tces
tissue and cell engineering society

newsletter 6

Compiled and Edited by
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Contents

From the editors 1

Focus on Research: Tissue Engineering at the Open University 1

Research Article: Designed Peptide-Based Hydrogels for Regenerative Medicine 2

Bioreactor Design and Stem Cell Processing Workshop Review, Buxton, June 2006 3

Featured Review Article: Meeting the Needs of Monitoring in Tissue Engineering 4

TCES Travel Bursary Details 5

Forthcoming Conferences 5

From the editors……

If you wish to contribute to the TCES newsletter (next edition out Summer 2007) 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 and TERMIS conferences this year by checking out our website www.tces.org

Felicity and Vivek.

Focus on Research: Tissue Engineering at the Open University

The Open University is well known for innovative teaching, but have you heard about its research portfolio which has recently expanded in the area of tissue engineering? This is focussed around modelling and repairing the injured nervous system, in particular the spinal cord and peripheral nerves. The group recently attracted a substantial Wellcome Trust grant in collaboration with the Open University stem cell group and colleagues at UCL and QMUL. This involves creating 3D culture models of the inhibitory environment that follows spinal cord damage, with a view to understanding the cellular events and developing therapeutic interventions to reduce or overcome the inhibition of neuronal growth. It will build on our previous tissue engineered spinal cord repair approaches and will facilitate the development of a new generation of implantable devices using cells, diffusible factors and biomaterials in combination.

Another 3D culture model, this time of the peripheral nerve, is currently being used to investigate the effects of the cancer treatment photodynamic therapy (PDT) on nerves. Surgeons report some sparing of nerves during PDT, but little scientific investigation of this phenomenon has been undertaken. This project gives an example of how we are using tissue engineered culture models in research which could impact directly on surgical practice, particularly in treatment of tumours where nerve damage is a serious side-effect (e.g. prostate cancer).

Peripheral nerve repair is another key area of interest and collaborations are maintained with Robert Brown's group at UCL to develop tissue engineered conduits for bridging gaps in peripheral nerves. These conduits are rationally designed by a multidisciplinary team and are mainly based on endogenous proteins (collagen, fibronectin) which can be engineered to form scaffolds for tissue repair. One of the aims of this work is to restore the mechanical properties of nerves. This is critical since if a repaired nerve is not free to glide

over surrounding tissues, or cannot bend and stretch, then function is likely to be compromised. Another research aim of the group at the Open University therefore is to continue to investigate peripheral nerve biomechanics. An exciting new direction enables nerve movement to be studied using ultrasound in human volunteers (a PhD student is currently sought to work on this nerve biomechanics project, see website for details).

The Open University campus in Milton Keynes houses the biomedical research labs which are among the best in the country and include confocal, electron and 3D time lapse fluorescence microscopy, high specification cell culture suites, and excellent molecular and histological analysis facilities. The central mission of the OU is to be "Open to people, places, methods and ideas" and we are keen to apply this philosophy to our research as well as our teaching. We maintain strong links with collaborators from many disciplines and locations, and are always keen to build more, so please come and talk to us at meetings, look at our website, and feel free to drop in if you are ever near Milton Keynes!

www.open.ac.uk/science/biosci/research/phillips

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Research Article: Designed Peptide-Based Hydrogels for Regenerative Medicine

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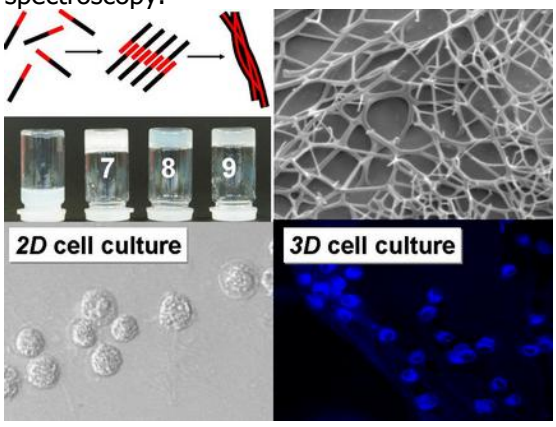
Spontaneous formation of macroscopic hydrogels from small molecule building blocks via self-assembly provides a route toward designed functional biomaterials. Peptides are suitable candidates for this type of designed biomaterial as they are inherently biocompatible, are available in a wide range of chemical functionalities and they constitute nature's language, in that small peptides such as RGD, YIGSR, IKVAV, etc. can direct cellular behaviour.[1] Significant progress in this area has been made by the groups of Zhang[2] and Stupp[3], who used oligo-peptides using >10 amino acid residues as building blocks.

Our approach is to use much smaller peptide building blocks, comprising di- and tri-peptides. The advantage of using much smaller building blocks is that it will give us better control/tunability of the self-assembled structures as well as a significant cost reduction. Short peptides are converted into hydrogelators by modification with aromatic π-stacking residues, such as fluorenylmethoxycarbonyl (Fmoc). These aromatic ligands are known to stack together and drive the self assembly from single molecules to fibrous networks. These networks are believed to be stabilised further by hydrogen bond interactions as demonstrated by circular dichroism, FTIR and fluorescence spectroscopy. [4]



Short peptides modified with aromatic stacking groups self assembled to form fibrous architectures of similar dimensions to the extracellular matrix as shown by cryo-scanning electron microscopy. These structures have been used for 2D and 3D cell culture of bovine chondrocytes.

The amino acid sequence within these short peptide building blocks were shown to control the architecture and the physical properties of the assembled structures. Combinations of

Fmoc-dipeptides were identified that formed fibrous hydrogels that were i) stable under cell culture conditions, ii) of similar dimensions to the fibrous components of the extracellular matrix and iii) capable of supporting cell culture of chondrocytes in 3D.[4]

A key issue in self-assembly is allowing the self-assembly process to occur under near-equilibrium conditions, thus avoiding mis-assembly. We have recently demonstrated that the self assembly process of these peptides can be triggered selectively using enzymes, under thermodynamic control, thereby assisting formation of well ordered structures. We demonstrated the use of proteases, enzymes that catalyse the hydrolysis of peptide bonds in dilute aqueous media, in reverse, by catalysing the synthesis of self assembling peptides.[5]

We are currently working on the full characterisation of the self assembled peptide structures and on means to control mechanical properties of these materials by rational incorporation of favourable interactions into the structures. Ultimately we wish to exploit these materials in controlling and directing the behaviour of (stem) cells in 3D cultures.

Vineetha Jayawarna, Richard J. Williams, Andrew M. Smith, Julie E. Gough, Rein.V. Ulijn

School of Materials & Manchester Interdisciplinary Biocentre (MIB),
The University of Manchester.

See a review in this area recently published by Rein and colleagues in the latest edition (April 2007) of *Materials Today*.

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[1] R.J. Mart, R.D. Osborne, M.M. Stevens, R.V. Ulijn, Peptide-Based Stimuli-Responsive Biomaterials. Soft Matter. In Press.
[2] S. Zhang, Fabrication of novel biomaterials through molecular self-assembly. Nature Biotechnol. 2003, 21, 1171-1178.
[3] S.I. Stupp, Biomaterials for Regenerative Medicine. MRS Bull. 30, (2005) 546-553.
[4] V. Jayawarna, M. Ali, T.A. Jowitt, A.F. Miller, A. Saiani, J.E. Gough, R.V. Ulijn, Nano-structured hydrogels for 3D cell culture through self-assembly of Fmoc-dipeptides. Adv. Mater., 2006, 8, 611-614.
[5] S. Toledano, R.J. Williams, V. Jayawarna, R.V. Ulijn. Enzyme triggered self-assembly of peptide hydrogels via reversed hydrolysis. J. Am. Chem. Soc., 2006, 128, 1070-1071.

Bioreactor Design and Stem Cell Processing Workshop Review, Buxton, June 2006

From the 18th to the 22nd of June, 2006, the emblematic Dome of Buxton hosted the Bioreactor Design and Stem Cell Processing Workshop, an event co-organised by The University of Keele and The University of Sheffield. This workshop was mainly focused on providing delegates with a comprehensive understanding of the use of bioreactors in stem cell culture and tissue engineering, its potentials and pitfalls.

A comprehensive range of subjects were approached such as, standard and advanced bioreactor designs, scale-up and the challenge of quality assurance, clean room design, maintenance and regulatory aspects, and clinical stem cell based therapies. The talks were given by academic and industrial international leaders on this area, including Professor Alicia El Haj (Keele University, UK), Professor Paul Hatton (Sheffield University, UK), Professor Martijn Van Griensven (LBI, Vienna), Dr Sebastian Concaro (Chalmers, Sweden), Dr Nuno Neves (University of Minho, Portugal), Professor David Williams (Loughborough University, UK), Dr Anette Jork (CellMed AG, Germany), Professor Jon Dobson (Maniacal, UK) and Dr Darren Burke (Enduratec, Bose, USA).

Other then providing a solid and up-to-date scientific program, this workshop revealed a very strong and well structured pedagogic component. The students attending this course were divided in four working groups and a tutor was assigned to each group. In between lectures, the students were asked to combine the knowledge they had acquired during the lectures with their creativity and "working under pressure" skills in several group exercises. During these exercises the students had a fixed period of time to design research

projects or strategies that could tackle some of the issues raised during the lectures attended so far and to present it to the workshop's audience. After every exercise each group was evaluated by a panel composed of some of the tutors and given a score. The winning group was announced during the last evening of the workshop.

Delegates attending the Bioreactor Design and Stem Cell Processing Workshop Review, Buxton

During the course there were also hands-on demonstrations of different types of bioreactors, some commercially available, and others developed and actively used by the University of Keele as research tools. There was also the possibility of visiting the facilities of ISTM, University of Keele, including a clean room.

Upholding the pattern of this workshop, both tutors and students were asked to demonstrate their skills at regular intervals. After a taste of British gastronomy at the Pavilion Gardens, everyone had to exercise their artistic skills in a Karaoke competition. It was worth seeing, and some times listening! For those who got somewhat frustrated with the artistic content of the workshop, the last evening reserved an enchanting surprise: a visit to The Chatsworth House. Located at Derbyshire, this is one of the Treasure Houses of England. The dense and enigmatic atmosphere in each room made it almost possible to breathe in the centuries of history sheltered by those walls. The evening had a perfect finale, with a refined dinner in the Burlington Room.

On behalf of all the students who attended this workshop, I would like to thank and acknowledge the organization of this meeting which added a valuable piece to our education.

Cassilda Reis
Cell and Tissue Engineering Group
ISTM – Keele University

Featured Review Article: Meeting the Needs of Monitoring in Tissue Engineering

Tissue engineering is a rapidly growing field that aims to develop biological substitutes that restore, maintain or improve tissue function. The focus of research to date has been the underlying biology required for tissue-engineered therapies. However, as tissue-engineered products reach the marketplace, there is a pressing need for an improved understanding of the engineering and economic issues associated with them. This is motivated by the lack of commercial viability of many of the initial therapies that have been produced. It has been suggested in the literature that this is partly due to poor process and system design in tissue production, as well as a lack of process monitoring and control. This review argues that principles of design, measurement and process monitoring from the physical sciences are needed to move tissue engineering forward, and that much of the technology needed to realize this is already available.
Regenerative Medicine 2007; 2 (2): 145-160.

Melissa L Mather, Stephen P Morgan, & John A Crowe
Applied Optics Group, School of Electrical and Electronic Engineering, University of Nottingham

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.

TERMIS 2007

TERMIS-EU (Tissue Engineering & Regenerative Medicine International Society - European Chapter)

Regents College, Regents Park, London
4th - 7th September 2007

www.termis.org/eu2007/

This year the TCES annual meeting will be held jointly alongside the TERMIS meeting in September. There will be dedicated TCES sessions with TCES invited speakers and presentations from TCES members. This will provide an excellent opportunity for PhD students and early stage career scientists to present their work at these sessions alongside senior international scientists. All TCES members are encouraged to attend this meeting which will be held in central London at Regents Park College. An added advantage is that this is very close to all the main shopping, theatre and nightlife in London.

Forthcoming Meetings

Commercial Opportunities & Legal Issues in Stem Cells

Newcastle University and the North East England Stem Cell Institute (NESCI), UK
10th May 2007

www.ncl.ac.uk/nuls/research/conferences

StemCell2007: Plastic, Reconstructive, and Aesthetic Surgery Stem Cell and Tissue Engineering Symposium

19 Mayıs University Congress and Culture Center Kurupelit, Samsun, Turkey
10th – 12th May 2007

www.stemcell2007.org

Regenerate 2007: TERMIS-North America

Westin Harbour Castle, Toronto, Canada
13th – 16th June 2007

www.regenerate-online.com

ECM VIII: Bone Tissue Engineering

Congress Centre, Davos, Switzerland
25th – 28th June 2007

www.ecmjournal.org/ecm_meetings/ecm8

The UK Society for Biomaterials

King's College London, UK
5th - 6th July 2007

www.uksb.org.uk/

Manchester Stem Cell Meeting

The University of Manchester, UK
16th – 18th July 2007

www.stemcellmanchester.co.uk