

# Dermatopoietin® (IL-1a)

## Revolutionary polypeptide in skin care



**EVENSWISS**



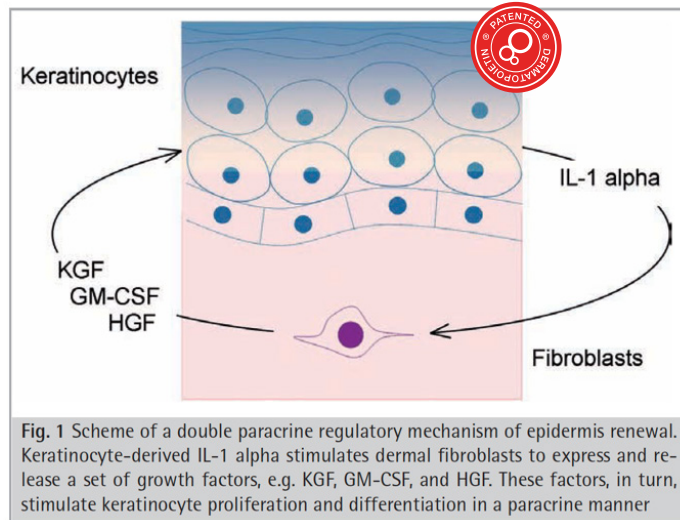
WITH DERMATOPOIETIN®

IL-1a – trademark name Dermatopoietin®. IL-1a, a cytokine of 159 amino acids, is best known for its role in the regulation of the immune response. IL-1a acts as a messenger regulating skin homeostasis,<sup>1,2</sup> and it is highly and constitutively expressed by keratinocytes in the epidermis. The target cells of epidermal IL-1a are dermal fibroblasts. IL-1a does not only stimulate their proliferation but also activates the production of procollagen and collagenase, as well as the expression of several growth and differentiation factors for epidermal cells.

Keratinocyte-derived IL-1a induces fibroblasts to express growth factors which act back on the epidermis and stimulate its regeneration. The expression of IL-1a by keratinocytes and the production of collagen 15 have been shown to decline in ageing skin.

IL-1a is shown to be an innovative active ingredient for cosmetic products with skin rejuvenating (anti-ageing) properties. It acts on the surface of skin by stimulating keratinocytes, the main cells of the epidermis, to produce and release endogenous IL-1a. The physiological function of this cytokine is to stimulate the fibroblasts in the dermis to increase the expression of collagen and elastin which leads to denser and tighter skin, and eventually to an improved skin elasticity and reduced wrinkles

Topical IL-1a thus affects deep skin structures without penetrating skin by triggering a cascade of reactions, which propagate from the surface to the depth of skin.



**Fig. 1** Scheme of a double paracrine regulatory mechanism of epidermis renewal. Keratinocyte-derived IL-1 alpha stimulates dermal fibroblasts to express and release a set of growth factors, e.g. KGF, GM-CSF, and HGF. These factors, in turn, stimulate keratinocyte proliferation and differentiation in a paracrine manner

## WHAT IS DERMATOPOIETIN® (DP)?

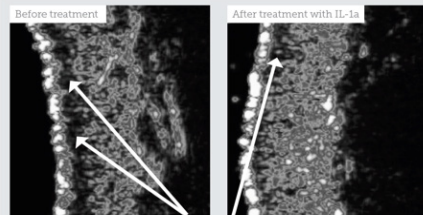
DP is the main active ingredient of the EVENSWISS® products.  
It is protected by a patent and it is the interaction of two main polypeptides:

### 1- Interleukin-1 Alpha

- Interleukin 1 Alpha (IL1A): protein stripes of 159 amino-acids, non-penetrable
- It is produced and released by Keratinocytes in the Epidermis
- Biological Name: Interleukin-1 Alpha
- Registered Trademark and Patented: Dermatopoietin®
- INCI Name: sh-polypeptide-17

### 2- Hexadelatine

- Stripe of 6 proteins
- Hexadelatine do not penetrate into the living cells of the epidermis it is restricted to stay on the SC

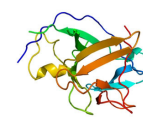


SLEB: subepidermal low echogenic band, a reliable marker of skin (photo-)ageing.

Figure 3.

Ultrasonography at 20 MHz is a technique to visualise skin architecture. Light pixels reflect skin proteins, dark pixels proteoglycans, lipid and/or water. The dense structure on the left side is the epidermis (keratin). Undemeath the epidermis is the dermis with the main protein collagen. The SLEB, which partially disappears after treatment with IL-1a, is part of the dermis.

## DERMATOPOIETIN®



**IL1A**  
159 amino-acid

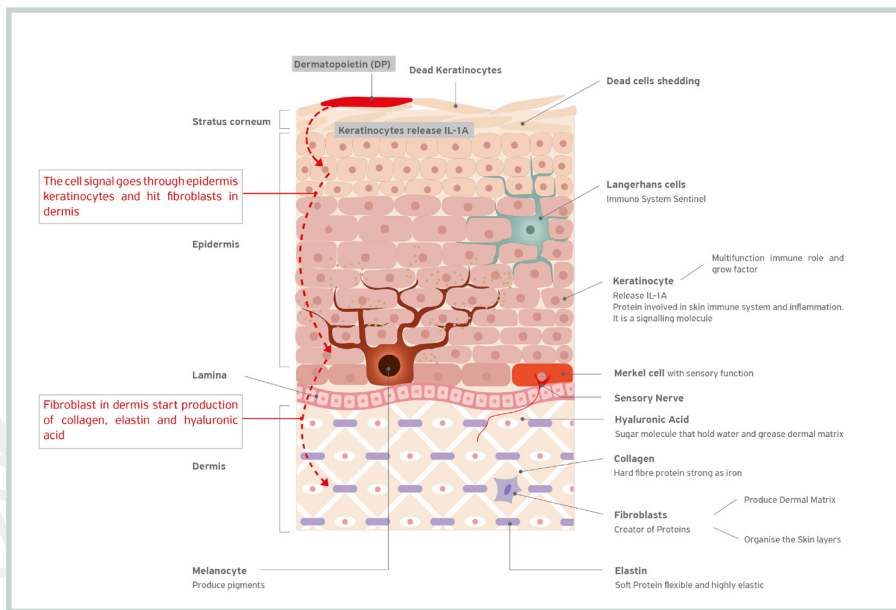
**Hexadelatine**  
6 amino-acid

## Abstract

Interleukin-1 alpha (IL-1 alpha) is an epidermal cytokine that is constitutively produced by human keratinocytes in substantial amounts and plays an important role in normal skin homeostasis. Comprehensive bibliography highlights the role of Interleukin-1 alpha as the master regulator of skin architecture and functions. At picomolar concentrations IL-1 alpha stimulates dermal fibroblasts to produce a cascade of growth factors (KGF, GM-CSF, and HGF) required for keratinocyte growth. IL-1 alpha stimulates collagen turnover in dermis by tight regulation of both collagen synthesis and degradation pathways. IL-1 alpha stimulates dermal fibroblasts to produce glycosaminoglycans, particularly hyaluronic acid. IL-1 alpha plays a role in keeping skin barrier function in norm. IL-1 alpha production and action in skin may be affected by extrinsic or intrinsic factors, e.g. chronologic aging or cortisol action. It provides a basis for the use of recombinant human interleukin-1 alpha as an active ingredient in dermatologic and cosmetic applications with focus on anti-age and anti-cellulite products.

# THE MECHANISM OF DERMATOPOIETIN®

## THE SIGNALLING COSMETICS®



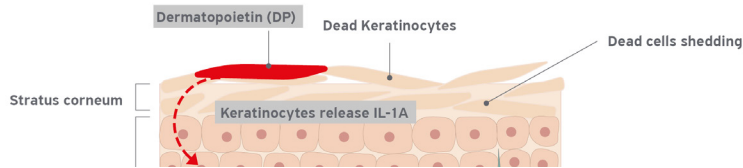
Dermatopoietin® (DP) = interleukin-1 alpha (IL-1 a) is a well-known polypeptide abundant in human skin. Its main physiological activity in skin is to promote skin renewal.

It stimulates keratinocytes in the epidermis to produce more IL-1 a, thereby generating a “chain reaction” of IL-1 a penetrating the epidermis (see scheme at right). Upon arriving in the dermis, it activates the fibroblasts to produce collagen, elastin and hyaluronic acid.

Once DP touches the surface of the skin (Stratus Corneum) it activates Keratinocytes, that release the IL-1A. (The Activation of the Keratinocytes occurs by a biochemical signal transmitted to the membrane receptors. The signal is translated by receptors).

The signal goes through Epidermis and Hits Fibroblasts in the Dermis. The natural and endogenous reaction of Fibroblast is to start producing proteins, particularly Elastin, Collagen and Hyaluronic Acid.

## HOW THE SIGNALLING COSMETICS® WORKS



The DP polypeptide send message to the first alive Keratinocytes on the Stratus Corneum. In that moment DP polypeptide send message and receptors of Keratinocytes take the message and translate. The message is recognised as endogenous and perfectly safe.

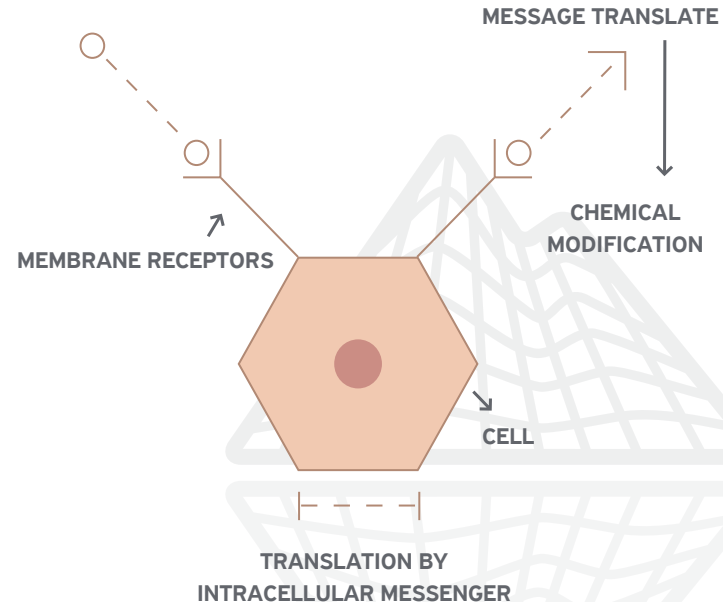
Keratinocytes cells have membrane receptors that receive physical or chemical signals. Some of them are called **Intracellular Messenger (steroids, organic molecules, peptides, etc).**

Receptors translate the external signal in chemical/biochemical intracellular signal.

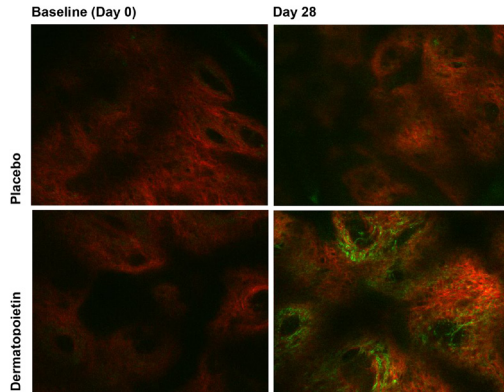
This trigger a cascade effect to amplify the signal.

The molecular circuit involved into translation and transmission includes receptors, channels, enzymes and regulatory proteins.

TRASDUCTION  
information -> messaging -> chemical modifications

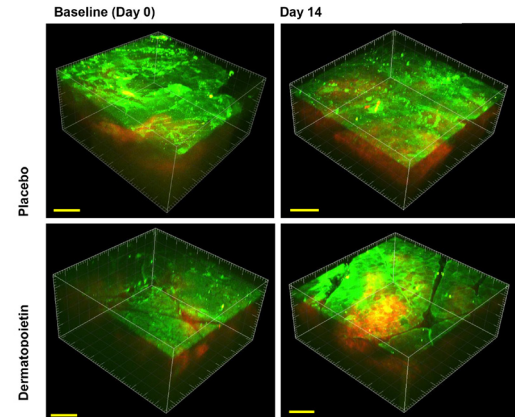


A 4-week treatment of aging skin with Dermatopoietin strongly increases the collagen, elastin and hyaluronic acid content of the dermis.



## Experiment 1

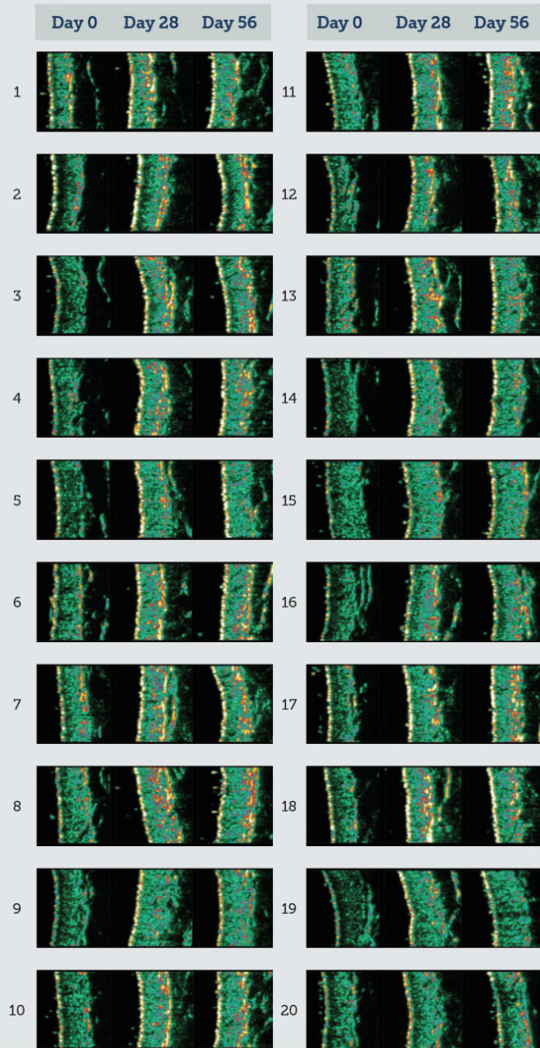
Two-photon microscopic pictures from the dermis at 80 µm skin depth. Comparison of Dermatopoietin versus Placebo and Baseline versus 4-week treatment. Pictures were obtained from the same skin spot. Clearly visible is the increase of collagen (red) and elastin (green). Dermatopoietin concentration: 150 µg/L.



## Experiment 2

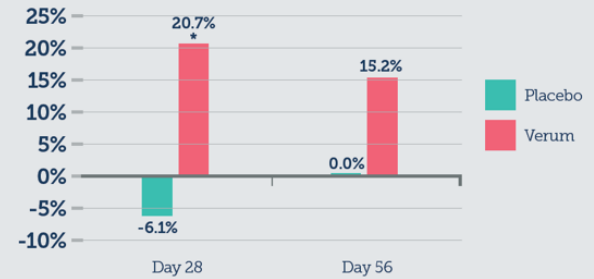
Three-dimensional 2-photon microscopic composite pictures showing the green autofluorescence in the epidermis and dermis as well as collagen (red, second harmonic generation) in the dermis. Clearly visible is the increase of collagen after two weeks in the skin of the forearm treated with Dermatopoietin at a concentration of 30 µg/L.

Figure 4.



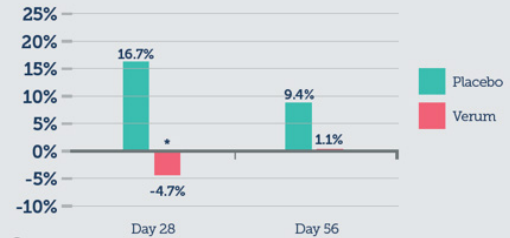
**Figure 4** - shows the ultrasonograms of 20 volunteers at baseline and after 28 and 56 days of treatment with a cosmetic formulation containing IL-1a.

Striking is the clear improvement of skin density and the partial disappearance of SLEB in all volunteers.



**Figure 5.**

Change of gross skin elasticity (R2) after 28- or 56-day treatment with either verum or placebo. R2 indicates the elastic portion of skin relaxation after its mechanical deformation. Only the formulation containing IL-1a improved skin elasticity. The difference between verum and placebo at Day 28 was significant with a p-value of 0.03.



**Figure 6.**

Change of viscoelasticity (R6) of skin after a 28- or 56-day treatment with verum or placebo, respectively. The difference between verum and placebo at Day 28 was significant with a p-value of 0.0008.