



## Treating ageing skin with a growth factor serum

Dr. Ahmed Al-Qahtani, president and founder of AQ Skin Solutions, discusses the use of a conditioned growth factor (GF) serum to prevent skin ageing

Aside from being the largest human organ, the skin falls under special consideration for being directly exposed to the environment. Being exposed to environmental insults such as ultraviolet radiation and other toxins, means that the skin can also undergo extrinsic ageing. Ageing is the synergistic result of both intrinsic and extrinsic ageing factors, which affect tissue function and structure.<sup>1</sup> These ageing processes produce damaging reactive oxygen species, or free radicals<sup>2</sup>, particularly as a result of photo damage due to UV light exposure. Consequences of the interwoven molecular pathways of intrinsic and extrinsic ageing include the reduction of procollagen production and increase of collagen degradation in the extracellular matrix (ECM), which manifests as fine lines and wrinkles, discolouration, eyelid bags, circles around the eyes, and sagging of the facial and periorbital areas. With emerging evidence revealing the shared fundamental molecular basis between chronological ageing and damage-induced ageing, exciting new opportunities for the proliferation of effective anti-ageing therapies are within reach. One research breakthrough to combat and reverse the underlying causes of ageing is the use of topical products employing growth factor (GF) technology.

### WHAT IS GROWTH FACTOR (GF)?

Growth factors (GFs) are specialised proteins that act as chemical messengers. The GFs discussed presently comprise extensive signalling pathways between the dermal and epidermal layers of the integumentary system.<sup>3</sup> They are found naturally in body cells including fibroblasts, which are responsible for the synthesis of the ECM

and collagen. Closely related to GFs are cytokines, which are associated with the immune system and play a key role in the modulation of inflammation for wound healing and skin regeneration.<sup>5</sup> GFs and cytokines are derived from macrophages, epidermal keratinocytes, and fibroblasts. Both are involved in cell differentiation, angiogenesis, production and distribution of collagen and elastin, and the regulation of essential cellular activities; therefore, they support healthy skin structure and function by promoting cell growth, organising the ECM and promoting cell recovery. Such topical GF technologies have also been found to produce cosmetic benefits as well.<sup>6</sup> AQ serums (AQ Recovery, Active, and Eye Serum) utilise the skin's own renewal mechanisms to reverse the signs of ageing, supplementing healing processes with essential components, which stimulates repair of ageing and photo-damaged skin. They are topical cosmeceuticals featuring GFs, skin conditioning agents, and antioxidants used in combination to improve the appearance of the skin, in terms of fine lines, wrinkles, age spots, tone and texture.

### AQ GF TECHNOLOGY IN WOUND HEALING AND REVERSING THE EFFECTS OF AGEING SKIN

My discovery of the use of GFs in aesthetics came as a result of my interaction with third-degree burn victims in their wound healing and cell regeneration therapies. A healthy skin biopsy was taken from the patient, and fibroblast (skin) cells were isolated using advanced cell sorting technology. The desired fibroblasts were replicated under sterile conditions and purified to obtain specific growth factors. The growth factors were isolated, purified, and placed



Figure 2: Photographs of significant wound healing visible in a patient using GF technology serum (AQ Recovery Serum) over a period of 29 days

under skin grafts and applied at the wound site. This resulted in the regeneration of the wound site and the emergence of new healthy, smoother skin with little to no scarring. Through my extensive research in the use of growth factors for medical application in wound healing and creation of artificial skin grafts, I came to recognise the potential for the application of GFs in the treatment of ageing skin; the molecular pathways of dermal ageing, both intrinsic and extrinsic, bear various similarities to that of a dermal wound, including the induction of inflammation by both acute photo-damage and trauma wounds. Knowing that inflammation results in elevated levels of free radicals and proteolytic enzymes, which promote the breakdown of the dermal ECM, I understood that successful wound healing would require a transition of the damaged cells from the inflammatory

stage to the granulation stage; such transition involves a variety of GFs and cytokines (i.e. TGF- $\beta$ s, PDGF, GM-CSF, and Interleukins).<sup>7,9</sup> These GFs act as primary signalling molecules, which initiate the repair process by promoting cell growth, and promote the production of the ECM components required for repair. Supporting studies have shown that stimulation of fibroblast growth using GFs and cytokines results in the synthesis of essential ECM components such as collagen, glycosaminoglycans, and elastin.<sup>8,9</sup> Therefore, I set out to formulate a serum containing precisely the composition of cell signalling molecules required to induce healing and regeneration to ageing skin. The correct combination and balance of the various GFs listed (Table 1) seem to play a crucial role in the remodelling and strengthening of damaged dermal tissue. Since ageing results in decreased levels of necessary GFs, reversal of the

signs of ageing requires supplementation of those GFs involved in skin repair<sup>9</sup>, and an appropriate medium for adequate delivery and absorption.

#### MODE OF ACTION OF THE TOPICAL GF SERUM VIA PATENTED AQ GF TECHNOLOGY

Although hydrophilic molecules larger than 500 Dalton typically have difficulty penetrating the stratum corneum, GFs and cytokines (>15,000 Dalton) are nevertheless able to penetrate the skin. Unlike collagen and elastin, these molecules do not comprise cytoskeletal proteins, yet they share the ability to create a signalling pathway. This cell-to-cell signalling allows them to communicate more deeply into the skin via epidermal keratinocytes, reaching as deep as the fibroblasts of the dense, irregular, fibrous connective tissue of the dermis. These molecules possess a further advantage in that they penetrate the skin predominantly along vertical pathways, such as through the pore of a hair follicle, through sweat glands, or through microlesions of the interfollicular stratum corneum. For the latter avenue, applying our serum in conjunction with microdermabrasion or micro-needling is particularly useful, as GF penetration can be significantly increased. The AQ serum formulation includes a unique delivery system in which conditioned media contains free-floating phospholipids, which can form micelles in aqueous solution, thus aiding the absorption of the larger GFs and cytokines. Soluble proteoglycans, or more specifically, glycosaminoglycans (GAGs), are also present in the media; studies have shown that GAGs can affect the activity and stability of proteins and signalling molecules within the ECM and also serve as lubricants in the ECM.<sup>10</sup> Our body produces its own GAGs that hydrate the dermal layer from within and also interact with various families of GFs. The hydrolysed GAGs contained in our formulation are similar to super moisturisers that can penetrate where simple surface moisturisers cannot. Furthermore, the addition of selected antioxidants and skin conditioning agents to our serum formulation facilitates the regenerative effects of the GFs and cytokines present. In sum, the AQ serum formulation not only allows for optimum penetration and absorption of the skin-regenerative GFs, but is also designed to fully promote the reversal of damage and promotion of health within the skin.

**Dr. Al-Gahtani** is a National Institutes of Health (NIH) scientist and is accredited with numerous scientific publications as well as his patented GF technology (U.S. Pat. 8,518,879). He is a longstanding member of the American Association of Immunologists and is an assistant professor with the faculty of medicine at United Arab Emirates University.



Table 1. List of growth factors, cytokines and other proteins identified in AQ Recovery, Active, and Eye Serum and their functions in the skin.

<b>TGF-<math>\beta</math>s (<math>\beta</math>1, <math>\beta</math>2, <math>\beta</math>3):</b>	Stimulates collagen production
	Stimulates fibroblast collagenesis
	Stimulates glycosaminoglycan production
	Increases fibronectin synthesis
	Inhibits matrix degradation
	Facilitates cell chemotaxis
<b>PDGF</b>	Controls fibroblast activation of collagen synthesis
	Stimulates fibroblast collagenesis and glycosaminoglycan production
	Stimulates angiogenesis
	Stimulates wound contraction
<b>GM-CSF</b>	Facilitates cell chemotaxis
	Improves leukocyte function
	Activates neutrophils, eosinophils, and monocytes/macrophages
<b>Interleukins (ILs)</b>	Stimulates proliferation and differentiation of haematopoietic cell lines
	Regulate cell homeostasis
<b>IL-3, IL-6</b>	Enhance neutrophil functions
<b>IL-7, IL-8</b>	Function as anti-inflammatory agents and stimulate wound healing

#### REFERENCES:

- Farage MA, Miller KW, Elsner P, Maibach HI. 'Intrinsic and extrinsic factors in skin ageing: A review', *Int J Cosmet Sci*, 30 (2008), pp. 87-9.
- Miyachi Y. 'Phototaging from an oxidative standpoint', *J Derma Sci*, 9(2) (1995), pp. 79-86.
- Bornberg M, Plettenberg H, Krumann J. 'Phototaging of human skin', *Photochem Photobiol*, 15 (2000), pp. 239-244.
- Babu M and Wells A. 'Dermal-epidermal communications in wound healing', *Wounds*, 13 (2007), pp. 183-189.
- Barrientos S, Stojadinovic O, Golinko MS, Brem H, Tomic-Canic M. 'Growth factors and cytokines in wound healing', *Wound Rep Reg*, 16 (2008), pp. 585-601.
- Schouert JM, Luu TK, Moy RL. 'Improved texture and appearance of human facial skin after daily topical application of Epidermal Growth Factor (EGF) Serum', *J Drugs Dermatol*, 1(5) (2002), pp. 613-620.
- Mateo RB, Reschner JS, Abina JE. 'Interleukin-6 activity in wounds', *Am J Physiol* 265 (1994), R1840-R1844.
- McCartney-Francis N, Mzel D, Wong H, Wahl L, Wahl S. 'TGF-beta regulates production of growth factors and TGF-beta by human peripheral blood monocytes', *Growth Factors*, 4 (1990), pp. 27-35.
- Rappolee DA, Mark D, Banda MJ, Werb Z. 'Wound macrophages express TGF $\alpha$  and other growth factors in vivo: analysis by mRNA phenotyping', *Science* 241 (1988), pp. 708-712.
- Moulin V. 'Growth factors in skin wound healing. Review article', *Eur J Cell Biol*, 68 (1995), pp. 17.
- Kirby CP, Lynch SE. 'Role of growth factors in cutaneous wound healing: a review', *Crit Rev Oral Biol Medical*, 4 (1993), pp. 729-760.
- Canalis E. 'Skeletal growth factors and aging', *J Clin Endocrinol Metabol*, 78(5) (1994), pp. 1009-1010.
- Georges S, Heymann D, Padines M. 'Modulatory effects of proteoglycans on proteinase activities', *Meth Mol Biol*, 836 (2012), pp. 307-22.