NSW Stem Cell Network

6th Stem Cell Workshop

"Tissue Engineering & Stem Cell Business"

Wednesday 6 April 2005
12:30 pm to 6:00 pm
Room 9BC
The Australian Technology Park, Redfern, NSW

Major Sponsor

MSMR
NSW MINISTRY FOR SCIENCE & MEDICAL RESEARCH

NSW First for Biotechnology Week
4–8 April 2005

Celebrating NSW Success in Biotechnology
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Welcome to the 6th Stem Cell Workshop *supporting stem cell research and the emerging stem cell industry in Australia.*

We are thrilled to be co-hosting this Workshop with the Tissue Engineering Network as part of the "NSW, First for Biotechnology", special week of events organized by the NSW Department of State & Regional Development.

The marriage between Tissue Engineering and Stem Cell research is growing stronger and the plenary speaker Dr Shulamit Levenberg from Haifa, Israel will give you a taste of its true potential. Dr Levenberg's research team has produced blood vessels by growing human embryonic stem cells on 3D scaffolds. Heart disease, for example could be treated using stem cell derived-blood vessels. The therapeutic potential is limitless and extends to growing entire organs.

These are exciting times for the Australian stem cell community, with the Federal Government's review of the use of human embryonic stem cell soon underway. Each State will eventually need to pass its own legislation. To clarify exactly what is under review and how the system works, the NSW Ministry for Science and Medical Research's policy advisor, Ms Kerry Doyle, will be presenting the whole story with plenty of time left for discussion.

NSW is fortunate to be one of the leaders in stem cell research in Australia having received two of the three National Health and Medical Research Council (NHMRC) licenses to grow human embryonic stem cell lines from excess IVF embryos. Each of the three stem cell groups are well on their way to creating new human embryonic stem cell lines that could one day have therapeutic application for a wide range of conditions such as spinal cord injury and diabetes.

The potential of stem cells from non-embryonic as well as embryonic sources is being actively explored around Australia, and this Workshop reflects the exciting developments in both areas. In Session 1, we will hear from respected national and local experts presenting their latest research in stem cells and tissue engineering. Following on in Session 2, leaders in the commercialization of stem cells will let us in on their business successes and pitfalls.

Thanks go to the chairpersons, Dr Stephen Livesey from the Australian Stem Cell Centre and Dr Kelvin Hopper from Innovation Dynamics for giving of their time and expertise.

We would also like to thank the major sponsor The NSW Ministry for Science and Medical Research, and the Australian Stem Cell Centre, for supporting Dr Levenberg's visit to Australia. Thanks to Australian Technology Park Innovations for sponsoring the Cocktail Hour, and promoting the Networking, which is critical for research collaborations and business developments. Also, thanks to our other sponsors Leica-Microscopes, Stem Cell Technologies and Chemicon that have been so committed to supporting the NSW Stem Cell Network.

Enjoy this Workshop and we look forward to keeping in touch with you through the Network.

Kind regards,

Dr Daniella Goldberg & Prof Bernie Tuch
Convenors of the NSW Stem Cell Network

NSW Stem Cell Network

NSW First for Biotechnology Week
4–8 April 2005

6th Stem Cell Workshop

Tissue Engineering and Stem Cell Business

Presented by
NSW Stem Cell Network and Tissue Engineering Network

12:30pm	Registration
1:00pm	Welcome **Assoc Prof Debora Picone, CEO, South Eastern Sydney & Illawara Area Health Service**
Session 1: TISSUE ENGINEERING Chair: Dr Stephen Livesey, Australian Stem Cell Centre	
1:10pm	Growing Human Embryonic Stem Cells on 3D Scaffolds **Dr Shulamit Levenberg, Haifa, Israel**
1:45pm	Engineering Surfaces and Scaffolds for Stem Cells **Assoc Prof Justin Cooper White, Division of Chemical Engineering, The University of Queensland**
2:10pm	Engineering Human Cartilage using Fetal Cells **Prof Pauline Doran, The University of New South Wales, NSW**
2.35pm	Business of Tissue Engineering – An Experience **Dr Steven Mercer, Tissue Therapies P/L, QLD**
3.00pm	Afternoon Tea
Session 2: THE BUSINESS OF STEM CELLS Chair: Dr Kelvin Hopper, Innovation Dynamics, Sydney	
3:30pm	Turning Embryonic Stem Cells into a Growing Business **Dr Megan Munsie, Stem Cell Sciences, VIC**
3.55pm	Human trials on Adult Stem Cells **Prof Silviu Itescu, Mesoblast, VIC**
4.20pm	Review of the Commonwealth Legislation on Embryonic Research – the Complete Story **Ms Kerry Doyle, NSW Ministry for Science & Medical Research**
4.45pm	**Future Events for the NSW Stem Cell Network**

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GROWING HUMAN EMBRYONIC STEM CELL ON THREE DIMENSIONAL SCAFFOLD

Embryonic stem cells hold promise for providing an essentially infinite supply of cells for cellular therapies, but the control of their proliferation and differentiation to form complex, viable three-dimensional (3D) tissues is challenging. We hypothesize that combining the appropriate chemical and physical cues could possibly create a supportive environment to direct differentiation and organization of human embryonic stem (hES) cells into three dimensional (3D) tissue structures. We tested this by creating a series of 3D culture conditions using matrigel and biodegradable scaffolds.

We found that polymer scaffolds, designed to resist contraction under the compressive stress exerted by the cells, promoted proliferation, differentiation and organization of hES cells into 3D structures. Furthermore, variation of growth factor conditions induced formation of human tissue-like structures including cartilage, liver, and neural tissues. In addition, hES cells cultured on polymer scaffolds organized into an endothelial tube-network, thus vascularizing the tissue *in vitro*.

When transplanted into SCID mice, the constructs maintain their viability and continue to express specific human proteins in defined differentiated structures. Moreover, the implants appear to recruit and anastamose with the host vasculature. This approach provides a unique culture system for addressing questions in cell and developmental biology, and provides a potential mechanism for creating viable human tissue structures for therapeutic applications.

Shulamit Levenberg

Department of Biomedical Engineering, Technion, Haifa, Israel

Dr Levenberg received her PhD at 1999 from the Weizmann Institute of Science, specializing in Molecular Cell Biology. She completed her postdoctoral training (1999-2004) at Prof Langer's group at MIT, who is world renowned for his work on tissue engineering. During this time, Dr Levenberg received a tenure-track faculty appointment in the Technion's (Israel Institute of Technology) department of Biomedical Engineering at the level of a senior lecturer.

At the Technion, Dr Levenberg is now establishing state of the art laboratories for conducting interdisciplinary research in the subjects of tissue engineering from hES cells and glaucoma.

Dr Levenberg has received the EMBO long term fellowship for her postdoctoral research and won the ASAIO William Kolff young investigator award.

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Australian StemCell Centre

Engineering surfaces and scaffolds for stem cells

Research into the creation of new tissues within host *in vivo* environments is crucial to improving the quality of life for many thousands of people world-wide with failing or faulty organs and deficient soft tissues. One popular solution to this organ/tissue shortage is through the generation of replacement functional tissues within engineered extracellular matrices (or scaffolds) made from synthetically- and biologically-derived polymers. The engineered polymeric constructs provide the preliminary structural, and ultimately, biological support for the development of the new tissue. Ideally, the scaffold is completely absorbed by the body to leave only the newly developed functional tissue. Replacement tissues are grown from a host of cell types, most of which are autologous and specific to the tissue to be replaced (e.g. chondrocytes for cartilage etc.).

More recently, researchers have ventured into the use of stem cells as the possible 'holy grail' starting position with respect to generating all replacement tissues from a single source. In this paper, the five critical elements of Tissue Engineering (TE) will be described, and thereafter, an overview of our research outcomes to date in the synthesis of new biopolymers, and the manufacture, surface modification and *in vitro* and *in vivo* assessments of 3D porous, polymeric scaffolds with a number of cell types, inclusive of stem cells, will be detailed and future developments and directions discussed.

Justin J. Cooper-White

Tissue Engineering and Microfluidics Laboratory, Australian Institute for Bioengineering and Nanotechnology, Division of Chemical Engineering, The University of Queensland

Justin Cooper-White is an Associate Professor of Bioengineering at The University of Queensland with expertise in biomaterials, tissue engineering, non-Newtonian fluid mechanics and microfluidics. Recently relocated from the University of Melbourne in March 2004, his team, the 'Tissue Engineering and Microfluidics' (TE&M) laboratory, focus on the development of novel tissue bioscaffolds and bio-microfluidic devices.

A/Prof Cooper-White has published over 50 refereed articles (book chapters, journal and conference papers) since obtaining his PhD in 2000 and is a reviewer for numerous granting bodies and international journals within these research fields. He is regularly invited for plenary and keynote talks at national and international conferences and has attracted over $5 million of national and international research grant funding since 2001. A/Prof Cooper-White is Vice President of the Australian Society of Biomaterials (2004 - current) and past President (2002-2004) of the Australian Society of Rheology.

SOME OF THE COMMERCIAL CHALLENGINEERING HUMAN CARTILAGE USING FOETAL CELLS

Tissue-engineered cartilage has potential applications for the repair of damaged and diseased joints, in toxicity testing as a substitute for animals, and in medical research. Cartilage formation is achieved *in vitro* by cultivating living cells on biodegradable polymer scaffolds. Ideally, as the cartilage matrix develops, the scaffold dissolves and disappears. The cells are usually differentiated chondrocytes isolated from adult or juvenile cartilage tissue; however, there is increasing interest in using stem and progenitor cells for cartilage tissue engineering. There are relatively few reports of three-dimensional neocartilage production using human chondrocytes; most studies of cartilage engineering have been carried out using animal models such as bovine calf, horse or rabbit.

The ultimate objective of our tissue engineering work is to develop cartilage constructs *in vitro* with the same biochemical, structural and mechanical properties as native tissues. The success of cartilage engineering depends on the provision of culture conditions appropriate for cell differentiation and rapid synthesis of extracellular matrix. Aspects of the physical culture environment, including mixing, mass transfer, hydrodynamic regime and mechanical pressure, play important roles in cartilage development.

In this work, three-dimensional cartilage tissues were produced under controlled conditions in recirculation column bioreactors using human foetal chondrocytes. Polyglycolic acid mesh was applied as a biodegradable scaffold for cartilage development. The quality of bioreactor-produced cartilage was influenced significantly by a range of culture and bioreactor operating conditions. Application of composite scaffolds and periodic medium flow reversal in the bioreactor yielded tissue-engineered cartilage with glycosaminoglycan contents similar to those in adult human cartilage. Tissue-engineered osteochondral composites were also developed by co-culturing foetal bone and cartilage cells in the same bioreactor device.

Pauline M Doran

School of Biotechnology & Biomolecular Sciences, The University of New South Wales

Professor Pauline Doran is a chemical engineer with research experience in microbial, plant and animal cell culture systems. After completing her PhD at Caltech in the USA, Prof Doran worked as a postdoctoral scientist at the University of Delft, The Netherlands, before returning to Australia and joining the staff of UNSW.

Prof Doran was awarded an ARC Queen Elizabeth II Research Fellowship for work on bioreactor development for culture of differentiated plant tissues and organs. She has been involved in cartilage tissue engineering studies using bioreactor systems for about 6 years.

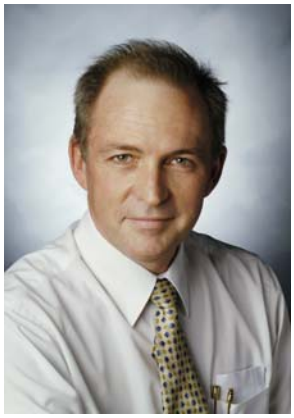
SOME OF THE COMMERCIAL CHALLENGES OF TISSUE ENGINEERING

Biotechnology is only taking the first practical steps in the clinical application of cell, tissue and hopefully in the future, organ engineering. Understanding the relevant cell biology and technical requirements for therapeutic use of these discoveries is challenging – and exciting for the potential it holds. This makes the commercialisation of tissue engineering particularly challenging.

Commercial success with cell biology requires an alignment of many critical factors each of which can be spectacularly difficult to achieve. Ultimately many disparate interests have to understand the story and be committed to the journey.

Great technology is not enough. Capital providers have to like its potential as well as the IP position; scientists have to feel that they are valued and will receive appropriate professional and financial recognition and tertiary institution commercial relations have to be creative and clever in delivering benefits valued by the institution(s). The technology has to be capable of delivering multiple revenue streams with different timelines and if the company is listed, the market has to like the story and the pipeline of good news the company has to deliver.

Some practical examples of satisfying these disparate requirements will be reviewed in the presentation.



Steven Mercer

Tissue Therapies Ltd, CEO

Steven Mercer is a medical graduate with postgraduate surgical training and a variety of technology oriented management experience, particularly in the commercialisation of cell based biology. After working with IBM in Australia and New York on the development of clinical, diagnostic and bedside ITC systems, Dr Mercer was the General Manager of Smith & Nephew Surgical Aust & NZ before successfully moving to biotechnology consulting and establishing the first TGA GMP licensed human clean room cell culture laboratory in Australia.

Dr Mercer became CEO of Tissue Therapies at the end of September 2004. Tissue Therapies Ltd is a listed biomedical company with exclusive rights to commercialise the VitroGro® platform discoveries of the scientific team at the Queensland University of Technology headed by Assoc Prof Zee Upton and Dr David Leavesley.

TURNING STEM CELLS INTO A GROWING BUSINESS

Stem Cell Sciences Ltd (SCS) is an Australian biotechnology company with a leading intellectual property and technology position in the area of stem cell research.

The company was founded in Melbourne in 1994 to commercialise discoveries from the Institute for Stem Cell Research (ISCR) at the University of Edinburgh and Monash University in Melbourne. Operating as a 'virtual' company until 2001, the company has quickly expanded from its Australian base in recent years to become a globally active organization, employing more than 50 staff in Melbourne, Kobe and Edinburgh.

The company's business plan builds on a suite of patented technologies to provide a range of highly purified stem cells and terminally differentiated cells for immediate application in cell-based gene and drug screening and future application in human cell-based therapies.

The collaborative academic relationships of SCS give access to a constant stream of commercially relevant and potentially valuable innovations in the stem cell field, either for internal development or licensing to third parties.

SCS has grown its business over the last ten years through approximately equal proportions of private capital investment and revenues derived from non-exclusive research and licensing agreements with major biopharmaceutical company partners.

This presentation will focus on the developmental pathway of the company, its strengths in terms of technology platform and IP position, as well as pitfalls encountered along the way.

Megan Munsie

Stem Cell Sciences, Development Manager

Dr Megan Munsie joined SCS as a Senior Scientist in 2001. She has recently been appointed Development Manager of the Australian operation and has previously held the position of Program Manager. Dr Munsie has had a long association with SCS. As a post-graduate she was an APAI scholarship recipient with SCS as the industry partner.

The expertise of Dr Munsie is in derivation and differentiation of murine embryonic stem cells specifically with respect to reprogramming of somatic nuclei through nuclear transfer. In 2000, Dr Munsie published the first proof-of-principle for therapeutic cloning demonstrating that somatic cell nuclei can be reprogrammed to pluripotency in a mouse model. Dr Munsie has also had over 12 years experience as an Embryologist in IVF clinics in Melbourne and the Gold Coast.

CLINICAL DEVELOPMENT AND COMMERCIALISATION OF ADULT STEM CELLS

Mesoblast Limited is an Australian biotechnology company committed to the development of novel treatments for orthopaedic conditions, including the commercialisation of a unique adult stem cell technology aimed at the regeneration and repair of bone and cartilage.

Mesoblast Limited has the world wide exclusive rights for a series of patents and technologies that have been developed over more than 10 years by scientists at the Hanson Institute and the Institute for Medical and Veterinary Sciences in Adelaide which relate to the identification, extraction, culture, and use of adult Mesenchymal Precursor Cells (MPCs). The technology has already achieved excellent results in the regeneration and repair of large bone fractures, and is currently being evaluated for the treatment of vertebral fusion, osteoporosis-related fractures of the spine and hip, and cartilage regeneration involving vertebral discs and large joints such as the knee.

Unlike embryonic stem cells, adult stem cells have no ethical concerns, and have not been associated with risk of cancer formation. Moreover, mesenchymal type adult stem cells possess unique immunomodulatory properties that result in their not being seen as foreign by immune cells of an unrelated recipient. Consequently, Mesoblast aims to develop allogeneic MPC products from universal donors for use in unrelated recipients and manufactured in centralized facilities. This will result in significantly reduced cost-of-goods, generation of a high-margin business model, and the ability to meet pricing limits set by reimbursement authorities, enabling widespread uptake of the new therapies.

The company has also acquired a 33.3% interest in Angioblast Systems Inc, an American company developing the platform MPC technology for the treatment of cardiovascular diseases, including repair and regeneration of blood vessels and heart muscle. Mesoblast and Angioblast have a Joint Expenditure Program to fund and progress the core technology to enable separate Investigational New Drug (IND) applications to the United States Food and Drug Administration (FDA).

Mesoblast's strategy is to rapidly complete pre-clinical and clinical milestones in order to progress product commercialization and position itself for strategic corporate partnerships.

Silviu Itescu

Mesoblast Ltd, Director and Chief Scientific Adviser

Professor Silviu Itescu is the founder of Mesoblast Limited and Angioblast Systems, Inc. Most recently as the Director of Transplantation Immunology at New York's Columbia University Medical Center, Prof Itescu has established an outstanding international reputation in the fields of stem cell biology, autoimmune diseases, organ transplantation and heart failure. His experiences range from laboratory research to new drug development and clinical evaluation.

Prof Itescu recently pioneered novel approaches to the use of adult stem cells for the treatment of heart disease and is leading international collaborative trials in this area. Prof Itescu was an advisor on cell therapy for cardiovascular diseases to both the US President's Council on Bioethics and the US FDA Biological Response Modifiers Advisory Committee (BRMAC). He has consulted for many international pharmaceutical companies and has been an advisor to biotechnology and health care investor groups.

THE REVIEW OF COMMONWEALTH LEGISLATION ON EMBRYONIC RESEARCH – THE COMPLETE STORY

The national scheme regulating human embryo research and prohibiting human cloning was agreed at Council of Australian Governments (COAG) on 5 April 2002. The COAG agreement has a number of key features including a restriction on the use of excess ART embryos created before 5 April 2002 and a review of the Commonwealth legislation which was to commence two years after the Commonwealth legislation was enacted. The nation regulatory scheme is made up of Commonwealth and State legislation, the Commonwealth *Prohibition of Human Cloning Act 2002* and the *Research Involving Human Embryos Act 2002* and the NSW *Human Cloning and other Prohibited Practices Act 2003* and *Research Involving Human Embryos (New South Wales) Act 2003* as well as legislation from all other jurisdictions.

Owing to the Federal election in October last year the Commonwealth legislation is now scheduled to be reviewed in the coming months with a report due to the Commonwealth in December 2005. The review of the NSW legislation may be carried out concurrently and will be undertaken under the auspices of the Minister for Science and Medical Research. Matters to be taken in account in the review of the legislation include developments in medical and scientific research and the potential therapeutic applications of such research. Accordingly, the review could include an examination of whether the current Australian ban on therapeutic cloning or Somatic Cell Nuclear Transfer should be lifted.

The Commonwealth review will be undertaken by *independent* persons chosen by the Hon. Julie Bishop the Minister for Ageing, with agreement from each State and Territory. The review process will involve consultation with the Australian, State and Territory governments, relevant agencies and a broad range of persons with expertise in or experience of relevant disciplines and will also involve an extensive public consultation phase. NSW is keen to use the Stem Cell Network as one mechanism for consulting its stakeholders to assist it in making an appropriate submission to the Commonwealth review. Accordingly, this discussion will focus on NSW position to date and key issues and questions for stakeholders to consider.

Kerry Doyle

NSW Ministry for Science & Medical Research, Executive Director, Policy and Operations

Ms Kerry Doyle's responsibilities as Executive-Director include providing support during the debate at the Council of Australian Governments (COAG) on human cloning and embryo research, which resulted in the implementation of the nationally consistent scheme to prohibit human cloning and certain other practices and regulate research involving human embryos.

Since 1994, she has worked in various positions in NSW Government, in areas including education, health, treasury, environmental policy and industrial relations. Prior to entering Government, she lectured and tutored at the University of Wollongong and was an educator in the school and theatre sectors in NSW. Ms Doyle previously held the position of Director of the BioUnit, NSW Cabinet Office, until 1 December 2003, when the BioUnit became the core of the newly established Ministry.

Her current role in the Ministry involves mobilising and directing programs and resources across Government to facilitate the effective implementation of policies and programs relevant to science and medical research strategy, including managing a range of BioFirst Programs, including the BioFirst Awards & Bio-Link.

NSW Stem Cell Network

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