Nutrex Technology Co. Ltd.

PROJECT NAME (Ingredient Trade Name): SABI (Growth factor complex) **Active Ingredient Scientific Name:** EGF, aFGF, bFGF, IGF-1, KGF-2, VEGF, SOD **Submission Date:** 2010/04/16
Description of Product: SABI contains high potency growth factor complex and is designed to re-invigorate human skin's natural recovery function. Two to three weeks of intensive skin care will encourage skin's natural recovery function and restores youthful skin texture and radiance quicker than any other skin care products.

1. Supporting Evidence (Efficacy/Functionality):

Provide all supporting literature and research studies, publications, protocols, and analytical assessment.

- Mechanism of Action/s (MOA)

Skin aging is mediated by combinational effects of time (intrinsic aging) and environmental factors (extrinsic aging) on cellular and extracellular infrastructure. These are two independent, clinically and biologically distinct, processes that affect the skin structure and function simultaneously. Growing evidence now suggests that the two aging processes have converging biochemical and molecular pathways that lead to photoaging of skin. The common mechanisms of the two aging processes may provide several unique opportunities to develop new antiaging therapies. Recent advances in understanding the role of endogenous growth factors in the aging process provide one such opportunity to develop novel antiaging cosmeceutic products.

A growth factor is a naturally occurring substance capable of stimulating cellular growth, proliferation and cellular differentiation. Usually it is a protein or a steroid hormone. Growth factors play an important role in reversing the effects of skin aging mediated by chronological and environmental factors. Excessive oxidation of intra- and extracellular components result in breakdown of collagen and elastin network in the dermis and produce the effect of facial aging.

Topical application of human growth factors in multiple clinical studies has been shown to reduce the signs and symptoms of skin aging, including statically significant reduction in fine lines and wrinkles and increase in dermal collagen synthesis. Figure 1 shows a schematic of the process of photodamage and wound healing.

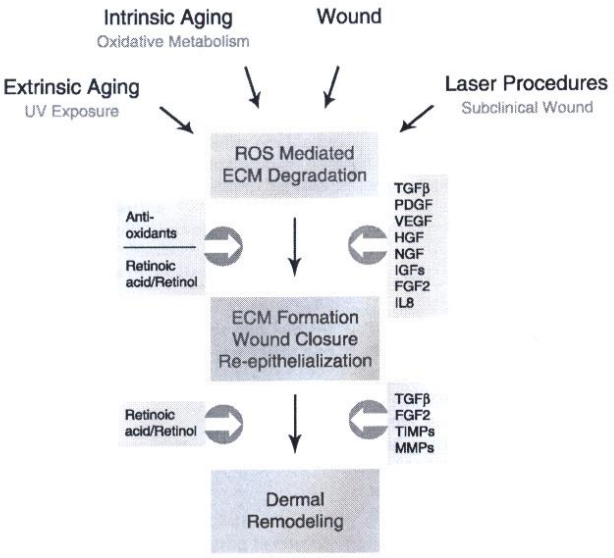


Fig. 1. Healing and remodeling of skin damaged by the effect of intrinsic aging, extrinsic aging, wound, or laser procedures.

1-1-1. acidic Fibroblast Growth Factor (aFGF)

Heparin-binding growth factor 1 is a protein that in humans is encoded by the FGF1 gene.[2][3]

The protein encoded by this gene is a member of the fibroblast growth factor (FGF) family. FGF family members possess broad mitogenic and cell survival activities, and are involved in a variety of biological processes, including embryonic development, cell growth, morphogenesis, tissue repair, tumor growth and invasion. It acts as a mitogen for a variety of mesoderm- and neuroectoderm-derived cells in vitro, thus is thought to be involved in organogenesis. Three alternatively spliced variants encoding different isoforms have been described.[4]

aFGF is a potent mitogenic and chemotactic agent for vascular endothelial cells, dermal fibroblasts, and epidermal keratinocytes, the principal cellular constituents of skin. To explore its potential to heal chronic dermal wounds, we applied pure recombinant human aFGF topically to full-thickness excisional injuries in healing-impaired genetically diabetic mice. Therefore, aFGF has potential therapeutic applications for promoting healing of dermal ulcers, especially in healing-impaired individuals.

Functions of aFGF:
- Improve elasticity of skin by synthesizing collagen and elastin
- Promote hair growth & prevent decolorization

1-1-2. basic Fibroblast Growth Factor (bFGF)

Basic fibroblast growth factor, also known as bFGF, FGF2 or FGF-**β**, is a 16.3 kDa protein with 154 amino acid residues and a member of the fibroblast growth factor family[5,6]. bFGF stimulates the growth of fibroblasts, myoblasts, osteoblasts, neuronal cells, endothelial cells, keratinocytes, chodrocytes, and many other cell types[7].

bFGF also plays an important physiological role in tissue regeneration and wound healing[8-10], accelerates angiogenesis during early wound healing process[11], and stimulates endothelial cell proliferation, migration, and collagen production[12] (Fig. 2, 3).

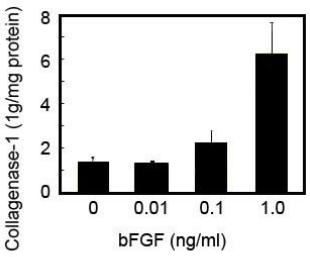


Fig. **2**. Activity of bFGF.

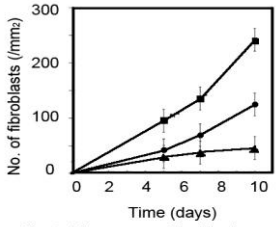


Fig. **3**. Time course fibroblast proliferation. Number of fibroblasts in the sustained release group (■), single application group (●), and control group (▲).

bFGF reduce irradiated soft tissue injury and improve random skin flap viability[13](Fig. 4). bFGF is an effective growth factor in the surgical healing of irradiated wounds.

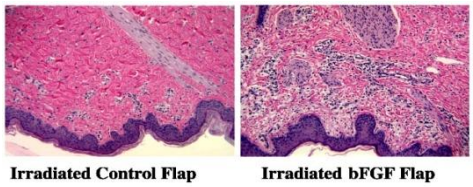


Fig. 4. Histologic findings of intracuticular injection flaps (phosphate-buffered saline control vs intracuticular basic fibroblast growth factor injected flaps.

Functions of bFGF:

- Reduce and prevent lines and wrinkles by actively generating new skin cells
- Skin rejuvenator involves in normal growth, healing, & wound repair
- Strengthen skin elasticity by inducing the synthesis of collagen and elastin
- Help blood circulation in the scalp and revitalizing hair follicles

1-1-3. Epithelial Growth Factor (EGF)

Human EGF is a 6 kDa protein with 53 amino acid residues and three intramolecular disulfide bonds[14]. EGF is a growth factor that plays an important role in the regulation of cell growth, proliferation, and differentiation by binding to its receptor EGFR[15].

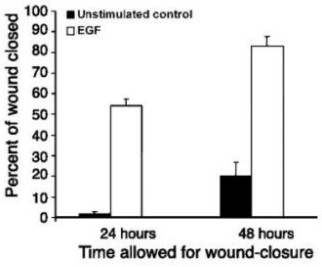


Fig. 5. Wound healing activity of EGF

EGF plays important roles in normal wound healing in tissues such as skin, corrnea, and gastrointestinal tract. EGF is a strong chemoattractant for fibroblasts and ephithelial cells and an important factor mediating wound healing processes[16-18](Fig. 5).

EGF treatment significantly accelerated healing compared to Silvadene vehicle treated injuries (Fig. 6). EGF accelerates of healing of epithelial wounds by promotion of keratin expression of the corneal epithelium (Fig. 7).

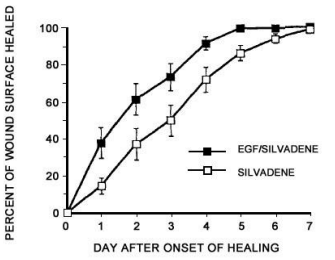


Fig. 6. Epidermal regeneration of paired, partial thickness wounds created with a Padget dermatome and treated with 10 ug EGF per gm Silvadene or treated with Silvadene alone.

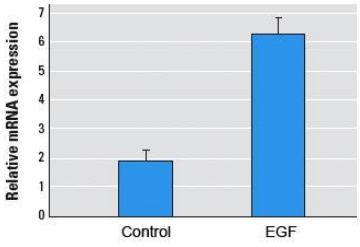


Figure 7. Effect of EGF on the expression levels of keratin 6a in UROtsa parental cells grown in serum-containing medium.

The discovery of EGF won Stanley Cohen a Nobel Prize in Physiology and Medicine in 1986 and was patented for cosmetic use by Greg Brown in 1989[19](Fig. 8).

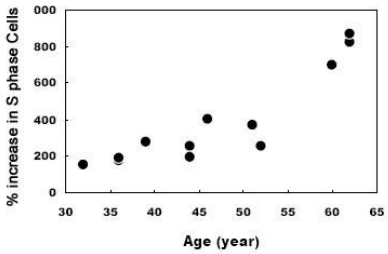


Fig. 8. New Cell increase Relative to Control after applying cream with EGF 60 days.

Functions of EGF:
- Reduce and prevent lines and wrinkles by actively generating new skin cells
- Enhance tone for skin that brimming with vitality & energy
- Nourish skin that appears smoother, brighter & regains its youthful look

1-1-4. Insulin-like Growth Factor-1 (IGF-1)

Insulin-like growth factor-1 (IGF-1), also called somatomedin C is a single chain polypeptide of 70 amino acid residues cross-linked by three disulfide bridges [20].

IGF-1 affects the growth and differentiation of the variety of tissues. It is mitogenic for wide range of cells including fibroblasts, osteoblasts, smooth muscle cells, fetal brain cells, neuroglial cells and erythroid progenitor cells[21] (Fig. 9,10). Almost every cell in the human body is affected by IGF-1, especially cells in muscle, cartilage, bone, liver, kidney, nerves, skin, and lungs. In addition to the insulin-like effects, IGF-1 can also regulate cell growth and development, especially in nerve cells, as well as cellular DNA synthesis [22].

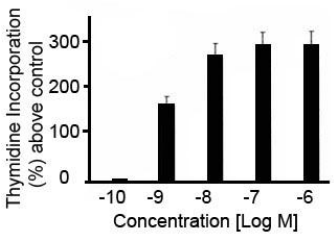


Fig. 9. Keratinocytes were stimulated with IGF-1.

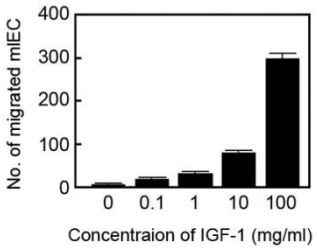


Fig.10. Activity of IGF-1.

IGF-1 is produced primarily by the liver as an endocrine hormone as well as in target tissues in a paracrine/autocrine fashion [23].

IGF-I expression promotes an average increase of 15% in muscle mass and a 14% increase in strength in young adult mice, and remarkably, prevents aging-related muscle changes in old adult mice, resulting in a 27% increase in strength as compared with uninjected old muscles. Muscle mass and fiber type distributions were maintained at levels similar to those in young adults [24].

IGF-1 has been manufactured recombinantly on a large scale using both yeast and *E. coli*. Several companies have evaluated IGF-1 in clinical trials for a variety of indications, including growth failure, type 1 diabetes, type 2 diabetes, amyotrophic lateral sclerosis (ALS aka "Lou Gehrig's Disease"), severe burn injury and myotonic muscular dystrophy (MMD).

Functions of IGF-1:
- Treat the appearance of lines and wrinkles
- Increases skin's own collagen & elastin levels and reduce blotchiness
- Refine texture glides effectively and slim your face and body with a fat burning effect

- Strengthen hair while stimulating hair follicles to produce strong hair shaft

1-1-5. Keratinocyte Growth Factor-2 (KGF-2)

KGF-2 (FGF-10) is a member of the fibroblast growth factor (FGF) family. FGF family members possess broad mitogenic and cell survival activities, and are involved in a variety of biological processes, including embryonic development, cell growth, morphogenesis, tissue repair, tumor growth and invasion[25].

KGF-2 exhibits mitogenic activity for keratinizing epidermal cells, but essentially no activity for fibroblasts, which is similar to the biological activity of FGF7 (KGF, Fig.11). KGF-2 is required for embryonic epidermal morphogenesis including brain development, lung morphogenesis, and initiation of lim bud formation. This growth factor is also implicated to be a primary factor in the process of wound healing[26-30].

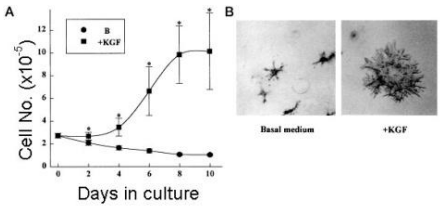


Fig. 11. A, Time course of the effect of KGF on mammary epithelial cell growth. B, Morphology of mouse mammary epithelial cell colonies. x40.

Palifermin (trade name Kepivance, marketed by Biovitrum) is a human recombinant keratinocyte growth factor (KGF) produced in *Escherichia coli*. KGF stimulates the growth of cells that line the surface of the mouth and intestinal tract. Human Genome Sciences (HGS) and GlaxoSmithKline (formerly SmithKline Beecham) are devel-oping topical and injectable formulations of repifermin, keratinocyte growth factor-2 (KGF-2), also known as fibroblast growth factor-10 (FGF-10) for the potential treatment of wound care, oral and intestinal mucositis, and inflammatory bowel diseases.

The growth and development of hair follicles is influenced by a number of different growth factors and cytokines, particularly members of the fibroblast growth factor (FGF) family. Keratinocyte growth factor (KGF or FGF-7) is a recently identified 28-kd member of the FGF family that induces proliferation of a wide variety of epithelial cells, including keratinocytes within the epidermis and dermal adnexa. KGF is an important endogenous mediator of normal hair follicle growth, development, and differen-tiation[31,32].

Functions of KGF-2:
- Reduce and prevent lines and wrinkles by actively generating new skin cells.
- Refine texture glides effectively and light up skin.
- Delivery of KGF to the base of the follicles which helps strengthen hair while stimulating hair follicles to produce strong hair shaft.

1-1-6. Vascular Endothelial Growth Factor (VEGF)

Vascular endothelial growth factor (VEGF) is a chemical signal produced by cells that stimulates the growth of new blood vessels. It is part of the system that restores the oxygen supply to tissues when blood circulation is inadequate. VEGF is a symmetric homodimeric molecule with two receptor binding interfaces lying on each pole of the molecule. Through alternative splicing six VEGF isoforms were identified[33].

VEGF is a sub-family of growth factors, specifically the platelet-derived growth factor family of cystine-knot growth factors. They are important signaling proteins involved in both vasculogenesis (the de novo formation of the embryonic circulatory system) and angiogenesis (the growth of blood vessels from pre-existing vasculature). VEGF's normal function is to create new blood

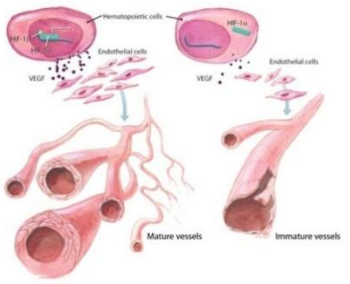


Fig.12. VEGF induces vasculogenesis by increasing production and proliferation of endothelial cells.

vessels during embryonic development, new blood vessels after injury, and new vessels (collateral circulation) to bypass blocked vessels (Fig.12)[34].

When VEGF is overexpressed, it can contribute to disease. Solid cancers cannot grow beyond a limited size without an adequate blood supply; cancers that can express VEGF are able to grow and metastasize. Overexpression of VEGF can cause vascular disease in the retina of the eye and other parts of the body. Drugs such as bevacizumab can inhibit VEGF and control or slow those diseases.

Functions of VEGF:

- Angiogenesis
  ↑ Migration of endothelial cells
  ↑ mitosis of endothelial cells
  ↑ Matrix metalloproteinase activity
  ↑ αvβ3 activity
- creation of blood vessel lumen
- creates lumen
- creates fenestrations
- Chemotactic for macrophages and granulocytes
- Vasodilation (indirectly by NO release)

1-1-7. Superoxide Dismutase 1 (SOD1)

Superoxide dismutase 1, soluble (amyotrophic lateral sclerosis 1 (adult)), also known as SOD1, is a human protein and gene. This gene encodes one of three forms of the human superoxide dismutase.

SOD1 binds copper and zinc ions and is one of three isozymes responsible for destroying free superoxide radicals in the body. The encoded isozyme is a soluble cytoplasmic and mitochondrial intermembrane space protein, acting as a homodimer to convert naturally occurring, but harmful, superoxide radicals to molecular oxygen and hydrogen peroxide[35](Fig. 13, 14).

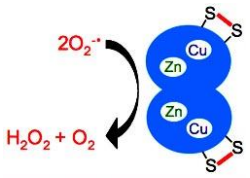


Fig.13 SOD – Reacts with the harmful free radical to form Hydrogen Peroxide radical

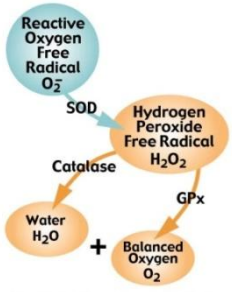


Fig.14. SOD – Reacts with the harmful free radical to form Hydrogen Peroxide radical.

Mutations (over 100 identified to date) in this gene have been linked to familial amyotrophic lateral sclerosis[36]. The most frequent mutations are A4V (in the U.S.A.) and H46R (Japan). The most studied ALS mouse model is G93A. Rare transcript variants have been reported for this gene.

Mice lacking SOD1 have increased age-related muscle mass loss (sarcopenia), early development of cataracts, macular degeneration, thymic involution, hepatocellular carcinoma, and shortened lifespan.

Cosmetic uses of SOD1

SOD is used in cosmetic products to reduce free radical damage to skin, for example to reduce fibrosis following radiation for breast cancer. Studies of this kind must be regarded as tentative however, as there

were not adequate controls in the study including a lack of randomization, double-blinding or placebo. Superoxide dismutase is known to reverse fibrosis, perhaps through reversion of myofibroblasts back to fibroblasts.

[References]

1. Metha RC, Fitzpatrick RE. Endogenous growth factors as cosmeceuticals. Dermatolgic Therapy 2007, 20; 35-359.

2. Dionne CA, Crumley G, Bellot F, Kaplow JM, Searfoss G, Ruta M, Burgess WH, Jaye M, Schlessinger J (Oct 1990). "Cloning and expression of two distinct high-affinity receptors cross-reacting with acidic and basic fibroblast growth factors". EMBO J 9 (9): 2685-92. PMID 1697263.

3. Jaye M, Howk R, Burgess W, Ricca GA, Chiu IM, Ravera MW, O'Brien SJ, Modi WS, Maciag T, Drohan WN (Aug 1986). "Human endothelial cell growth factor: cloning, nucleotide sequence, and chromosome localization". Science 233 (4763): 541-5. PMID 3523756.

4. "Entrez Gene: FGF1 fibroblast growth factor 1 (acidic)

5. Gospodarowicz D. Biological activities of fibroblast growth factors. Annals of the New York Academy of Sciences, 638: 1-8, 1991.

6. Gospodarowicz D., *et al*. Structural characterization and biological functions of fibroblast growth factor. Endocrinol. Rev. 8: 95, 1987.

7. Rieck P., *et al*. Human recombinant bFGF stimulates corneal endothelial wound healing in rabbits. Curr Eye Res. 11(12):1161-72, 1992.

8. Werner S., *et al*. Large induction of keratinocyte growth factor expresson in the dermis during wound healing. Proc. Natl. Acad. Sci. USA, 89: 6896-6900, 1992.

9. Hu C., *et al*. Basic fibroblast growth factor stimulates epithelial cell growth and epithelial wound healing in canine corneas. Vet Ophthalmol. 12(3): 170-175, 2009.

10. Parker NP., *et al*. Effects of basic fibroblast growth factor-2 and hyaluronic acid on tracheal wound healing. Laryngoscope. 119(4): 734-739, 2009.

11. Komori M., *et al*. A single Local Application of Recombinant Human Basic Fibroblast Growth Factor Accelerates Initial Angiogenesis During Wound Healing in Rabbit Ear Chamber. Anesth Analg, 100: 830-834, 2005.

12. Katsuya K., *et al*. Accelerated wound healing through the incorporation of basic fibroblast growth factor-impregnated gelatin microspheres into artificial dermis using a pressure-induced decubitus ulcer model in genetically diabetic mice. JPRAS, 58(8): 1115-1123, 2005.

13. David BH., *et al*. Improving Surgical Wound Healing with Basic Fibroblast Growth Factor after Raditaion. Laryngoscope 115: 412-422, 2005.

14. Herbst RS. Review of epidermal growth factor receptor biology. International Journal of Radiation Oncology, Biology, Physics 59 (2): 21–6, 2004.

15. Carpenter G, and Cohen S. Epidermal growth factor. The Journal of Biological Chemistry 265 (14): 7709–12, 1990.

16. Schultz G., *et al*. EGF and TGF-alpha in wound healing and repair. J Cell Biochem. 45(4): 346-52, 1991.

17. Gabriel A., *et al*. Wound healing, Growth factors. eMedicine. May 27, 2009.

18. Brown GL., *et al*. Enhancement of wound healing by topical treatment with epidermal growth factor. N Engl J Med, 321: 76-79, 1989.

19. US patent 5618544. Method of decreasing cutaneous senescence.
20. Rinderknecht E, and Humbel RE. The amino acid sequence of human insulin-like growth factor I and its structural homology with proinsulin. J Biol Chem. 25;253(8): 2769-76, 1978.

21. Chatelain P., *et al*. Paracrine and autocrine regulation of insulin-like growth factor I. Acta Paediatr Scand Suppl. 372:92-5, 1991.

22. Marvin YL, and Kim HT. Chondrocyte apoptosis induced by collagen degradation: inhibition by caspase inhibitors and IGF-1. J Orthop Res. 22(1):140-144, 2004.

23. Todorović V., *et al*. Insulin-like growth factor-I in wound healing of rat skin. Regul Pept. 9;150(1-3): 7-13, 2008.

24. Elisabeth RB., *et al*. Viral mediated expressio of insulin-like growth factor I blocks the aging-related loss of skeletal muscle function. Proc. Natl. Acad. Sci. USA 95: 15603-15607, 1998.

25. Paul WF., *et al*. Human KGF Is FGF-Related with Properties of a Paracrine Effector of Epithelial Cell Growth. Science 245: 752-755, 1989.

26. Kopp J., *et al*. Accelerated wound healing by in vivo application of keratinocytes overexpressing KGF. Mol Ther. 10(1): 86-96, 2004.

27. Werner S., *et al*. Large induction of keratinocyte growth factor expression in the dermis during wound healing. Proc Natl Acad Sci USA. 89(15): 6896-900, 1992.

28. Lisa SC., *et al*. Human Keratinocyte Growth Factor Effects in a Porcine Model of Epidermal Wound Healing. J Exp. Med. 178: 865-878, 1993.

29. Marchese C., *et al*. Human keratinocyte growth factor activity on proliferation and differentiation of human keratinocytes: differentiation response distinguishes KGF from EGF family. J Cell Physiol. 144(2): 326-332, 1990.

30. Xia YP., *et al*. Effects of keratinocyte growth factor-2 (KGF-2) on wound healing in an ischaemia-impaired rabbit ear model and on scar formation. J Pathol. 188(4): 431-438, 1999.

31. Guo L, Degenstein L, Fuchs E. Keratinocyte growth factor is required for hair development but not for wound healing. Genes Dev. 1996 Jan 15;10(2):165-75.

32. Danilenko DM, Ring BD, Yanagihara D, Benson W, Wiemann B, Starnes CO, Pierce GF. Keratinocyte growth factor is an important endogenous mediator of hair follicle growth, development, and differentiation. Normalization of the nu/nu follicular differentiation defect and amelioration of chemotherapy-induced alopecia. Am J Pathol. 1995 Jul;147(1):145-54.

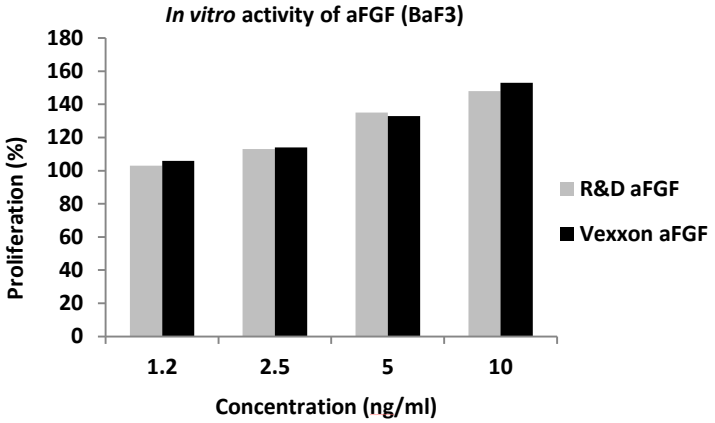
33. Margit Stimpfl, Dan Tong, Barbara Fasching, Eva Schuster, Andreas Obermair, Sepp Leodolter and Robert Zeillinger. Vascular Endothelial Growth Factor Splice Variants and Their Prognostic Value in Breast and Ovarian Cancer. Clinical Cancer Research (2002) 8, 2253~2259.

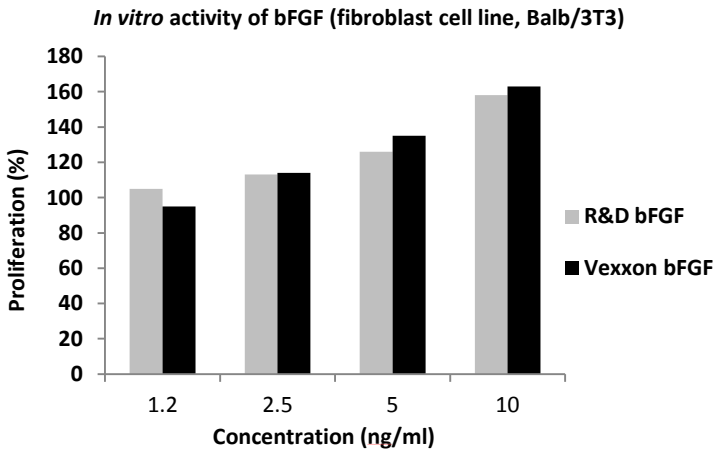
34. Ramirez-Bergeron, D.L. et al. (2006) Dev. Cell 11:81.

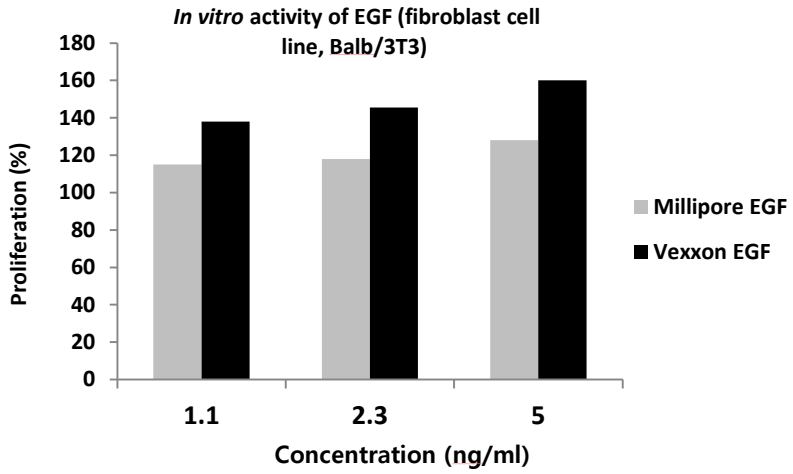
35. Trends in oxidative aging theories. Free Radic Biol Med. 2007 Aug 15;43(4):477-503.

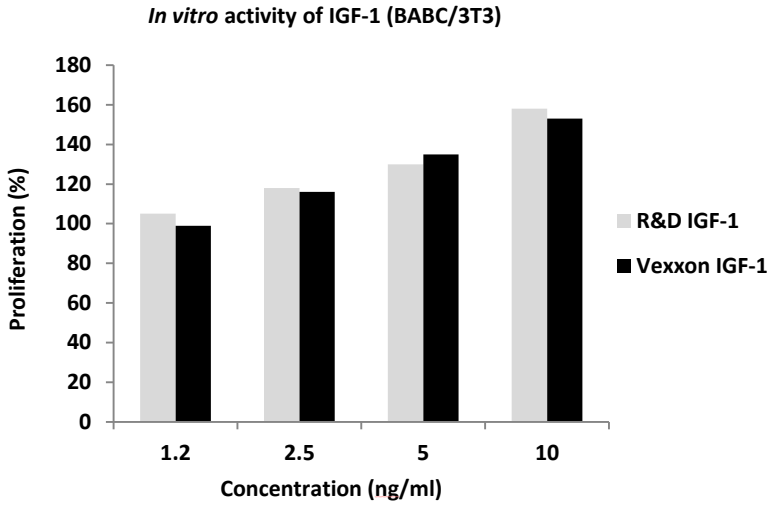
36. Seetharaman SV, Prudencio M, Karch C, Holloway SP, Borchelt DR, Hart PJ. Immature copper-zinc superoxide dismutase and familial amyotrophic lateral sclerosis. Exp Biol Med (Maywood). 2009, 234(10):1140-54.

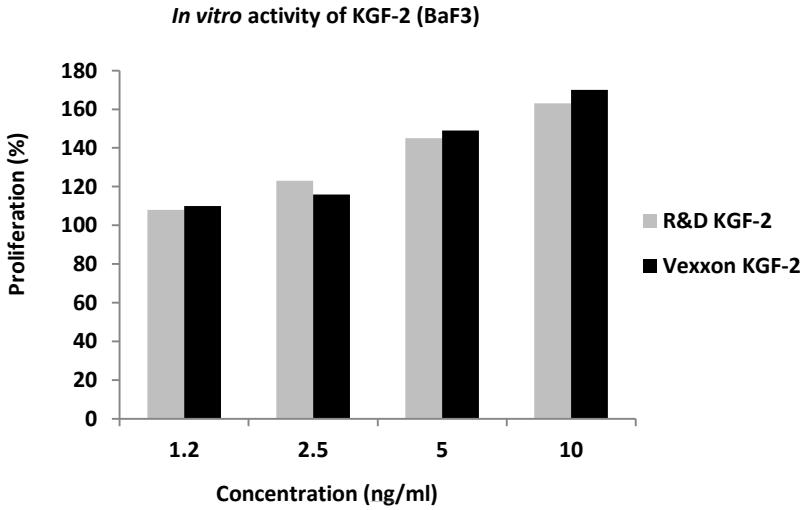
- Chemistry/Characterization data
- *In vitro* bioassay dat

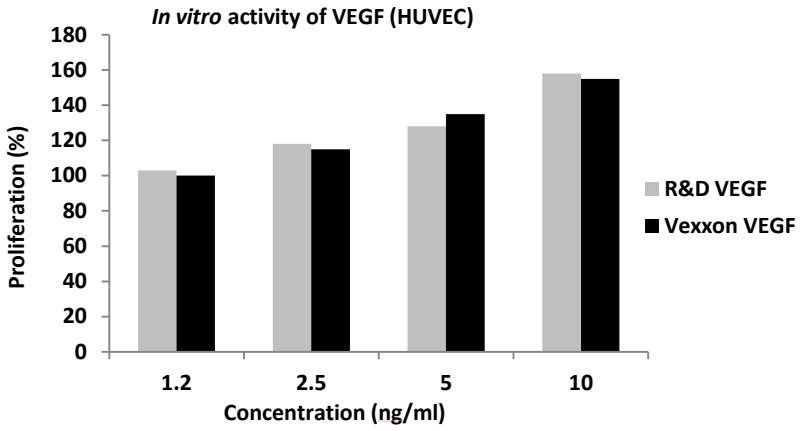


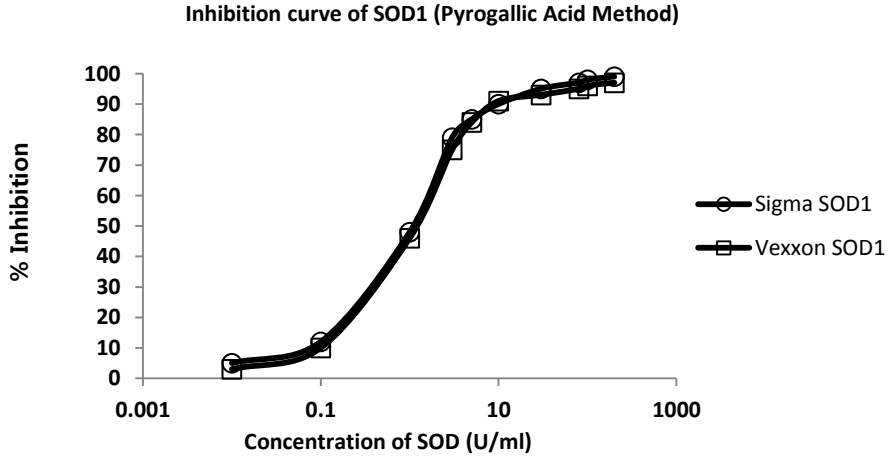



In vitro activity of EGF (fibroblast cell line, Balb/3T3)
Proliferation (%)
180
160
140
120
100
80
60
40
20
0
1.1
2.3
5
Concentration (ng/ml)
Millipore EGF
Vexxon EGF

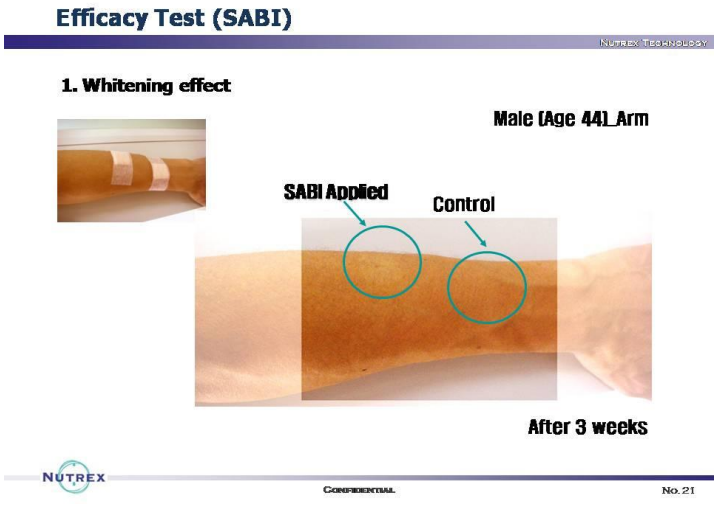

In vitro activity of IGF-1 (BABC/3T3)
Proliferation (%)
180
160
140
120
100
80
60
40
20
0
1.2
2.5
5
10
Concentration (ng/ml)
R&D IGF-1
Vexxon IGF-1

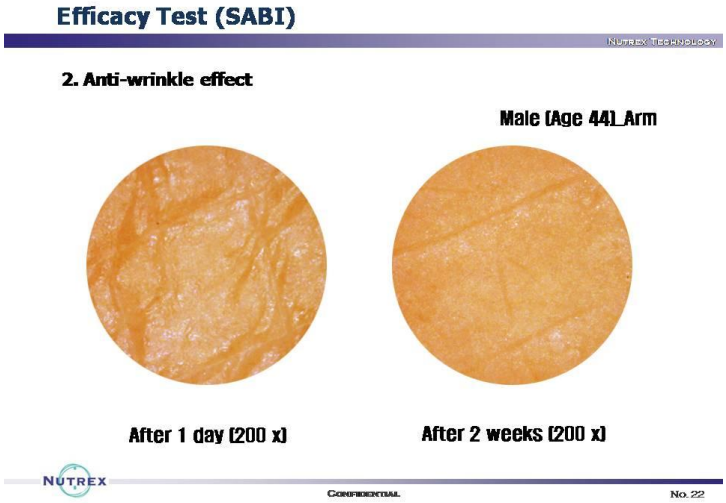

In vitro activity of KGF-2 (BaF3)
Proliferation (%)
180
160
140
120
100
80
60
40
20
0
1.2
2.5
5
10
Concentration (ng/ml)
R&D KGF-2
Vexxon KGF-2





- *In vivo* testing (Laboratory, Animal, and Human Clinical Studies)
- *In vivo* testing





- Clinically tested
  - Provide studies done by Company on the ingredient.
  - Total number of clinical studies completed: 3 times
  - Study design? (number of subjects, duration of the study/ies, double-blinded, placebo-controlled, case controlled, etc.)
    - 1: 30 persons, 4 weeks
    - 2: 10 persons, 4 weeks
    - 3: 10 persons, 4 weeks
  - Percent response rate?
  - Dose and delivery form used in the study/ies 0.06 mg and nanoliposome
- Published or not published, and in which journal/s?
- Recommended Delivery form/s: Water solution or powder
- Recommended dose/s? (mg per day) : 0.06 mg (~20 ppm/3 ml use)
- Collaborating Organizations, professors or University Affiliations
  - Hang-Cheol Shin (Professor, Bioinformatics Dept. Soongsil University)
- Conclusions from the studies
  - Promotes normal skin cell division and regeneration
  - Increases skin elasticity and moisturizing ability, while prevents post-inflammatory hyper-pigmentation
  - Improves the aging and dehydration of skin induced by UV exposure

2. Intellectual Property / Exclusivity

Provide an IP Portfolio summary to include:

- Provide patent information
  - Provisional/non-provisional/PCT/
  - How is the patent unique, compared to competition?
  - Number of patents?
  - Patent Type? (Process, Application, Combination, Composition, or other)
  - Patent Number/s, title, abstract, claims and application/issue dates

No.	Type	Title	Application, Registration No. (Y/M/D)	Owner	Remarks
1	Patent	METHOD FOR PREPARING SOLUBLE AND RECOMBINANT PROTEINS USING PDI AS A FUSION PARTNER	10-2008-7001981 (2008/01/24)	Nutrex Technol. Co. Ltd	Korea Applied
2	Patent	PROCESS FOR PRODUCING RECOMBINANT PROTEIN USING NOVEL FUSION PARTNER	10-2008-7001982 (2008/01/24)	Nutrex Technol. Co. Ltd	Korea Applied
3	Patent	METHOD FOR PREPARING SOLUBLE AND RECOMBINANT PROTEINS USING PDI AS A FUSION PARTNER	PCT/KR2005/003 543 (2005/10/24)	Nutrex Technol. Co. Ltd	PCT Applied
4	Patent	PROCESS FOR PRODUCING RECOMBINANT PROTEIN USING NOVEL FUSION PARTNER	PCT/KR2007/006 792 (2007/12/24)	Nutrex Technol. Co. Ltd	PCT Applied
5	Patent	METHOD FOR PRODUCING RECOMBINANT PROTEIN USING PotDAS A FUSION PARTNER	10-0890188 (2009/03/17)	Nutrex Technol. Co. Ltd	Korea Registered
6	Patent	METHOD FOR PRODUCING RECOMBINANT PROTEIN USING RNA POLYMERASE AS A FUSION PARTNER	10-0890189 (2009/03/17)	Nutrex Technol. Co. Ltd	Korea Registered
7	Patent	METHOD FOR PRODUCING RECOMBINANT PROTEIN USING RpoS AS A FUSION PARTNER	10-0890186 (2009/03/17)	Nutrex Technol. Co. Ltd	Korea Registered
8	Patent	METHOD FOR PRODUCING RECOMBINANT PROTEIN USING Crr AS A FUSION PARTNER	10-0890185 (2009/03/17)	Nutrex Technol. Co. Ltd	Korea Registered
9	Patent	METHOD FOR PRODUCING RECOMBINANT PROTEIN USING slyD AS A FUSION PARTNER	10-0890184 (2009/03/17)	Nutrex Technol. Co. Ltd	Korea Registered
10	Patent	METHOD FOR PRODUCING RECOMBINANT PROTEIN USING MALATE DEHYDROGENASE AS A FUSION PARTNER	10-0890183 (2009/03/17)	Nutrex Technol. Co. Ltd	Korea Registered
11	Patent	METHOD FOR PRODUCING RECOMBINANT PROTEIN USING Tsf AS A FUSION PARTNER	10-0890187 (2009/03/17)	Nutrex Technol. Co. Ltd	Korea Registered
12	Patent	PREPARATION METHOD OF RECOMBINANT PROTEIN BY USE OF A FUSION EXPRESSION PARTNER	PCT/KR2008/005 256 (2008/05/09)	Nutrex Technol. Co. Ltd	PCT Applied
13	Patent	METHOD FOR PREPARING SOLUBLE AND RECOMBINANT PROTEINS USING PDI AS A FUSION PARTNER	12/091291 (2008/04/23)	Nutrex Technol. Co. Ltd	USA Applied
14	Patent	PREPARATION METHOD OF RECOMBINANT PROTEIN BY USE OF A FUSION EXPRESSION PARTNER	12/676982 (2008/08/24)	Nutrex Technol. Co. Ltd	USA Applied

■ Describe exclusivity options (MLM, all markets, global, etc.)