

Beethoven Saal

8.30-10.00

## V 9

***Tissue engineering***

## V 9-1

***Tissue engineered skin: present and future******E. Middelkoop***

**Prof. Dr. med. Esther Middelkoop, Vereniging Samenwerkende Brandwondencentra Nederland, Postbus 1015, 1940 Beverwijk, NL, Email: emiddelkoop@rkz.nl**

The author will give an overview of the present situation regarding skin replacement materials and techniques, with their respective pro's and con's. Some clinical cases using the presently available techniques will be presented, as well as evaluation techniques for measuring clinical outcome parameters. The directions of the latest developments on this subject in basic research (scaffold design, use of mesenchymal stem cells) will conclude this presentation.

## V 9-2

***Keratinocyte Grafting – simplifying the delivery of cells from the laboratory to the patient******S. McNeil***

**Prof. Sheila McNeil, University of Sheffield, Department of Engineering Materials, Sir Robert Hadfield Building, Mappin Street, Sheffield S1 3JD, UK, Email: s.macneil@sheffield.ac.uk.**

Adult human cultured keratinocytes have been used successfully in the treatment of patients with extensive full thickness burns injuries since the early 1980s following publication on a methodology for culturing adult keratinocytes in 1975. Survival of cultured autologous keratinocytes on patients for more than two decades strongly suggests that the cultured cells contain inherent keratinocyte stem cells capable of continued proliferation. However, despite this relatively early and encouraging clinical success, the next phase of tissue engineered skin "products" has been largely disappointing in terms of clinical uptake by the NHS and in terms of commercial success. In this field, as in no other of tissue engineering, research has gone to the basic and pragmatic through a swift cycle of over-inflated expectations to the current state of

hopefully more realistic expectations for cultured skin cells. The approach that we have taken within the University of Sheffield and the spin-out company CellTran Ltd, is to go back to the early methodology of culturing autologous keratinocytes as sheets of cells and seek to improve on the technology for taking cells to the laboratory to the patient and for developing a patient centred cell therapy which will be clinically successful.

We have developed a chemically defined plasma polymerised surface containing 20 % carboxylic acid groups which supports the attachment and proliferation of keratinocytes. Autologous keratinocytes are initially expanded in the laboratory using conventional methodologies and then transferred to the plasma polymer surface for no more than 2 days before transfer to the patient's wound bed. This allows rapid transfer of cells from the laboratory to the patient where this is the priority – for major burns patients and ease of timing of transfer of cells from the laboratory for repeated applications in chronic wound patients. Supplying the cells to patients on an easy to handle polymer disc (currently 6 cm diameter) obviates the necessity of the surgeon or district nurse handling spray-on cells or fragile sheets of cultured cells. The application of the plasma polymer containing cells to the wound bed is compatible with other on-going treatment regimes for burns therapy and chronic wounds. Our current challenge is to further improve on the culture methodology to avoid the use of bovine serum or murine mouse feeder cells (both routinely used in the initial methodology for expanded keratinocytes). We have established that we can obtain rapid expansion of non-differentiated human keratinocytes grown on irradiated human lung fibroblasts (MRC5s which have been used in the production of human vaccines for some 30 years) in the absence of any foetal calf serum. This system is in pre-clinical evaluation at present prior to clinical assessment. Our clinical data to date shows accelerated healing of burns injuries and slow steady sustained healing of chronic non-healing wounds with repeated applications of autologous cells.

In summary, we have undertaken a programme of redesigning the culture and delivery of keratinocytes from the laboratory to the patient to make this as low-tech and easy to handle and patient friendly as possible.

**V 9-3*****Engineering of nerve regeneration******G. Terenghi***

**Prof. Giorgio Terenghi, University of Manchester, Plastic Reconstructive Surgery Research, Room 3.102, Stopford Building, Oxford Road, Manchester M13 9PT, Email: anni.gibbon@manchester.uk**

The current repair method to bridge nerve defects is to use autologous nerve grafts, which provide the regenerating axons with natural guidance channels, Schwann cells and extracellular matrix molecules. Because the harvesting of a nerve graft results in comorbidity and the functional recovery following nerve repair is poor, an alternative method of nerve reconstruction is needed. Biocompatible nerve conduits have been acknowledged as an alternative solution, as their surface micro-geometry may be combined with cultured cells, growth factors and extracellular matrix molecules to form a tissue engineered nerve graft.

The addition of cultured Schwann cells within the conduit has proved to have a crucial role, and by using a stable genetic labelling method for identification of transplanted cells we have been able to demonstrate their active participation in the regenerative process, as well as their optimal concentration. Further improvements are provided by coating of conduit with extracellular matrix macromolecules, which increases Schwann cells proliferation and consequently axonal regeneration.

More recently, interest has been directed toward the use of stem cells because of their potential to differentiate towards any cell phenotype. We have been able to differentiate adult bone marrow mesenchymal stem cells toward cells expressing phenotype and functional characteristics of Schwann cells. Furthermore, their transplantation in bioengineered nerve conduits has proved beneficial in promoting enhanced nerve regeneration.

There is a clear need for a tissue engineering approach which would enhance functional recovery after peripheral nerve surgery. Development in cell cultures, genetic manipulation and biotechnology indicate that the concept of a bioengineered nerve implant as an alternative to the use of autologous tissue is becoming closer to clinical reality.

**V 9-4*****Tissue engineering of cartilage******G. van Osch***

**Dr. Gerjo van Osch, Erasmus Orthopaedics and dept. Otorhinolaryngology, Room Ee1655, Po Box 1738, 3000 DR Rotterdam**

Regeneration of collagen is a limiting factor in cartilage repair and cartilage tissue engineering. To improve cartilage repair it is necessary to understand wound healing processes. We investigated experimental addition of enzymes to improve integration of graft in surrounding cartilage and the use of growth factors to further stimulate collagen repair.