

CURRENT RESEARCH: RESTORE BURN AND WOUND RESEARCH

Current Research – 1 Genes activated in the burn wound

In 2007 the Stoke Mandeville Burns and Reconstructive Surgery Research Trust was relaunched as *Restore Burns and Wound Research*. This was done not only to emphasise our unique clinical focus but also to emphasise that we are not a single institute charity. Appropriately, the first project to come to fruition in this period was an entirely new model of a thermal injury with an acute wound that was devised by research fellow Tze Kong. As with previous models, we targeted the clinical scenario of a burn in a human subject. Again, the skin due for excision in breast reduction patients proved to be an optimal site for analysis; fully consented subjects had a stereotyped contact burn made on the under surface of their breast at the start of their operation. This was done using an electrical thermode developed and characterised by restore which delivered a precise and known energy to the skin contact area. At various time points during the operative procedure, the same skin was removed and snap frozen for comparison with similar skin from unburned areas. Tze screened messenger RNA – the precursors of proteins and key intracellular signals using a gene array *transcriptomic* approach. In doing this, he revealed many hundreds of potential signals that are changed in the very earliest burn wound environment. Further, he took this work one stage further and looked at the molecular changes that occur with the clinical treatment of immediately cooling the same injury. This revealed many mediators that are implicated in reducing the discomfort of the acute injury and which also may be involved in decreasing inflammation and scarring. This unique work expected to be published this year.

Current Research 2. the role of stem cells in burn wound healing

Our next project explored the systemic nature of the acute burn in more detail. Stem cells are cells found in all multi-cellular organisms that have the ability to divide and to differentiate. Currently, they are an area of intense research as one hypothesis is that they offer a wound the possibility of repair by *regeneration* rather than scarring. It is believed that stem cells are released from suppressed adult bone marrow after a significant systemic insult. Andreas Fox, the fellow who evolved this study, set out to establish for the first time what happens to bone marrow-derived stem cells (proangiogenic progenitor cells) in the first few days after a significant burn. Given the relative infrequency of substantial body surface area burns, and the tightly defined inclusion and exclusion criteria of the protocol, Andreas set about increasing the number of potential patients with new burns by attaining ethical approval for a multi-centre collaboration with The St Andrew's Centre for Burns in Chelmsford, Essex. Spending many hours at the bedside he took sequential blood samples from patients with burns greater than 20% total body surface area (TBSA) and included in this number were patients intubated on the Intensive Care Unit: successfully navigating the ethical approval of patients unable to provide immediate consent to investigation. As a result, with the expertise of the University of Oxford and NHSBT Stem Cell Research laboratory, he was able to show that there is a surge of stem cells released in to the peripheral blood from the bone marrow following a major burn, and we remain focussed on understanding the significance in relation to healing through future studies.

This study provided the foundation for our next strategic goal of growing endothelial progenitor cells (ECFCs) from a patient with a new burn in the laboratory. Undertaken by fellow Thanassi Athanassopoulos, he successfully established how to grow ECFCs in culture to the extent that they began to form a new network of blood vessels when supported by dermal fibroblasts or bone marrow mesenchymal stem cells. This new vasculature raised the exciting prospect that ECFCs could be used therapeutically to enhance how rapidly artificial skin (skin substitutes) integrate when applied to resurface a burn wound. Currently, such substitutes are applied to provide both temporary and permanent cover to the burn surface. Examples include modified collagen matrices that can be seeded with cells such as fibroblasts and keratinocytes. However, these have a considerable drawback in that they often fail to incorporate into the host tissues. If existing artificial skin can be seeded with ECFCs and supporting cells to establish an intrinsic vascular network, theoretically this could enhance the speed at which such topical treatments integrate to 'seal' the wound. This area is under investigation by our current DPhil research fellow, Miss Jennifer Kean, who has had initial success with growing a vasculature network from such stem/progenitor cells on skin substitutes such as Integra®. Jennifer will complete her project in 2012 and we look forward to its publication.