

AusBiotech 2011: Healing touch

Australian labs are conducting pioneering research into tissue regeneration, such as the new treatment for severe burns, NovoSkin.

Tim Dean (Australian Life Scientist) | 17 October, 2011 10:49 | [Comments](#) | [Like](#)



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Many people may not be aware that Australian labs and biotech firms are among the world leaders in tissue regeneration research. Issues affecting the field will be surveyed at the AusBiotech 2011 Conference in the Tissue Regeneration and Biomaterials session, chaired by Professor Stephen Prowse, CEO at the CRC for Wound Management Innovation.

According to Prowse, wound management still doesn't receive the attention it should given the impact it has on the health sector. Just chronic ulcers alone – nasty wounds that are reluctant healers, with many people carrying them around for months, if not years – could be cost up to \$4 billion a year to treat, with around four to five hundred thousand individuals afflicted at any one time.

That's around two to three per cent of the national health budget, yet wound management receives a substantially smaller fraction of research dollars.

Researchers such as Prowse and his CRC, along with many others around the country, are involved in a wide range of projects, including: investigating the biochemical changes that prevent effective healing of things like ulcers, and looking at various therapeutics to circumvent those biochemical blocks; investigating the role of genetics, epigenetics and

microRNA in wound healing; developing new therapies and wound dressings; and looking at and improving wound treatment diagnostics and processes.

One particularly exciting project is being conducted by Professor John Greenwood, who is the Director of the Burns Unit at the Royal Adelaide Hospital, through NovoSkin, a joint venture between his company, Skin, along with PolyNovo, which is owned by Calzada. NovoSkin is developing new treatment for burns which seeks to not only radically reduce costs, also dramatically improve the outcomes for severe burns.

Burning problems

With severe burns, it's sometimes difficult to decide which is worse: the affliction or the cure. Burns can cause horrific wounds, which need to be treated carefully and methodically over an extended period of time if the patient is to avoid the complications of infection as well as end up without serious scarring.

Once the burn wound itself has been cleaned and cleared, the wound needs to be stabilised while preventing healing from beginning before a skin graft can take place. If healing begins prematurely, and the wound

Even if the wound can be managed before contraction sets in, enacting a successful skin graft is no easy task. First the skin needs to be taken from an appropriate donor site.

This process itself carries the risk of producing a new wound, particularly as the dermis – which is inevitably partially removed when taking the graft – cannot regenerate the same way the epidermis can. According to Greenwood, many patients even find the donor site to be a greater source of pain and discomfort than the burn site – which is certainly saying something.

And consider a poor individual who has suffered burns to over 50% of their body: they simply lack sufficient unaffected skin to provide enough grafts for the burn regions. Even once a graft is successful, it's rare that the grafted skin matches like-for-like with the burn region, leaving visible seams and noticeably different skin grades.

The gold standard treatment for severe burns for the last three decades has been Integra, produced by Integra Neurosciences. Integra is a dermal template formed from bovine collagen and shark chondroitin with a pseudoepidermis of non-porous silicone that effectively acts to seal the wound.

Once the burn region is excised, Integra is placed in the wound site and remains there until a skin graft can be placed over the top, at which point the collagen integrates into the body.

Integra has been a boon to burns surgeons, but it has its drawbacks, says Greenwood. The first is that it's particularly prone to infection, and the other is its very high cost, at around \$5,000 for an A4-sized sheet.

The combination of these two drawbacks can result in some very unfortunate outcomes: "The whole amount can become infected, and it can all fall off overnight, sometimes leaving up to \$250,000 of material on the floor. Then you have a patient who doesn't just have an open wound, but now an open infected wound, which is often a mortal situation," says Greenwood.

"What we really want is a material that can be implanted; which can be integrated into the wound; is biodegradable, so it disappears; is biotolerated, so it doesn't cause any adverse reactions; which will act as a scaffold for dermal ingrowth; but restricts the formation of dermal scarring by compartmentalising the normal healing mechanism into small 500 micron blocks, which means you don't get much in the way of contraction," he says.

"Ideally it'd also be extremely cheap to make, and would be completely synthetic, so it's not likely to become infected, and can be used as a scaffold to grow the composite cultured skin."

It was while in pursuit of such a miracle material that Greenwood was in Melbourne in 2004 investigating some new collagen treatments. While there he also met with some scientists from PolyNovo, a spin-off company from the CSIRO, who mentioned a new material they had developed called NovoSorb, which is a cunningly clever biodegradable polyurethane polymer.

"When I met with them, I told them what I needed in terms of structure and what the material had to be able to do, and they said they could modify the chemistry to do whatever we wanted. They could even have it release things like anaesthetics or growth factors as the material breaks down."

The end result is what NovoSkin calls its Biodegradable Temporising Matrix (BTM). It functions in a similar way to Integra, being placed into the excised wound site, and it fully integrates into the wound within 10 days, preventing it from contracting and developing unsightly scar tissue.

Using BTM raised up the possibility of using it with another technology Greenwood is developing, called Composite Cultured Skin (CCS). This is where a small amount of the patient's skin is harvested and cultured into a patch large enough for a graft on to the affected site – all without causing the manifold problems of taking large sheets of skin from donor sites.

The problem in the past with using cultured skin is that it takes around 21 days to grow before it can be grafted. Integra would be unlikely to last that long, but the BTM is able to keep the wound stabilised for long enough for the CCS to be placed over the top.

Cool solution

NovoSkin has already conducted two trials on pigs, first to determine the best formulation of PolyNovo's magic material for the BTM, and the second demonstrating that the BTM yields better results than Integra, with it showing smaller wound contraction with none of the BTM sites becoming infected, compared to two thirds of the Integra sites.

The next step is to begin human trials, with NovoSkin receiving the go-ahead from the regulators to start on two trials for small wounds to demonstrate efficacy. After that it'll be on to a major burn wound pilot trial and then a multi-centre trial. The first human trials are expected to kick off in September of this year.

The hope is to produce a new burn treatment that won't only be more effective than the current industry gold standard, but is also substantially less expensive, thus opening it up for use in developing countries, not just the wealthy ones that can afford Integra.

However, there's considerable inertia to overcome, with Integra having a strong following in the burn treatment community. With sufficient positive results from the upcoming trials, along with proven capability to manufacture and distribute NovoSkin, we could see Australia further cement its reputation as a pioneer in innovative wound management treatments.