Tissue engineering: the fabric of recovery

Professor Sheila MacNeil outlines her multifaceted tissue engineering research and explains how developments in the field have enabled the creation of life-changing solutions for patients.

To begin, what inspired you to work in tissue engineering? What are the most fascinating and unique aspects of your research?

I was inspired to work in tissue engineering by hearing of the great strides being made in the 1980s in culturing skin cells for patients with extensive burns injuries. This led to a long-standing collaboration with the Burns Unit in Sheffield. My group cultured skin cells for patients with severe burns and we developed an improved and simpler methodology for delivering these laboratory expanded cells from the lab to the patient, which we commercialised as MySkin®.

Throughout, the common theme of my group’s work has been to collaborate closely with clinicians to get a good understanding of the clinical problem and then come up with the simplest solution, deliver significant benefit for patients and make the technology more adoptable by more clinicians.

MySkin® is the UK’s first and only commercially available complete service for the culture and delivery of patients’ skin cells to treat extensive burns. How does MySkin® improve upon traditional skin grafts?

MySkin® is not actually a skin graft, it is a way of delivering laboratory expanded keratinocytes (the cells that form the upper barrier layer of the skin) to help achieve a new barrier in burns patients, or indeed, on top of wide-mesh conventional skin grafts, when there are insufficient skin grafts to manage a patient with extensive burns injuries quickly enough.

To treat chemical burns in the damaged eye, limbal stem cells are needed from the healthy eye. Working in collaboration with the L V Prasad Eye Institute in India, the Sheffield University team has sought to develop a membrane to assist in this. How have you approached this objective?

Our prior experience in developing MySkin® helped in analysing what was needed for regeneration of the cornea. We developed an excellent collaboration with the Institute’s Dr Virender Sangwan, who described how traditional practice (for the preceding 12 years) was to take a small biopsy from the patient’s undamaged eye, expand the limbal stem cells in culture and then put them on small pieces of human amniotic membrane. Our first thoughts were that we could readily replace this human donor membrane with a synthetic membrane. Then we started to ask ourselves whether it was really necessary to always culture the cells in the laboratory.

Could we do as well if we worked from very small pieces of the cornea from the region known as the limbus? This is when things became exciting. Virender immediately offered to test the concept by combining small pieces of the limbus with the existing human amniotic membrane, showing that the concept works for this donor tissue.

Your work also focuses on improving the mesh material currently used in the pelvis for surgical procedures to treat stress urinary incontinence (SUI) and pelvic organ prolapse (POP). How will the materials you are working with enhance the effectiveness of these treatments?

The distensible polyurethane tape that we’re working with has a lot more bounce and give in it than the strong but relatively rigid polypropylene (PP) mesh used currently. PP works well in abdominal hernia repair but the pelvic floor has been compared to a trampoline, which needs to withstand years of organs bouncing up and down on it. If you make your trampoline out of a rigid material it can eventually tear rather than bounce back. To address this, we have selected a particular polyurethane that combines the strength that is needed with a lot more bounce than PP.

It is very important that tissue engineering technology does not compete with an existing clinical method that works, but provides something extra. In the case of MySkin®, it provides an extra source of keratinocytes...
ADVANCEMENTS IN BIOMATERIALS and tissue engineering technologies and expertise have enabled scientists to dedicate their research to providing additional solutions for patients who have extensive burns when there are insufficient skin grafts to treat them and rapidly restore skin barrier function. Without quickly regaining an intact skin barrier layer patients are at risk of infection or even death.

Professor Sheila MacNeil is an expert in tissue engineering at the University of Sheffield, where her work with the Biomaterials and Tissue Engineering Group has consistently sought to put the patient first through a focus on soft tissues for clinical benefit.

SPEEDING UP SKIN GROWTH
MacNeil’s dedication to the field is exemplified by her development of MySkin® in collaboration with Professor Robert Short through CellTran Ltd, the spinout company they co-founded to bring research innovations out of the lab and into the clinic. Commercially available since 2004, MySkin® provides a treatment option when conventional skin grafting is not available. For instance, when patients suffer severe burns to more than 60 per cent of their body there is not enough unaffected skin to use to graft the damaged areas.

In the early 1990s, when MacNeil began her research, the best method of culturing the patient’s skin cells – into small sheets – was slow and had poor success rates. In life threatening burn injuries, it is critical to create a skin barrier as soon as possible in order to avoid infections, so treatment needs to be simple and swift. This is where plasma polymerisation comes in. This surface engineering method allows the development of a very thin continuous surface for skin cells to adhere to that can then be coated onto a medical-grade wound dressing. With the cells facing downwards, they are able to leave the dressing and enter the wound bed.

Relatively inexpensive to manufacture, fast and easy to use, it is little wonder that MySkin® has been adopted by 11 of the UK’s 13 major burns institutes to treat over 300 patients since 2008. It provides burns surgeons with a readily available commercial service, brings about a life-saving skin barrier sooner and has helped heal chronic wounds where previous best practices could not. In short, the development of MySkin® from lab research into a commercially sustainable product has proved to be a highly valuable benefit to both the patient and the health services.

ADVANCED CORNEA REPAIR
MacNeil has also been working to improve upon the traditional methods for treating corneal blindness in collaboration with Dr Virender Sangwan from the L V Prasad Eye Institute – an internationally renowned centre for eye treatments and cutting-edge research in India.

The traditionally used cultivated limbal epithelial transplantation (CLET) procedures require access to special clean rooms and dedicated staff to

In fruitful collaborations with scientists in the UK and abroad, researchers at the University of Sheffield endeavour to produce new and improved soft tissue damage treatments.
work on the expansion of limbal cells in cultures – they also present increased risk of contamination.

Simple limbal epithelial transplantation (SLET), as the name implies, is a simpler approach to corneal restoration – with the same success rate as the more complicated CLET (76 per cent). Instead of expanding corneal cells in a culture, a tiny strip of limbal tissue is taken from the healthy eye, divided into smaller pieces and then placed on an amniotic membrane that sits on the damaged cornea. With cell cultivation taken out of the equation, SLET can be offered to patients in situations when access to the resources that CLET demands is not feasible. So far, more than 200 patients have received the novel treatment, with Sangwan actively spreading awareness and other groups successfully adopting the method.

MacNeil and Virender are continuing to pioneer in the field; using electrospinning, they have developed a synthetic biodegradable membrane to replace the need for human amniotic membrane. Using human donor tissue means there is always a risk of passing on bacterial or viral disease no matter how great the precautions, so there is still the need for a tissue bank at present. Representing an off-the-shelf product, the pair have approval to carry out the first human clinical study of the SLET technique on their synthetic membranes. If they are successful, surgeons will no longer require access to tissue banks, clean rooms or dedicated staff for cell expansion, making corneal restoration a whole lot simpler to achieve.

MECHANICAL FAILURE

Another important research area for MacNeil is the development of biomaterials for patients affected by stress urinary incontinence (SUI) and pelvic organ prolapse (POP).

Both SUI and POP have proven to be difficult issues for women to talk about, surrounded by a stigma that can lead to ignorance of the associated afflictions and treatment options. SUI is the involuntary leakage of urine under increased abdominal pressure, meaning it is more likely to occur while coughing, sneezing or simply exercising. POP occurs when the soft tissues keeping the bladder, vagina and rectum in place lose their elasticity and strength. Treatments for both employ a polypropylene (PP) mesh – but the material has been known to cause severe side effects in 5 per cent of patients treated for SUI and 25 per cent of those treated for POP. “They don’t just suffer the side effects of the material failing mechanically. It fails in such a way that it causes massive, painful side effects that can wreck patients’ lives,” explains MacNeil.

With UK National Health Service (NHS) Consultant Urologist Professor Christopher Chapple, MacNeil has developed a stronger, more elastic distensible polyurethane tape to replace PP mesh. Ultimately, it should encourage the body to adopt it more comprehensively as its design enables the patient’s cells to actually grow into the material. A more durable alternative could not be timelier. Awareness of the side effects of PP mesh failure may be belated but it is growing, and so too is scrutiny of its manufacturers and the surgeons using it.

MacNeil’s work is dedicated to improving patient outcomes, ensuring that high-quality research does not linger in the laboratory. By developing simpler, more cost effective methods that benefit practitioners too, MacNeil aims to make these treatments a viable option for anyone who needs them.

Pelvic floor biomaterials research.