

# A TOPICAL DISCUSSION

WHY ONE COMPANY BELIEVES **HUMAN GROWTH FACTORS** ARE THE WAY FORWARD FOR ANTI-AGEING SKINCARE

For years, antioxidants and AHAs have been the hallmarks of anti-ageing skincare. But as understanding about the process of intrinsic and extrinsic ageing advances, so too do practitioners' options in adding to their topical anti-ageing armoury. Perhaps the most notable development in this field of late is being spear-headed by SkinMedica, a company whose product range has seen many prominent industry figures in the US subscribing to the potential and, indeed, efficacy of what is being heralded as the next generation of cosmeceutical – human growth factors.

The potential for endogenous growth factors in reducing the effects of facial photodamage has long been studied in the US. However, Dr Richard Fitzpatrick brought the debate into sharp focus with the development of his SkinMedica TNS® (or Tissue Nutrient Solution) product range. "A pioneer in laser resurfacing, Dr Fitzpatrick developed a keen interest in wound healing and wanted to find a means of achieving faster recovery rates for ablated skin," explains Dr Gregory Nikolaidis, a consultant dermatologist and human growth factor proponent who worked with Dr Fitzpatrick during his laser therapy fellowship. "He partnered with California-based Advanced Tissue Sciences to evaluate the potential of a growth media that was being used to stimulate skin growth for Dermagraft® and TransCyte®, two FDA-approved burn and wound-healing products. Really he was looking for the ultimate wound dressing, but he soon realised that the solution offered the potential for so much more."

The solution, now known as NouriCel-MD™, was found to be rich in human growth factors, cytokines and soluble matrix proteins that had been secreted by a culture of fibroblasts taken from neonatal foreskin during Advanced

Tissue Sciences' processes for three-dimensional tissue growth. For Dr Fitzpatrick, the discovery was exciting. Like many, Dr Fitzpatrick was already interested in the role growth factors played in wound healing and given that, as Dr Nikolaidis explains, "he believed that the biochemical effects of intrinsic and extrinsic skin ageing were similar to wound formation and the process of wound healing", it wasn't too great a leap of faith for Dr Fitzpatrick to wonder what role growth factors, and consequently NouriCel-MD™, could play in the treatment of ageing skin."

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## WOUND HEALING AND SKIN AGEING

The correlation between wound healing and skin ageing certainly seems to carry weight.

Dr Fitzpatrick and Dr Nikolaidis view photo-damage as a chronic wound and use the term 'solar scar' to describe the body's cumulative exposure to UV. Just as in process of wound healing, UV damage induces inflammation which, over time, can result in the degradation of the extracellular matrix. "Inflammation results in the generation of Reactive Oxygen Species (ROS) resulting in the degradation of the extracellular matrix," reveals Dr Nikolaidis. "The transition from this inflammatory phase of wound healing to the granulation phase which follows is mediated by a variety of growth factors and cytokines. These have been found to be crucial for the reversal of photoageing."

In a paper published in 2005, Dr Fitzpatrick explains the role growth factors play in wound healing in some detail (1): "Wound healing is dependent on the synergistic interaction of many growth factors. After injury, cytokines and other growth factors flood the wound site to mediate the inflammatory response, promote new cell growth and decrease wound contraction and scarring. A cycle of collagen production and growth factor secretion continues in a type of autocrine feedback loop of continuous wound repair. The remodelling phase is the final step in the wound repair process and typically lasts several months. It is during remodelling that the extracellular matrix is reorganised, scar tissue is formed and the wound is strengthened. Type III collagen deposited during the proliferation phase is gradually replaced by Type I collagen, which is more tightly crosslinked and provides more tensile strength to the matrix."

It is this remodelling phase, explains Dr Fitzpatrick, which is key in treating the effects of photodamage. But as aged skin doesn't appear







↖ The SkinMedica TNS product range is distributed in the UK by Skin-Brands and includes: TNS Recovery Complex®, TNS Ultimate Daily Moisturizer, TNS Illuminating Eye Cream and TNS Lip Plump System.



DR RICHARD FITZPATRICK

to have a sufficient amount of growth factors and cytokines to facilitate this remodelling process, it makes sense to deliver growth factors topically. But which growth factors in particular are most effective in this process and how does this pertain to SkinMedica's TNS range?

#### PROVEN EFFICACY

The 96.3% NouriCel-MD™ solution used in SkinMedica's TNS Recovery Complex® is a proprietary blend of key growth factors," reveals Dr Nikolaidis. "It contains Transforming Growth Factor Beta (TGF-β), found to stimulate collagen secretion; Vascular Endothelial Growth Factor (VEGF), found to stimulate new blood vessel formation; Hepatocyte Growth Factor (HGF), which helps to stimulate new blood vessel formation; Keratinocyte Growth Factor (KGF), found to stimulate epithelial cell growth. Other components include: interleukins, soluble collagen, matrix proteins and antioxidants," he adds.

In Dr Fitzpatrick's pilot study published in 2003 (2), 14 patients with Fitzpatrick Class II or greater facial photodamage applied TNS Recovery Complex® to their face twice daily for 60 days. At baseline and at 60 days there were clinical evaluations of photodamage using the Fitzpatrick scale, 3mm punch biopsies of the lateral cheek and optical profilometry of the upper cheek. The peri-orbital region showed a statistically significant improvement ( $p=0.0005$ ); optical profilometry (silicone impressions) showed a statistically significant reduction in roughness ( $p=0.0075$ ) and shadowing ( $p=0.02$ ) in fine lines and wrinkles; and biopsies revealed new collagen formation in the Grenz zone, which



DR GREGORY NIKOLAIDIS

showed a 37% increase in thickness, and thickening of the epidermis by 27%. The conclusion: "the application of a mixture of topical growth factors may stimulate the repair of facial photodamage, resulting in new collagen formation, epidermal thickening and the clinical appearance of smoother skin with less visible wrinkling."

In a more recent study (3), evaluator-blinded clinical assessment of photographs taken with a VISIA-CR system using natural, diffused, cross-polarised and UV lights showed statistically significant improvements ( $p<0.05$ ) in wrinkles in the peri-orbital and cheek areas following twice daily application of TNS® at six months when compared with the baseline. Optical profilometry of the peri-orbital area also demonstrated a statistically significant ( $p<0.05$ ) reduction in wrinkles. But how do human growth factors affect such improvement in photodamaged skin?

#### SIGNALLING PATHWAYS

Some debate has raged over exactly how human growth factors can penetrate the stratum corneum given that many studies have shown, as Dr Fitzpatrick himself points out, "that hydrophilic molecules larger than 500 Da molecular weight have very low penetration through stratum corneum. Growth factors and cytokines are large hydrophilic molecules greater than 15,000 Da molecular weight." According to Dr Nikolaidis, growth factors do not need to penetrate deep into the dermis in order to stimulate new collagen production. "Pathways of cell-to-cell communications are well established," he says. "Growth factors and cytokines create a signalling pathway from the superficial cells to deeper ones, with keratinocytes in the upper dermis

#### REFERENCES

- (1) Richard E Fitzpatrick, Endogenous Growth Factors as Cosmeceuticals, American Society for Dermatologic Surgery, 2005; 31: 827-831
- (2) Richard E Fitzpatrick & Elizabeth F Rostan, Reversal of Photodamage with Topical Growth Factors: A Pilot study, J Cosmetic & Laser Ther, 2003; 5: 24-34
- (3) Stacy Smith, Therapeutic Clinical Research, San Diego, CA, Efficacy of TNS Recovery Complex in Facial Photodamage.

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affecting a response from the fibroblasts in the dermis. The stratum corneum is simply a loose layer of dead skin cells overlying live keratinocytes underneath. Prior to application of TNS Recovery Complex®, a manual wash or scrub can remove much of this layer and allow the product to reach the keratinocytes." And because human growth factors are a neutral pH, they are less irritating to the skin too.

Dr Nikolaidis reveals that he has seen great success with SkinMedica's TNS range and uses many of the products in conjunction with a retinoid to achieve optimal efficacy. "I've seen fantastic results with laser patients whose recovery downtime has improved dramatically with use of the TNS Recovery Complex®," he asserts. "I think the fact that well-respected figures in the US, notably Dr Tina Alster, director of the Washington Institute of Dermatologic Laser Surgery, and Dr Roy Geronemus, director of the Laser & Skin Surgery Centre in New York, are prepared to come out in support of the product says more than enough about its efficacy and suitability for use in aesthetic practice." ■