Wound Healing

Dermal wound healing involves many complex interactions between different biological processes. An understanding of these interactions is important for the development of new therapies for wound healing and our understanding of how drugs or environmental chemicals can affect it. Healing of dermal wounds can be divided into 3, overlapping phases; granulation tissue growth (leukocyte infiltration, angiogenesis, fibroblast activation), re-epithelialization (activation and differentiation of keratinocytes) and dermal re-modelling (connective tissue synthesis). These phases can be investigated sequentially in vivo or individual aspects can be followed using specific in vivo or in vitro models (see available models). For example, granuloma formation can be studied in vivo using dead space models and re-epithelialization using cultured keratinocytes. Cell culture systems can also be integrated to form a skin equivalent. Using a combination of techniques information can be obtained on the mechanism of action and specificity of the treatment or chemical being investigated.

Available models

In vivo

- Mouse models: full-thickness punch or incisional dermal wounds.
- Dead space models: rat carrageenan-sponge granuloma model. The sponges can be exposed (acute or chronic) to mediators or drugs via cannulas implanted in the sponges.
- Transplanted human skin.
- Transplanted cells or skin equivalents. Transfected cells or skin equivalents containing modified cells can be applied to dermal wounds.

In vitro

- Human skin fibroblasts and keratinocytes.
- Skin equivalents: human keratinocytes grown on a collagen gel or an acellular dermis. The gel can contain fibroblasts, pieces of dermis, leukocytes, endothelial cells or melanocytes and other cells of interest, depending on the wishes of the client and the problem to be investigated.

End points

- Wound closure/contraction (macroscopic and microscopic), collagen synthesis, cell infiltration, angiogenesis, mediator synthesis and release.
- Any other readout parameters can be performed upon request using standard biochemical, immunological and molecular biological methods.

Data in vivo mouse model

Figure 1. The synthesis and release of prostaglandin (PG) E₂ (ex vivo) by mouse 5 mm full thickness punch wounds at different times after wounding. Control = control skin (5mm biopsy), Moist wounds (5mm biopsy including wound) = covered with Op-Site. Dry wounds (5mm biopsy including wound) = uncovered wounds.

Figure 2. Collagen content of mouse full thickness punch wounds at different times after wounding.
Advantages

- Derphartox offers a range of in vitro and in vivo models which can be used to develop drugs for studying wound healing in 1 center.

- In addition to the preclinical services, Derphartox can also support you with the development, preparation and submission of the essential documents for early phase clinical trials when the decision is made to proceed to the proof of concept in humans.

Time lines

These will vary depending on the protocol.

Associated (disease) models

- Normal and diseased human skin explant culture
- The human skin transplant model of psoriasis
- Imiquimod mouse model of psoriasis
- Mouse oxazolone-induced delayed type hypersensitivity model (also for pruritus)

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References