduction. It is likely that topographical effects (and many effects) will start with adhesions and that the adhesions will directly affect the genome and proteome. To this end, I have two great PhD students, Manus Biggs and Fahsai Kantawong looking at the morphology of adhesions and proteomics of differentiation respectively.

As a young academic, the award of the TCES Early Stage Investigator Prize is of great value. Tenure is not always an easy thing to achieve – even with good publication record (I have around 40 papers) and growing success in the competition for grants (I have been awarded 3 grants as PI in 3 years) and I thank Alicia for promoting my availability! In my position, I need evidence from my peers that I am a successful researcher, and the award from the TCES is just this. The Centre for Cell Engineering is coming through a time of flux with the retirement of Adam and Chris, and Mathis taking on the directorship. However,

due to Mathis' promotion success, the award of a Royal Society / Wolfson refurbishment grant lead by Mathis (co-apps Nikolaj, Dr Catherine Berry, and myself) and the recent award of a third fellowship to the Centre (a Royal Society Dorothy Hodgkin Fellowship to Catherine), things are looking very positive in Glasgow.

I strongly recommend young researchers in Tissue Engineering to consider fellowship schemes as they are designed to allow creativity – although be warned as they also represent a very steep learning curve. Our success in the Centre with the fellowship schemes shows that Tissue Engineering is a priority area. I also very strongly recommend that young researchers apply to the TCES for the Early Stage Investigator Award. The TCES is a very good society and this award is good evidence of esteem, something every Head of Department will be happy to discuss with you, and I shall be making sure that my HoD knows about this award in the very near future!

Matthew Dalby
Centre for Cell Engineering
University of Glasgow

TCES Travel Bursary

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 Conference June 2007

TCES Spring Meeting: focus on early stage researchers. University of Oxford, UK.

Details of registration will be available on our website next year.

TERMIS 2006-7

Tissue Engineering and Regenerative Medicine International Society

European Chapter

Rotterdam Netherlands, Congress Center De Doelen.

8-11th October **2006**

www.etes2006.org

London, UK

5-8th September **2007**

Forthcoming Meetings

2nd Annual Tissue Engineering and Regenerative Medicine Conference - Hosting EuropaBio Policy Forum

Brussels, Belgium

7-8th November 2006

www.jacobfleming.com/buxus/generate_page.php?page_id=315

2nd International Conference on Biomaterials and Medical Devices - BiomMedD'2006

Iasi, Romania

9-11th November 2006

www.srb.ro/conference/biommedd2006/

Patenting, Regulating and Commercialising Stem Cells

Harrington Hall Kensington, London, UK
27-28th November 2006

www.c5online.com/Pharmaceutical_Biotech/pharmalaw.htm

BioMed 2006 - Kuala Lumpur International Conference on Biomedical Engineering 2006

Kuala Lumpur, Malaysia
11-14th December 2006

<http://biomed.um.edu.my/biomed2006>

BRITE Net - Tissue Engineered 3D culture models

Open University, Milton Keynes, UK
Organised by James Phillips (OU) and Felicity Rose (Nottm).
12th December 2006

Preliminary Programme**'Tissue engineering solutions for replacing animal experiments'**

Dr Laura Playle, National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs).

'An in vitro model of breast ductal carcinoma in situ'

Dr Felicity Rose, School of Pharmacy, University of Nottingham.

3-dimensional culture models in nervous system repair'

Dr James Phillips, Biological Sciences Department, The Open University.

'Manipulating thymic microenvironments to study thymus development and function'

Prof Graham Anderson, MRC Centre for Immune Regulation, University of Birmingham.

'3- dimensional cell aggregate formation in ultrasound standing wave traps'

Prof Terence Coakley, Cardiff School of Biosciences, Cardiff University.

'Construction of artificial haematopoietic microniches'

Dr Gerard Markx, School of Chemical Engineering and Analytical Science, University of Manchester.

'Modelling cell interactions in 3 dimensional brain and adipose tissue culture systems'

Dr Jane Loughlin, Biological Sciences Department, The Open University

'Porous polymer matrices for 3D cell Culture'

Dr Ross Carnachan, IRC in Polymer Science and Technology, University of Durham