

Growth factors – the body's own peptides control various cell functions

published in medical Beauty Forum 2012 (2), 16-18

Peptides have become a topic of intense biochemical research since they control a multitude of regulatory functions in the body. Also the growth factors are an object of research since they regulate the development of young organisms and initiate repair mechanisms and healing processes in the later course of life. It's not surprising though that they are also in the focus of cosmetics.

Peptides are prevalent in nature: they occur as components of the connective tissue, the nails and hairs but also as signalling substances and hormones. Various attempts have been made to use their effects for skin care purposes by integrating mare's milk, colostrum with its high content of proteins and antibodies, but also various other milk products into different skin care products. Peptides from different sources such as thymus, epiphysis, cartilages, liver, prostate, heart, and brain tissue have been synthetically recreated and mixed into cosmetic creams in the hope of improving the metabolism in the mature and atrophic skin, strengthening the immune defence and impeding the skin aging process. The attempts were rewarded with limited success though, narrowing down on improving the skin hydration, tightening the skin surface as well as on antioxidative effects¹.

Subsequently, synthetic peptides that stimulate the collagen synthesis were discovered; they became generally known as matrikines. Other oligopeptides, i.e. small peptides with low molecular mass influence the muscular synapses of mimic wrinkles hence they can be used for wrinkle reduction treatments.

Hormone-like effects

In the focus of interest are the natural peptides of the body with hormone-like effects. They are called growth factors. Time and again new growth factors have been discovered and the scientific findings on their functions have been accumulating in an exponential manner.

Various stimuli take part in the development, activation or release of growth factors. The reciprocal actions with their corresponding receptors trigger signalling cascades within or at the cells which then selectively increase or

retard or even incapacitate gene activities. The following survey covers a selection of skin relevant representatives – a snapshot of a definitely rather fascinating topic.

Fibroblast Growth Factor (FGF)

The Fibroblast Growth Factor is not a single component though: in the meantime it comprises a whole family of more than 20 growth factors. The FGF receptors are situated on the surface of the external cell membranes and convey the signals into the interior of the cell after the docking manoeuvre. This particular type of receptors also is called transmembrane receptors: the cells are induced to proliferate, differentiate or also migrate. FGF-1 is the most popular representative of the family. Besides its effects on the proliferation of fibroblasts (cells of the connective tissue) which, among other activities, are responsible for the collagen synthesis, FGF-1 also manipulates the endothelium cells that coat the inner surface of blood vessels. This activity has major effects on the formation of new blood vessels (angiogenesis). A further very important aspect for the skin is the wound healing process.

The term **Keratinocyte Growth Factor (KGF)** is synonymous with FGF-7. It regulates the epithelialisation during the wound healing process or more precisely, the process during which keratinocytes cover the wound area and form the epithelium – in the case of the skin, the epidermis, a squamous epithelium. Keratinocyte Growth Factor 2 is identical with FGF-10.

Epidermal Growth Factor (EGF)

Via its receptors, the EGF stimulates proliferation and cell growth. It impedes the apoptosis, or in other words the programmed cell death. However, in this way it can also support the growth and metastatic spread of tumours.

Vascular Endothelial Growth Factor (VEGF)

By activating the endothelium formation, the VEGF initiates the vascularisation (angiogene-

¹ H. Lautenschläger, Peptide – mehr als Botenstoffe und Hormone, Kosmetik International 2007 (9), 14-17

sis) during the embryonic development. It also manipulates other types of cells.

Transforming Growth Factor (TGF)

The TGF belongs to the family of cytokines. Cytokines also regulate the cell functions and stimulate their differentiation, growth and immune response. There are several TGF sub-families. TGF- α for instance is produced by tumour cells whereas TGF- β contributes to the wound healing process.

The **interleukins (IL)** are another type of growth factors that belong to the cytokine family. IL-1 removes damaged cells out of the connective tissue by intensifying the inflammatory processes. The group of interleukins also is characterized by a high degree of multifunctionality. IL-1 α stimulates the collagen synthesis in the skin².

Insulin-like Growth Factor (IGF)

IGF-1 is a representative of this group and participates in the carcinogenesis, cell proliferation and the inhibition of the apoptosis (programmed cell death).

Melanocyte Stimulating Hormone (MSH)

MSHs are signalling molecules that control various biological processes. The α -Melanocyte Stimulating Hormone (α -MSH) for instance induces the formation of pigments³.

Platelet Derived Growth Factor (PDGF)

The PDGF is divided into various factors that are released by the blood platelets and influence the wound healing process as well as the proliferation of fibroblasts. They are particularly found in the embryonic phase.

Hepatocyte Growth Factor (HGF)

Among other activities, the HGF enhances the collagen synthesis via fibroblasts and accelerates the proliferation during the wound healing process.

Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF)

Similar to the factors G-CSF und M-CSF which also belong to this specific group, GM-CSF stimulates the development of neutrophil granulocytes and macrophages, both are counted among the phagocytes.

In vitro und in vivo...

The conclusions usually drawn from biochemical studies and then applied to cosmetic and dermatological applications often neglect the complex cross-linkages and reciprocal actions that result from hormonal and signalling processes. Stimulating or inhibiting one factor naturally triggers secondary reactions which in individual cases may not even be aligned but may have corrective or even counterproductive effects (elsewhere). An uncontrolled use of individual factors may even have carcinogenic effects. Beyond that, also the multifunctional activities of the peptides with hormone-like effects have to be considered. Similar to the prostaglandins (hormone-like fatty acids) effects which have been known for quite some time by now, even varying effects at the local target receptors may be induced. The cause-effect relationships deduced from cell cultures ("in vitro") or isolated tissue only partly allow conclusions relating to the organism as a whole ("in vivo"). Hence, it can be maintained that there are only few reliable scientific statements on the actual "in vivo" effects of externally applied cosmetic products containing growth factors as well as on the clinical significance regarding comparable placebo products. The application of growth factors in cosmetic products generally is focused on the anti-aging treatment and the wound healing process⁴. Individual growth factors are isolated from stem cells or cell cultures. Others are produced synthetically.

Limits to efficacy

The highly concentrated growth factors of the colostrum or the stem cell extracts, both of major significance for the development of animal or vegetable organisms, are expected to support the long term rejuvenation treatments of adults. The question whether the growth factors identified in these multi substance systems finally get to the areas where they are needed still remains unanswered. It is doubtful that customary cosmetic emulsions are able to accomplish this task. It is a matter of fact that peptides as a substance group contained in milk products or as components of vegetable stem cell extracts show excellent skin care characteristics⁵ due to their specific structure

² Pomytkin I, Interleukin-1 Alpha, ein für die Hauterneuerung zentrales epidermales Zytokin, SÖFW-Journal 135 (9), 41-46 (2009)

³ Böhm M, Luger TA, α -Melanocyten stimulierendes Hormon, Der Hautarzt 2010 (6), 497-504

⁴ R. C. Mehta, R. E. Fitzpatrick, Cosmeceutical Science in Clinical Practice, New York 2010, Informa Healthcare, Chapter 4: Growth Factors, p 26-31

⁵ H. Lautenschläger, Spezielle Wirkstoffe und Grundlagen in der Korneotherapie, Kosmetische Medizin 2004 (2), 72-74

and, above all, due to the presence of additional components such as amino acids, vitamins, isoflavones, carbohydrates and essential fatty acids. The results can still be intensified by accompanying physical effects like radiofrequency treatments, electric stimulations, mechanical stimuli (shock waves, ultrasound, microdermabrasion etc.), even in time lapse mode, a fact that meets the customers' expectations in terms of cosmetic and dermatological treatments. In how far externally applied growth factors actually contribute to a successful treatment still remains to be quantified.

Conventional activation

It is presumed that the growth factors used in today's "cosmeceuticals" penetrate via the damaged skin barrier, sweat glands and the hair follicles⁶, since the high-molecular peptide structures practically impede the passage through the intact skin barrier – unless specific substances are added that improve the penetrability such as liposomes for instance. In connection with the difficult transport of exogenous growth factors and their doubtful arrival at their destination it is an interesting issue how the endogenous growth factors can be stimulated from the outside. Just to mention a few examples:

- Sodium ascorbyl phosphate or ascorbyl palmitate can penetrate the skin barrier and stimulate the collagen formation when combined with liposomes or nanodispersions.
- Vitamin A (Retinol) activates cell formation and collagen synthesis. In combination with penetration supporting nanodispersions, skin recovering vitamin A acid effects can be observed.
- A repigmentation of vitiligo affected skin is described in connection with vitamin D analogous substances and UV light.
- D-panthenol stimulates the cell proliferation on injured skin.
- Echinacea and butcher's broom extracts stabilize capillary blood vessels.
- Fruit acid treatments and microdermabrasion activate skin recovering processes.

Endogenous growth factors are activated in every one of the above-mentioned cases. The particular mechanism as well as the informa-

tion on which specific growth factor actually had been stimulated might not be known in detail. It is a matter of fact though that the so-called activators penetrate easily through the skin barrier whereas on the other hand it is rather complicated to transport high-molecular peptides into the skin.

It has to be stated though that endogenous growth factors can only be stimulated and function properly in presence of essential physiological components which however may not be the case with problem skins. It can be assumed that there are deficiencies in vitamins, specific fatty and amino acids as well as trace elements, a fact that needs to be considered in the first place when selecting the ingredients for cosmetic formulations.

Experience shows that repeated and intense treatments with fruit acids or other chemical peelings in order to intensify the skin recovery process on the so-called hard way may be counterproductive and even involve irreparable damages to the skin. There even seems to be a causal relation between frequent fruit acid peelings and subsequently developed rosacea. A physical parallel here is the skin damage caused by repeated sun exposure which leads to a premature aging of the skin. Moderate techniques like massages (mechanical stimulations), radiofrequency and infrared therapies as well as heat and cold treatments for instance are soft alternatives that have proved successful in inducing endogenous growth factors.

In this context, further interesting scientific results can be expected however besides the euphoric anticipations also the skin as an organism should be kept in mind. Miracles are certainly desirable although they occur extremely rarely.

Dr. Hans Lautenschläger

⁶ R. C. Mehta, R. E. Fitzpatrick, Endogenous growth factors as cosmeceuticals, *Dermatologic Therapy* 2007 (20), 350–359