

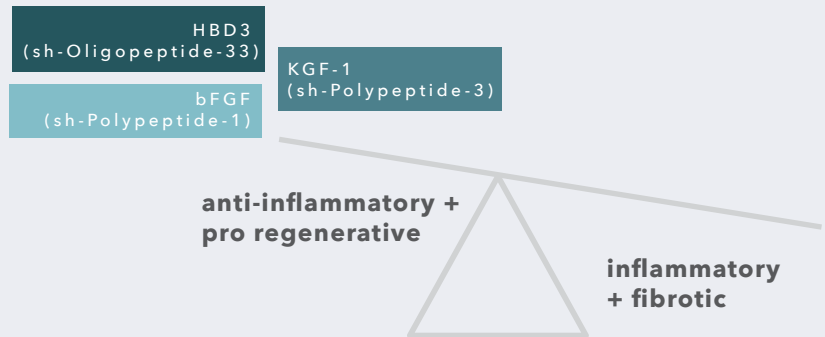
# PolyGF-3

## Vegan Growth Factor Ingredient Complex

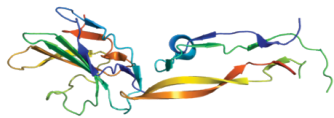
### Introduction:

PolyGF-3 is a complex of 3 recombinant (synthetic) human growth factors, combined synergistically to match the precise levels found in healthy young skin. The scientists at Cellese have studied the secretome of the human bone marrow stem cell for over 10 years to capture this ideal profile, using a bioinformatics approach to recreate and deliver optimal skin rejuvenation in a vegan, globally compliant ingredient.

The balance beam illustration shows the nature of growth factors and defensins as balancing protein biosignals, regulating and offsetting inflammatory and fibrotic bio signals - effectively canceling their aging effects.



### hBD3 (sh-Oligopeptide-33): Beta Defensin-3



hBD3 (sh-Oligopeptide-33):  
Beta Defensin-3

Defensins are a class of antimicrobial peptides naturally released by the human body. Beta Defensins, specifically the Beta Defensin-3 (hBD3) subtype, is native to the skin and is responsible for keeping skin homeostasis in check while supporting the skin microbiome. BD3 increases the maturity of skin immune cells, allowing them to work overtime, protecting and defending the skin from aging triggers, and reducing inflammation<sup>1</sup>. Not only does hBD3 reduce the growth of harmful microorganisms that can lead to acne<sup>2, 3</sup>, it also acts as a probiotic-like molecule keeping the skin-friendly microbes alive, leading to ultimate skin strength, resiliency, and health<sup>3</sup>. hBD3 is a potent anti-inflammatory that has shown efficacy in treating topical inflammatory conditions such as atopic dermatitis<sup>4</sup> and that affords it the ability to control the pathways that lead to skin aging. hBD3, being heavily involved in wound healing, increases the production of keratin, a key structural protein found in our skin, and the proliferation of epidermal keratinocyte cells, both of which improve the visible signs of aging skin<sup>5</sup> and strengthen the skins protective barrier<sup>6</sup>.

(1) Ferris LK, Mburu YK, Mathers AR, et al. Human beta-defensin 3 induces maturation of human langerhans cell-like dendritic cells: an antimicrobial peptide that functions as an endogenous adjuvant. *J Invest Dermatol.* 2013;133(2):460-468. doi:10.1038/jid.2012.319.

(2) Harder J, Tsuruta D, Murakami M, Kurokawa I. What is the role of antimicrobial peptides (AMP) in acne vulgaris? *Exp Dermatol.* 2013 Jun;22(6):386-91. doi: 10.1111/exd.12159. PMID: 23711061.

(3) M. Marta Guarna, Richard Coulson, Evelina Rubinchik, Anti-inflammatory activity of cationic peptides: application to the treatment of acne vulgaris, *FEMS Microbiology Letters*, Volume 257, Issue 1, April 2006, Pages 1-6.

(4) Sawamura, D., Goto, M., Shibaki, A. et al. Beta defensin-3 engineered epidermis shows highly protective effect for bacterial infection. *Gene Ther* 12, 857-861 (2005).

(5) Chieosilapatham P, Ogawa H, Niyonsaba F. Current insights into the role of human  $\beta$ -defensins in atopic dermatitis. *Clin Exp Immunol.* 2017;190(2):155-166. doi:10.1111/cei.13013.

(6) Purpera, Paula. (2020). Defensins: Skin-derived Antimicrobial Peptides with Antiaging Properties Learning Objectives.

(7) Kiatsurayanon C, Niyonsaba F, Smithrithee R, Akiyama T, Ushio H, Hara M, Okumura K, Ikeda S, Ogawa H. Host defense (Antimicrobial) peptide, human  $\beta$ -defensin-3, improves the function of the epithelial tight-junction barrier in human keratinocytes. *J Invest Dermatol.* 2014 Aug;134(8):2163-2173. doi: 10.1038/jid.2014.143. Epub 2014 Mar 14. PMID: 24633129.

## bFGF (sh-Polypeptide-1): Fibroblast Growth Factor

With aging comes a significant decline in the production of the most important structural protein for the skin, known as collagen. Collagen levels start to decline in production, with subsequent thinning of the skin, about 1% every year after the age of 20. The cells in our dermis (where the majority of the collagen lives) that are responsible for the production of this anti-aging protein are known as Fibroblasts. These cells can also become rather sluggish as we get older, leading to that lowered production of collagen. The primary growth factor (molecules the cells use to talk to one another, like text messages) that triggers the Fibroblast to grow and produce new versions of itself is the Fibroblast Growth Factor (FGF). FGF, in concert with KGF, has shown to rapidly enhance wound healing and collagen deposition in skin.<sup>1</sup> When these cells are given the instruction to grow and replicate via the FGF biosignal, the skin now has more Fibroblasts that are now pumping out more collagen and increasing skin elasticity. Collagen production is the holy grail of anti-aging, and the FGF gives your skin the opportunity to produce more of it. When it comes to anti-aging, synthesis of collagen and elastin are paramount to maintain a youthful appearance, and FGF has shown to activate these cellular processes in skin, acting as the master cellular control mechanism for anti-aging, reducing the appearance of lines and wrinkles.<sup>2</sup>

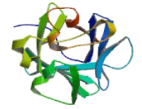


bFGF (sh-Polypeptide-1):  
Fibroblast Growth Factor

(1) Qu Y, Cao C, Wu Q, Huang A, Song Y, Li H, Zuo Y, Chu C, Li J, Man Y. The dual delivery of KGF and bFGF by collagen membrane to promote skin wound healing. *J Tissue Eng Regen Med*. 2018 Jun;12(6):1508-1518. doi: 10.1002/term.2691. Epub 2018 May 15. PMID: 29706001.

(2) de Araújo R, Lôbo M, Trindade K, Silva D, F, Pereira N: Fibroblast Growth Factors: A Controlling Mechanism of Skin Aging. *Skin Pharmacol Physiol* 2019;4:275-282. doi: 10.1159/000501145.

cells are produced, they change shape and form as they rise to the surface of the skin, eventually becoming dead skin cells at the surface which slough off naturally in roughly 30 days. This cell turnover cycle starts to slow down with age, and the ability for these vital skin cells to migrate slows as well. The main growth factor that triggers the mighty keratinocyte to grow and divide is the Keratinocyte Growth Factor (KGF). Keratinocytes, when healthy, produce their own types of collagen that keep the DEJ and skin barrier strong and intact. Regulating keratinocyte cell production, and allowing these cells to migrate, grow, and divide, is the hallmark of youthful, healthy skin. KGF has proven to protect epidermal stem cells from UV irradiation, acting as a cytoprotective agent<sup>1</sup>, while also increasing native hyaluronic acid synthesis for increased skin hydration.<sup>2</sup> One consequence of the skin aging process is the skin and its barrier become fragile, weak and susceptible to injury. Topically applied KGF has shown to improve the strength and resiliency of the skin<sup>3</sup>, while increasing the regenerative capacity of the epidermis, keeping a youthful and healthy cellular turnover cycle.<sup>4</sup>



KGF-1 (sh-Polypeptide-3):  
Keratinocyte Growth Factor

(1) Braun, Susanne, Krampert, Monika, Bodo, Enikoe, Kuemin, Angelika, Born-Berclaz, Christiane, Paus, Ralf, Werner, Sabine. (2006) Keratinocyte growth factor protects epidermis and hair follicles from cell death induced by UV irradiation, chemotherapeutic or cytotoxic agents *Journal Cell Science*, 119: 4841-4849.

(2) Karvinen, S; Pasonen-Seppanen, S; Hyttinen, JMT; Pienimaki, JP; Torronen, K, Jokela, TA; Tammi, MI, Tammi, R (2003) Keratinocyte growth factor stimulates migration and hyaluronan synthesis in the epidermis by activation of keratinocyte hyaluronan synthases 2 and 3. *J Biol Chem*, 278:49495-49504.

(3) Dou C, Lay F, Ansari AM, et al. Strengthening the skin with topical delivery of keratinocyte growth factor-1 using a novel DNA plasmid. *Mol Ther*. 2014;22(4):752-761. doi:10.1038/mt.2014.2.

(4) Pierce GF, Yanagihara D, Klopchin K, et al. Stimulation of all epithelial elements during skin regeneration by keratinocyte growth factor. *J Exp Med*. 1994;179(3):831-840. doi:10.1084/jem.179.3.831.

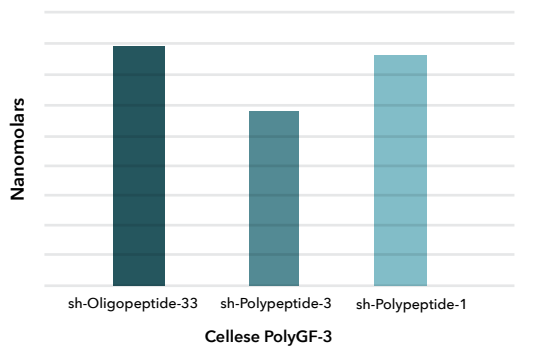
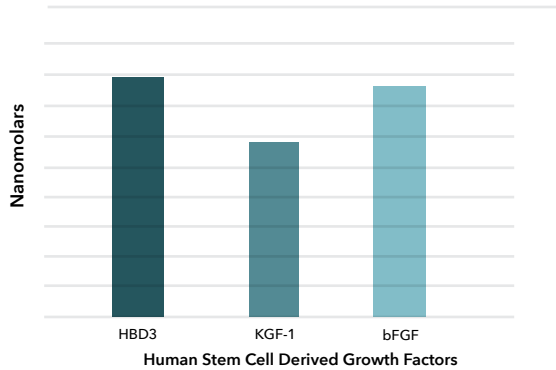
## KGF-1 (sh-Polypeptide-3): Keratinocyte Growth Factor

The most dominant cell in your epidermis, the layer of the skin just above the dermis, is the Keratinocyte. This cellular "king" of the epidermis is produced near the basement of the epidermis, in an area called the Dermal-Epidermal Junction (DEJ). New keratinocytes produced here come from a specific type of keratinocyte stem cell. As these

### Dosing Methodology

Cellese uses its 10+ years of experience in bioinformatics to deliver recombinant growth factors at nanomolar (nM) levels in line with the published literature and natural secretome levels found in human cell cultures. For standard

cosmetic products, dosing is targeted at 1x. For professional and medical grade dosing is recommended at 2x and 4x respectively.



↖ **Equivalent Nanomolar Delivery** ↗

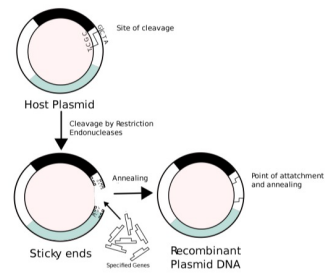
### What Are Growth Factors?

Growth Factors are signaling protein molecules that all cells in the human body use to communicate with one another. Think of these like text messages between cells, and each text is coded with a specific message. This communication between cells is rampant and healthy when we are young, but unfortunately the ability of cells to produce these molecules starts to decline as we get older, that healthy communication slows down, and that leads to aging setting in. Topically applied growth factors replenish what we had in abundance in our youth, giving the cells the ability to get back to a healthy communication level that will yield a profound anti-aging response.

### What Are Recombinant Growth Factors?

Growth Factors can come from two sources. They can be naturally derived and harvested from human cells, or we can produce them in the lab with recombinant technology. This is where we take a non-human bacterial cell and hijack its genetic machinery. We take human DNA that is coded for a specific protein (like

BD3, FGF or KGF), and implant it into the bacterial cell. This cell will now take orders from that DNA and produce multiple copies of the protein it was told to create. While these molecules are not derived from human cell sources directly, they are in fact molecularly identical and achieve the same biological effect. This is how most protein-based drugs, like Insulin, are produced today.



PROTEIN MANUFACTURING - GENE SPLICING

These proteins are identical to the human derived version in form and function, but not derived from an animal cell, and this can be considered vegan.

Cellese Has created the poly growth factor (PolyGF) technology platform to provide an exact synthetic analog of its human bone marrow stem cell condition media products. These products have performed exceptionally well in a clinical setting, and have been sold in Singapore and Europe for two years as cosmeceuticals in the medical aesthetic market. Patients and practitioners report excellent outcomes equivalent to human derived products. The following peer reviewed clinical studies have been published validating the PolyGF technology.

PolyGF-8: Topical combined growth factors improve the appearance of skin aging. *J Am Aca Dermatol.* 2019;81(4):AB256. doi:10.1016/j.jaad.2019.06.1132.

Sachdev, Mukta & Velugotla, Keerthi & Revanker, Sapna & Somasekhar, Geetha. An open-label, single-center, safety and efficacy study of eyelash polygrowth factor serum. *J Clin Aesthet Dermatol.* 2020;13(2):61-66. Published online 2020 Feb 1.