MCB

Medicos-Biotech Co., Ltd.

Beauty and Medical Healthcare Platform
“Living a healthy, wonderfully vibrant life”

Innovative technologies to change the world
With ESG

August 2023

Techonology Overview

Medicos Biotech

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– Technology platform and High productivity technology

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with brief conclusion

Techonology Overview

Purpose of this Proposal

- This proposal are prepared to explain **how difficult it is to get high-productivity spider silk materials** and how this material technology can innovate the existing **functional skin cosmetic, medical biomaterials, and petrochemical industries** and, as an alternative, change the world.

- Currently, there are only **five companies** worldwide capable of producing spider silk. There are two companies in the US, one company in Japan, one company in Germany, and one company (MCB) representing Korea. Among them, we explain you why MCB is ahead of other competitors in Spider silk original source technology.

Definition

- Spider silk has attracted the industrial filed since it is **5 times stronger than steel (per unit mass) and 3 times harder than DuPont's Kevlar.**
- **Properties of its High strength, High elasticity, Biodegradability, and Biocompatibility. (meet Bio-steel and Bio-harmony)**
- Applicable industries are functional skin Cosmetics, Medical treatment (Biomaterials, Scafford, Chronic wound healing, Spinal Cord healing, etc), and Substitute for petrochemical industry (chemical fiber, clothing), military fiber applications.
- The Spider silk protein produced by MCB is a spider species of ***Trichonephila clavipes*** (Golden orb-weaving spider) known to produce spider silk with the most excellent physical properties among spiders existing in nature, and among this species, the ***protein sequence of drag line silk*** with the highest tensile strength developed, and the proteins constituting the spider web consisting of repeating structures were produced in the form of recombinant proteins.
- Technology to high productivity, producing spider silk protein from recombinant strains.

ESG Agenda

- Biodegradability. Satisfies **the environmental** agenda, which is **E in ESG.**
- Base raw materials are eco-friendly materials, and the production process of raw materials is also 100% eco-friendly.
- In the case of medical use, the production process is based on fermentation, so it is environmentally friendly, and the same is condition for substitute on petrochemical industrial use. The process of natural decomposition of the product is also applicable.

Techonology Overview

Problems of conventional technology

- **The global market for new biocompatible materials is expected to grow to $250 billion in 2025, and the CAGR is about 14.7%, which is a rapidly growing field.**

1. But, as a matter of currently used materials, in the case of biomaterials, polymers, metals, and carbon-based ceramic materials have good mechanical strength, but have disadvantages such as biocompatibility and adhesive strength. In the case of hydrogels, although biocompatibility is excellent, but mechanical is disadvantage, that its application is limited due to poor strength.

2. Therefore, **spider silk protein**, which has its own antibacterial function, excellent physical properties, excellent biocompatibility and biodegradability, and is effective for cell recovery, is a dream material that can achieve innovation in the existing biomaterial field, MCB company uses it material was developed. Spider silk is a material of high industrial interest due to its excellent physical (tensile strength, elasticity) and biological (biocompatibility, biodegradability) properties. The physical delivery effect of the drug is high.

3. When producing the spider silk molecular weight size is enlarged and adjusted to the natural size, there is a problem in that productivity rapidly decreases. The production cost is very high, and production as a recombinant protein is not easy due to the very large protein size and repetitive structure, making it difficult to use it as an actual product.

➔ The productivity of **MCB's high productivity technology and molecular weight size control are judged to be ahead of its global competitors,** and MCB is already preparing on commercialization on functional skin cosmetics, medicals WOUND healing. Therefore, there are commercialized cases where it has been used as a medical material such as medical devices or medicines, and functional skincare cosmetics.

4. Additionally, Spider silk production technology requires a combination of technology and commercialization in three major areas. In other words, these are the **three key success factors essential** for commercialization of Spider silk. **First,** It is a combination of Metabolic engineering technology that can improve spider silk productivity and freely control protein molecular size, which is the source of Spider silk technology, and **the second** is Operation of an independent team for spider silk production and further R&D. The **third** is expertise in many abundant career medical team in the field of skin surgical treatment.

Techonology Overview

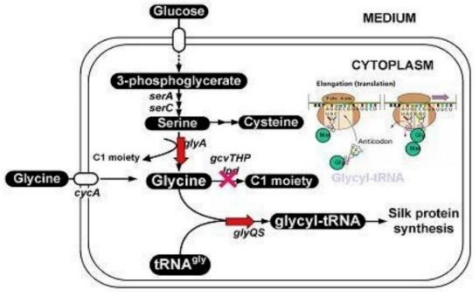
1. Metabolic Engineering

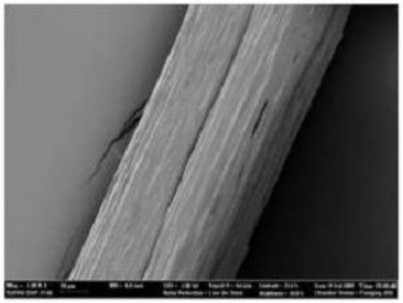
- MCB, the technology source of spider protein silks are coming from metabolic engineering. Metabolic engineering refers to a technology that optimizes the production of a target metabolite by manipulating the production pathway of the metabolite. Metabolic engineering progresses in the direction of maximizing the production of desired products by modifying the unique metabolic pathways of microorganisms through the overexpression of production pathway genes, the removal of competing pathway genes, or the introduction of foreign genes. Various chemicals that can be produced using microorganisms are widely used in energy, food, medicine, cosmetics, and chemical industries. MCB spider silk protein is developed by KAIST using metabolic engineering methods for mass production. It has the unique advantage of controllable molecular weight and, consequently, adjustable mechanical strength and degradation time, depending on the application. Compared to other global 4 companies, our production process ensures excellent productivity, which is expected to provide a favorable cost advantage.
- The spider silk protein produced by MCB is a recombinant protein derived from the drag line silk of Trichonephila clavipes (Golden orb-weaving spider), known for producing the strongest physical properties among natural spider silks. Through analyzing the protein sequence of the drag line silk, which exhibits the highest tensile strength among the spider silks of this species, we have manufactured a recombinant protein that mimics the repetitive structure present in the natural spider silk composition. There is a problem in that productivity decreases exponentially as the molecular size of the spider silk protein increases. Spider silk is a material of great industrial interest due to its excellent physical properties (tensile strength, elasticity) and biological properties (biocompatibility, biodegradability). It forms a unique structure due to its large molecular weight and repetitive sequence, resulting in high hydrophobic protein interactions and increased drug delivery efficiency. In the case of spider silk molecular weight control and production, it is important whether or not to have professional metabolic engineering technology background from a fundamental or long-term perspective of MCB. Co-founder of MCB, KAIST Vice President Lee Sang-yup and his team are world-renowned scholars who represent not only Korea but also the world in the field of research and development of the human microbial environment and metabolic engineering.
- Regarding the completion of patent technology transfer, as the KAIST-related development department is transferred to MCB, so if additional physical properties (molecular weight control, mass production efficiency expansion) need to be improved in the future, it can be promoted through the operation of MCB's own research and development team. Our spider silk protein has the characteristics of high productivity technology through metabolic engineering method developed and transferred by KAIST to MCB, molecular weight control according to the application field, mechanical strength and biodegradation time accordingly, and is superior to other companies. **MCB Productivity is secured.** It is expected to occupy an advantageous position in terms of cost of product.

Techonology Overview

1. Metabolic Engineering

- MCB, Ultra-high molecular weight silk fibers made by spiders have excellent strength and elasticity comparable to Kevlar, a high-strength synthetic fiber from DuPont, USA, and have been researched and developed for use in various fields such as the medical industry. Although many attempts have been made around the world, interest in this technology is higher because it has not been possible to artificially produce high molecular weight spider silk.
- This spider silk high productivity and mass production technology was successfully produced by a team led by Distinguished Professor Lee Sang-yup of KAIST about 10 years ago using E. Spider silk fibers made from this ultra-high molecular weight protein are characterized by their properties being stronger than steel. Professor Sang-Yup Lee's team found that a lack of glycyl-tRNA occurs in E. coli when spider silk protein is produced using systems metabolic engineering techniques such as comparative proteomic analysis. In addition, to solve this problem, KAIST researchers already reconstructed the metabolism of E. coli by amplifying or removing related genes more than 10 years ago, and successfully synthesized 285 kDa spider silk protein with the world's highest number of repeat units from E. coli. I was able to do it. In addition, after isolating and purifying the spider silk protein produced in Escherichia coli, it was produced in the form of silk fiber through spinning using biomimetic technology.
- As a result of measuring the physical properties of spider silk fibers already made at the time about 10 years ago, the tenacity was 508 MPa and the tensile modulus (Young's modulus) was 21 GPa, confirming the fact that it has the same strength as Kevlar. As a result, it was impossible to produce high-strength spider silk fibers because it was impossible to produce large spider silk proteins as large as 285 kDa in the past, but this research and development has made it possible.
- Dragline silk made by spiders has **excellent physical properties and can be used in various products such as surgical threads, artificial ligaments, body armor, parachutes, and steel cables supporting suspension bridges.** Spider dragline silk protein is composed of more than 40% glycine.





Techonology Overview

2. MCB Spider Silk technology

Why is it difficult to mass-produce spider silk, and why is it such a difficult technology to implement and maintain quality?

➔ This spider silk protein has attracted significant industrial interest due to its diverse potential applications, leading to numerous related research endeavors. However, due to the territorial behavior based on the spider's aggressive nature and its cannibalistic tendencies, farming and mass production are challenging, resulting in very high production costs.

➔ Moreover, When producing the spider silk molecular weight size is enlarged and adjusted to the natural size, there is a problem in that productivity rapidly decreases. The production of recombinant proteins is also complicated by the large protein size and repetitive structure, making commercialization of spider silk as an actual product difficult.

- When the size of the molecular weight of spider silk is increased and adjusted to the natural size, there is a problem in that productivity rapidly decreases. Natural sized spider silk protein (250~320 kDa) production was unobtainable.
- However, based on the papers and data from related academic circles, as can be seen, **most of the current competitors are using low molecular weight spider silk proteins of about 50 kDa**, and proteins with a maximum size of 200 kDa. This protein is smaller in size than the natural spider silk protein, and cannot fully utilize the characteristics of the naturally occurring ultra-high molecular weight spider silk protein.

Therefore, MCB is the first and only company to produce ultra-high molecular weight spider silk proteins similar to those present in nature. **In summary, MCB's Spider silk molecular weight control, and mass-production technology/productivity, in terms of these two points of view, compete with four global companies and have the following technological comparative advantages.**

1. Molecular size control (Quality) ; MCB can produce spider silk proteins in different sizes **from 3.5 kDa to 370 kDa.** This is to control the size of the protein by repeating the repetitive sequence of spider silk protein from 1 to 128 times. Research has confirmed that the larger the size of the protein, the more prominent the formation of crystalline structure, the better the hydrophobic interaction, the easier barrier formation and drug delivery, and the higher physical properties.

2. Productivity (Price for commercialization) ; The revealed global 4 companies production volume is less than **10 times** that of MCB company, and we have the price competitiveness of spider silk protein to the level where practical industrialization is possible based on the world's highest level of spider silk protein production and efficient and high purification rate. In terms of technology and productivity, we judge that other companies do not compete with MCB.

2. MCB Spider Silk technology

So, MCB's successful commercialization of spider silk, quality and productivity are summarized as follows.

- (https://doi.org/10.1073/pnas.1003366107). The spider silk protein commercialized by Our MCB is a material with very good physical and biological properties, similar to the spider silk protein that exists in nature, unlike other companies' spider silk proteins with low molecular weight. However, the larger the size, the lower the yield due to high cytoplasmic stress, so we produce spider silk proteins in sizes of 16mer (55kDa), 48mer (148 kDa), and 96mer (286 kDa) depending on the purpose and field of application, and optimize the purification process. The product is standardized and produced as a raw material line, and we have **technologies and strains** that can produce **from 3.5 kDa to 370 kDa** as needed. In the case of 4 existing global companies using spider silk protein, only one size is specified and used, and in our case, spider silk protein of various sizes is produced and standardized, so a wide range of applications is possible. Furthermore, since the production yield is more than 10 times higher than that known by other existing companies, we can aim for price competitiveness and practical industrialization.
- MCB spider silk protein is optimized for mass production technology and purification process through additional improvement and research based on the metabolic engineering method developed and transferred by KAIST to produce proteins of various sizes with very high productivity compared to other global 4 companies depending on the application field.

✓ **Currently, our protein production yield is based on standardized product lines of 16mer, 48mer, and 96mer spider silk.**

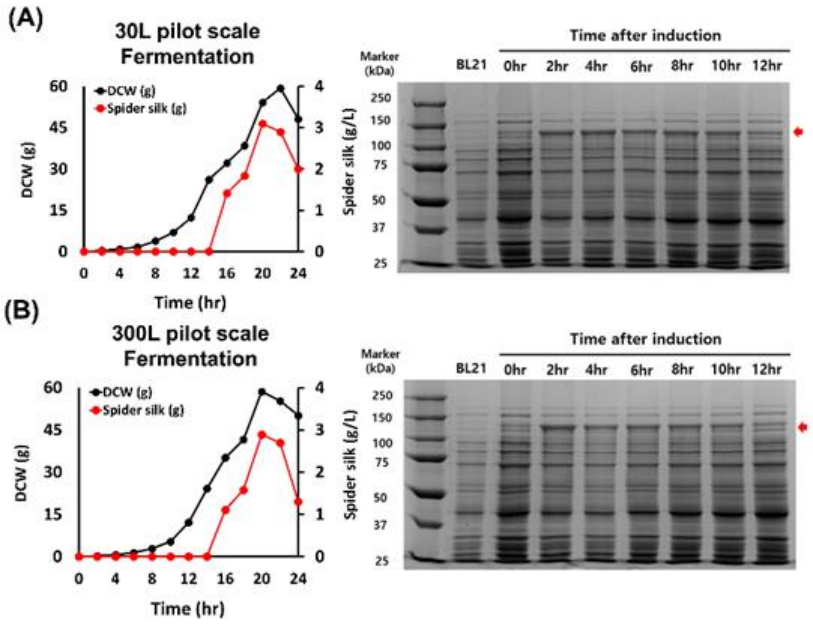
✓ **20g/L for 16mer, 15g/L for 48mer, and 7g/L for 96mer are produced based on fermentation broth (L). In the case of 7g/L mentioned above, it means the amount of protein produced by the strain per L of fermentation broth based on the production of 96mer spider silk protein, which is the highest molecular weight.**

- Currently, our laboratory located in Daejeon is equipped with facilities for purification such as two 5L lab scale fermenters, a compressor for cell disruption, an agitator, large-capacity UF/DF equipment, and a freeze dryer. In addition, the pilot scale 30L and 300L fermenters owned by Professor Lee Sang-yup's laboratory at KAIST have been used to optimize the scale-up process for large-capacity fermentation at the industrial level, and fermented liquid is secured and refined by carrying out continuous 300L fermentation every month.

2. MCB Spider Silk technology

Are there any problems with quality deterioration when the production volume is increased? A description of the rationale for increasing production without quality problems and confirmation of guarantees.

- We have optimized the scale-up process for large-capacity fermentation at the industrial level while carrying out pilot scale fermentation using 30L and 300L fermentors.
- As a result of fermentation with an optimized process, it was confirmed that the cell growth profile and protein production were stably expressed identically to the existing lab scale fermentation. In addition, by utilizing the developed process, continuous fermentation of 300L is carried out every month to secure and refine the fermentation broth.
- In addition, the part where we are making efforts to further improve production is the improvement of strain productivity, improvement of purification process efficiency, and more efficient mass purification system. If the production volume is improved through these efforts, mass production is possible regardless of quality degradation. , it will be able to further improve production efficiency.



<**Figure.** 30L and 300L pilot scale fermentation results>

Techonology Overview

2. MCB Spider Silk technology

- We optimized the scale-up process using 30L and 300L fermentors for industrial-level production of spider silk protein, and based on the optimized process, we commissioned the CDMO process to Korea located Binex Co., Ltd., a **GMP facility**, to produce and the purification process was established.
- In addition, we developed a simple and highly efficient mass purification process to improve the purification yield, standardize the quality of spider silk protein produced in the process, and conduct stability evaluation and efficacy evaluation. Through these efforts, we are currently producing spider silk protein on our own, and have already organized through internal meetings and research about additional equipment and processes required to establish a larger-scale mass purification system, so if investment is made, We together will be able to have production facilities with mass production settings right away.
- The part where MCB is making efforts to further increase production in order to expand additional production can be largely divided into facility facilities equipped with mass production settings including improved productivity of strains and improved mass refining process. In the case of improved productivity of strains, continuous efforts at the mcb research institute after the transfer of KAIST technology have innovatively improved production compared to the previous ones (16mer 20g/L, 48mer 15g/L, 96mer 7g/L), additionally increased strain screening and adaptive evolution (ALE) We are continuously improving additional production strains through strain selection.
- In addition, in the case of production facilities, pilot scale process optimization using 30L and 300L fermentors and production and purification process development in GMP facilities were carried out. Since the situation has already been sorted out through research, if investment is made, production facilities with mass production settings will be available immediately (within 3 to 6 months). Therefore, if these production facilities are in place, it will be possible to significantly improve production and secure more sufficient price competitiveness through a much more efficient production process.

So, a summary of the conclusions about what kind of superiority MCB can show through comparison with four global companies in these two key technologies, molecular weight size and productivity, is as follows.

1. The size of naturally occurring ultra-high molecular weight spider silk proteins is known to be between 250 to 400 kDa. The larger the size of the protein, the more prominent the formation of the crystalline structure of the spider silk protein through the repeated structure, and the superior physical and biological properties of the spider silk protein as a biomaterial. However, most of the four global competitors currently use low-molecular-weight spider silk proteins of about 50 kDa, and proteins of up to 200 kDa in size. This protein is smaller in size than the natural spider silk protein, and cannot fully utilize the characteristics of the naturally occurring ultra-high molecular weight spider silk protein. Therefore, MCB is the first and only company to produce ultra-high molecular weight spider silk proteins similar to those present in nature.

Techonology Overview

2. MCB Spider Silk technology

2. The productivity and output of other global competitors revealed are less than 10 times that of ours, and we are competitive in price of spider silk protein to the level where practical industrialization is possible based on the world's highest level of spider silk protein production and efficient and high purification rate. , we believe that other companies cannot compete with MCB in terms of technology and productivity.

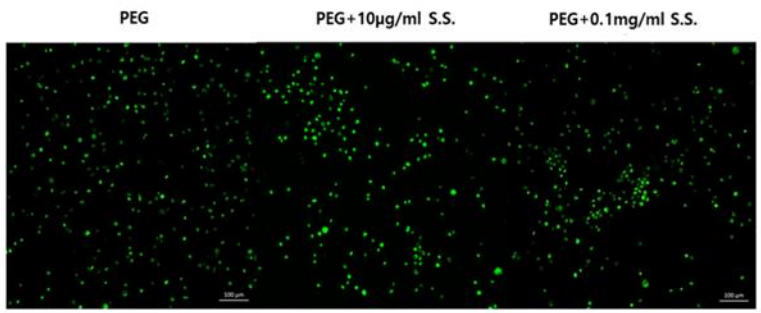
3. MCB, our proprietary technology, which can produce not only spider silk proteins of a specific size but also spider silk proteins of various sizes from 3.5 to 370 kDa, adjusts various physical properties and biodegradation period by adjusting the size of the protein according to the application field and use (**Functional skin cosmetics, Medical wound dressing and scaffords, Spinal injuries regeneration and other industrial usages**). Compared to competitors, it is possible to utilize a much wider range of spider silk proteins. Through an optimized refining process, **we have secured a purification yield of over 95%, completing registration of cosmetic raw materials and preparing technical documents for medical devices.** In fact, functional cosmetics are ready for commercialization, and wound dressing for medical treatment is planned to be completed in one clinical trial.

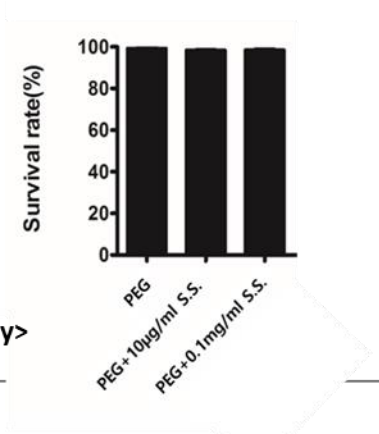
4. MCB spider silks are 7 times higher productivity than other competitors. And MCB Spider silk has attracted the level field since it is 5 times stronger than steel (per unit mass) and 3 times harder than DuPont's Kevlar. The protein size and high productivity technology of Medicos-biotech company's spider protein silk is ahead compared to global 4 competitors. **In other words, we have a competitive advantage over the four companies in terms of quality and price through commercialization.**

2. MCB Spider Silk technology

Additional explanation of the biocompatibility-related features of spider silk as a biomedical material

- Biocompatibility means that the material is non-toxic and non-damaging in the biological system (or host), which is a characteristic that a biomedical material must have. Biocompatibility can be confirmed by live/dead assay. As shown in the image figure below, it was confirmed that mouse C3H cells grew well without cell death when 10ug and 0.1mg of spider silk protein were contained, and it was confirmed that spider silk protein had excellent biocompatibility at the experimental concentration.
- **In particular, most of the materials (HA, Collagen, Gelatin, etc.) currently used as biodegradable biomaterials have excellent biodegradability, but their use as biomaterials is limited due to their poor physical properties. Spider silk protein has excellent biocompatibility and biodegradability as well as excellent physical properties, and since the physical properties and biodegradation period can be adjusted according to the size of the protein,** it can be said to be a dream biomaterial with infinite applications as a biomaterial.
- Furthermore, **spider silk protein has no allergic reaction and is well known as an antibacterial material. In addition, by providing a binding motif to cells, initial migration and cell adhesion are improved, and hydrophobic interactions and micelle structure formation are possible due to high molecular weight, which improves drug delivery effect and activates the action of existing products by interacting with various growth factors.**
- In addition, growth factors such as Cyclin D1, VEGF, TGF-b, Fibronectin, and Vimentin, which are involved in cell regeneration and collagen regeneration through stimulation of the canonical pathway of the Nf-Kb pathway, which is responsible for cell recovery in the immune response, are treated with spider silk protein. Therefore, these biological properties including biocompatibility of spider silk protein make spider silk protein a very good material as a biomaterial, and it will be a source technology related to biomaterials that can supplement the shortcomings of currently used materials and develop a better product.

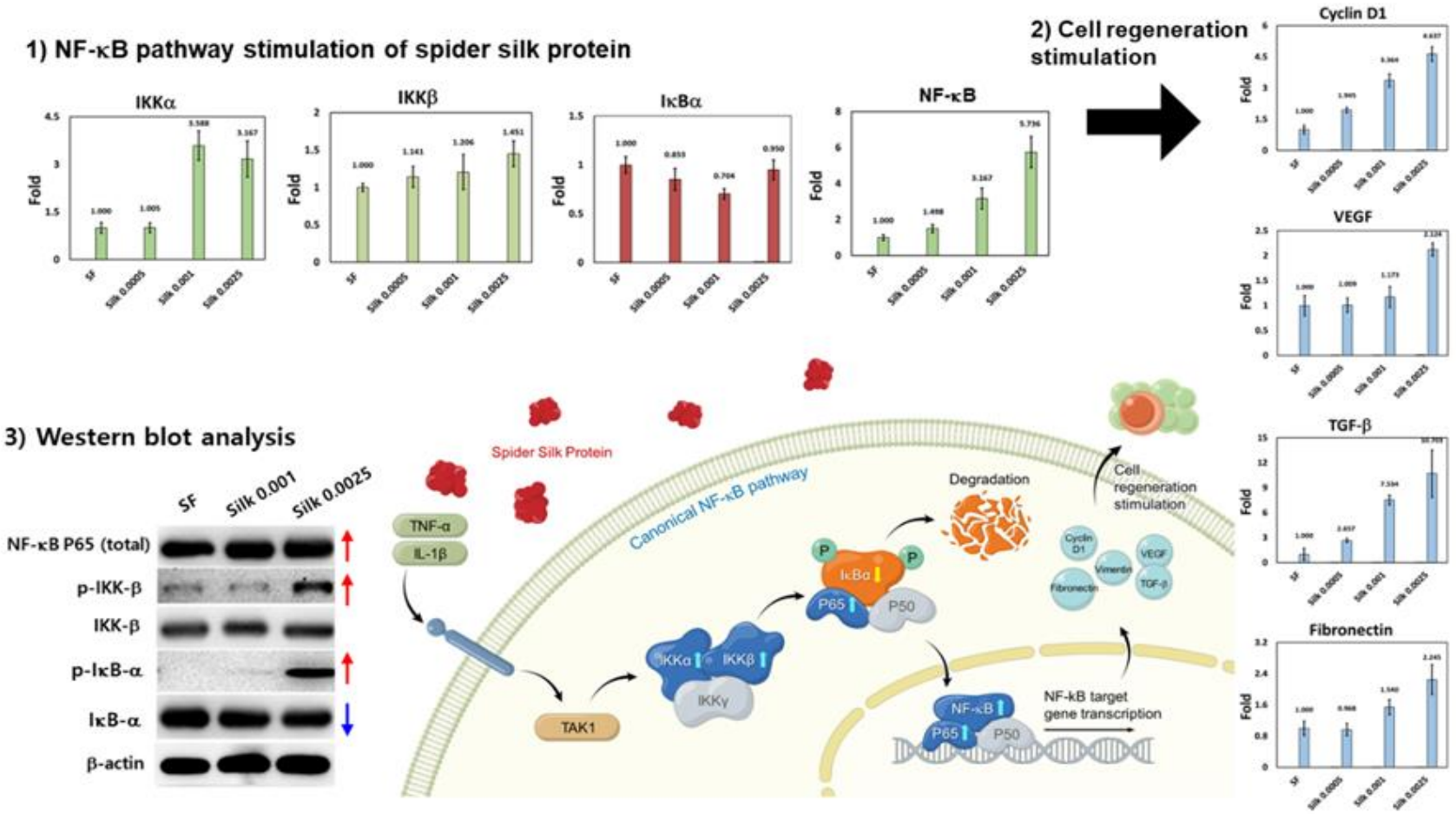




<Figure. Confirmation of biocompatibility through live/dead assay>

2. MCB Spider Silk technology

Additional explanation of the biocompatibility-related features of spider silk as a biomedical material

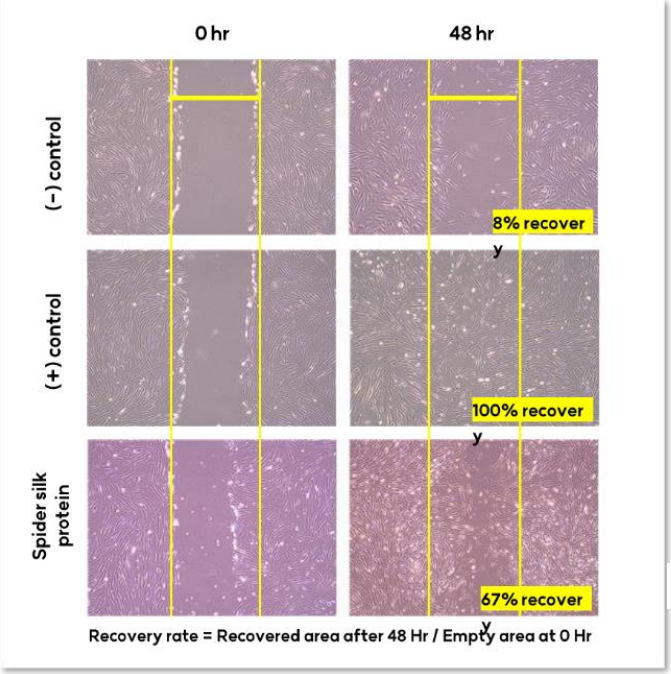


<Figure. Confirmation of mechanism of action of spider silk protein that promotes cell regeneration**>**

3. Cosmetics and Wound healing

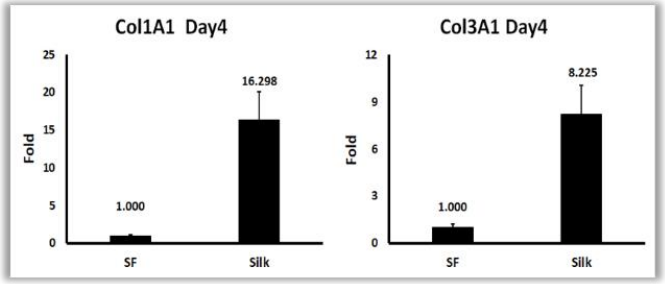
How spider silk protein can help prevent hair loss (Dr.Graft shampoo & treatment).

- Spider silk protein is a natural high molecular substance found in nature and consists of 37% Glycine, 21% Alanine, and 4.5% Serine&Proline. (Moisturizing and collagen regeneration. Moisturizing effect of crystal ring structure)
- Spider silk There has never been a material like this that is biocompatible, biodegradable, and non-irritating (allergic) to the skin. This brings a **premium effect**. Glycine helps synthesize collagen, which reduces wrinkles and skin elasticity, while Alanine binds well with epidermal cells to help reduce wrinkles and helps regulate skin moisture and maximize hydration. Serine and Proline help prevent skin aging by supporting keratin production and UV protection.



Confirmation of the healing effect of spider silk proteins in an in vitro scratch test. Even using only spider silk protein, 67% recovery was seen.

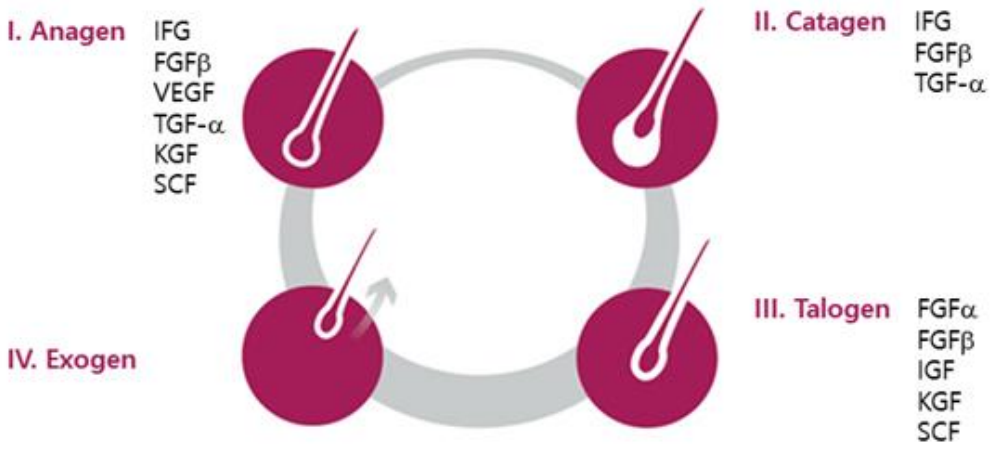
(Negative control: serum free medium: healthy control: medium with FES)



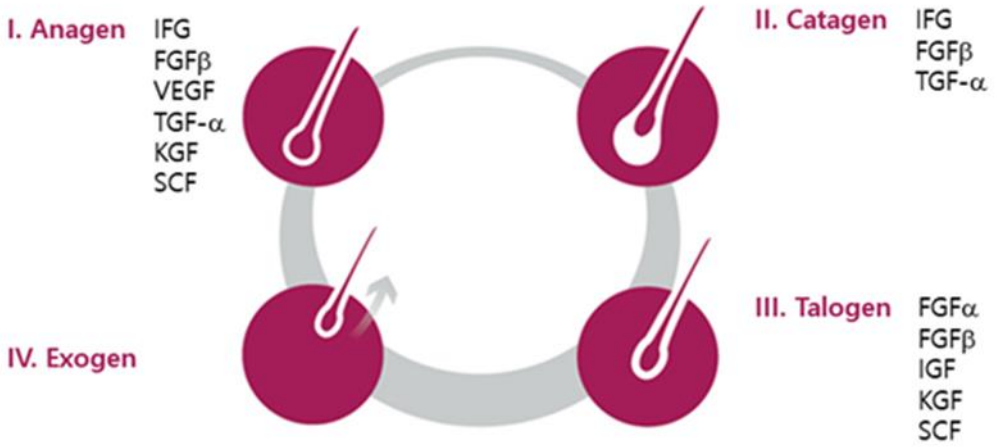
CollAI and COIQAI MRNA levels increased with application of spider silk protein iron

3. Cosmetics and Wound healing

- As above, spider silk proteins have a positive effect on cell growth and regeneration. The scalp is also a part of the skin, and it focuses on improving the scalp environment to prevent and alleviate hair loss, helping to improve the scalp through spider silk protein to help prevent and alleviate hair loss.
- In addition, ROS inhibition, collagen expression, antioxidant, hyaluronic acid expression, NO inhibition, whitening 2 types, filaggrin expression, inflammation 3 types, and positive effects on cell growth were confirmed through various in-vitro experiments.
- The cortex of hair lost due to physical damage (friction, combing, etc.) and chemical damage (product use, perm or dyeing procedure, etc.) of hair is disappeared when a wash-off type product containing spider silk protein is used. It was confirmed through other papers that the damaged cortex was restored.
- • MCB-Formula™, a combination of 7 growth factors, is a combination of SCF, IGF, VEGF, FGFβ, FGFα, TGF-β, and KGF that activates the dermal papilla that produces hair, promotes hair growth, and hair cell division related to hair quality. , It helps strengthen the production of peripheral blood vessels that supply nutrients to the hair follicles that support hair.



3. Cosmetics and Wound healing



- **Anagen: growth phase**
- **Categen: regression period**
- **Talogen: resting period**
- **Exogen: A new concept that does not involve growth factors. Can be modified with Return to anagen.**
- Hair generation is divided into 4 cycles as shown in the figure below, and each growth factor helps hair grow in various cycles, rather than one growth factor involved in one cycle.
- MCB-Formula™, a combination of 7 growth factors, greatly affects scalp regeneration, capillary blood flow and maintenance of hair follicles, and cell division.

1. Folliculogenesis: FGFb, SCF, and VEGF growth factors help to form healthy hair follicles, affecting the resting and growing phases of hair. It helps to form blood vessels around hair follicles and activates dermal papilla cells to promote hair growth.

2. Scalp regeneration: FGFa and TGF-b help regenerate healthy scalp. FGfa enhances the activity of KGF, which helps cell division, and KGF helps the activity of TFG-b. Because of these interactions, they are growth factors that can be found during growth, regression, and resting periods.

3. Cell division: IGF and KGF help form healthy hair follicles and scalp through skin cell division. In particular, IGF helps activate a growth factor called PDGFA/B, and it is a growth factor that helps in the creation of cells and blood vessels even in small amounts. Because of this role, it is involved in the entire hair cycle.

3. Cosmetics and Wound healing

How are Spider silk useful for functional skincare cosmetics such as anti-wrinkle and moisturizing.

<ROS inhibition>

- Skin aging is mainly divided into intrinsic aging process and extrinsic aging process. It means a phenomenon caused by a factor. Among them, reactive oxygen species (ROS) generated through respiration as well as external factors such as ultraviolet rays and stress are considered to be the main cause of skin aging. Reactive oxygen means oxygen with free radicals (free radicals), and since it is very reactive, oxidative stress that damages skin cells and tissues occurs. Oxidative stress accelerates skin aging by destroying skin antioxidants, oxidizing proteins, oxidizing DNA, cutting chains of connective tissue components such as collagen and hyaluronic acid, and participating in melanin production. Therefore, when excessive active oxygen is generated in the skin of the human body, the antioxidant defense system is destroyed, ultimately causing skin aging to be accelerated. **It was confirmed that the spider silk protein is effective in inhibiting the production of reactive oxygen species.**

→ **Test results :** When 'Spider silk protein' was treated at a concentration of 0.025% or less (0.005, 0.01, 0.025%), the amount of reactive oxygen species (ROS) produced in human keratinocytes induced by UVB was up to 52.73±0.77% compared to the UVB alone treatment group. Reduction was confirmed. Through this, 'Spider silk protein' is judged to be helpful in inhibiting the generation of reactive oxygen species (ROS) against ultraviolet B as the amount of ROS increased by UV-B irradiation decreases at a concentration of 0.025% or less.

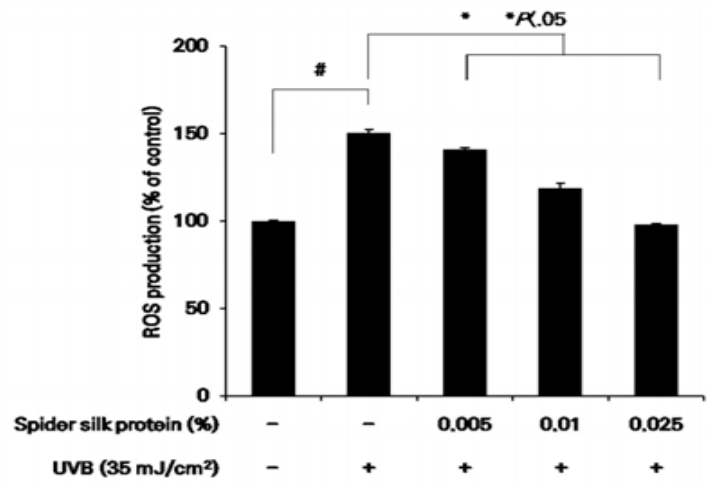


Figure 2. Changes in ROS generation in human keratinocytes (HaCaT cells) induced by ultraviolet B after treatment with the test substance 'Spider silk protein'.

(#P<.05, 음성대조군 대비 또는 *P<.05, UVB 처리군 대비) compared to negative control or Compared to the UVB treatment group)

3. Cosmetics and Wound healing

<Collagen Expression>

- As skin aging progresses, the epidermal layer lacks moisture, resulting in rough skin and an abnormal keratinization cycle of keratinocytes, resulting in the formation of an abnormal stratum corneum. In the case of the dermal layer, inhibition of collagen synthesis in dermal fibroblasts results in a lack of extracellular matrix, resulting in structural deformation of the reticular layer of the dermis. This structural transformation causes a decrease in skin elasticity and wrinkles. Collagen is a fibrous protein present throughout body tissues and is composed of various types, and type I collagen is mainly present in the skin. The procollagen expressed from the pro-collagen gene of dermal fibroblasts is secreted out of the cells and combined with each other to form type I collagen. Pro-collagen is produced when the pro-alpha 1 chain expressed in the COL1A1 gene and the pro-alpha 2 chain expressed in the COL1A2 gene form a triple helix structure. The production of type I collagen is balanced within normal skin tissue, so skin elasticity is controlled. In order to prevent such a skin aging phenomenon, a component capable of restoring the structure of the reticular layer of the skin by activating the function of dermal fibroblasts present in the dermal layer to promote collagen production is required. It was confirmed that spider silk protein increases COL1A1, which suggests that there is also a wound healing effect.

→ **Test results :** When human dermal fibroblasts were treated with 'Spider silk protein' at a concentration of less than 0.025% (0.005, 0.01, 0.025%), it was confirmed that COL1A1 mRNA expression was increased by up to 60.09±2.55% compared to the negative control group. Through this, 'Spider silk protein' is judged to help increase collagen production as the expression of COL1A1 mRNA in human dermal fibroblasts increases at a concentration of 0.025% or less.

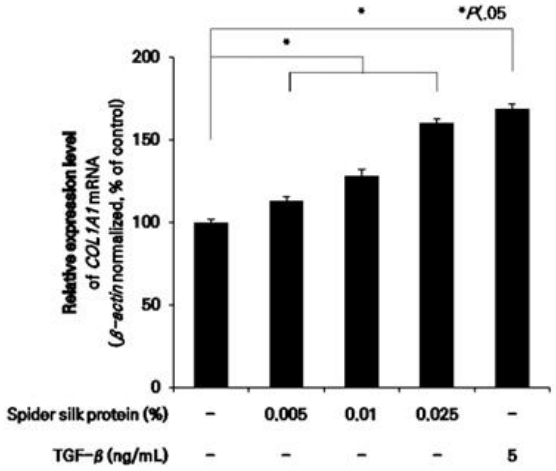


Figure 2. Changes in Type I Collagen (COL TA 7) gene expression in human dermal fibroblast cells (NHDFs) treated with the test substance 'Spider silk protein'.

(*P<.05, 음성대조군 대비) Compared to the negative control group)

3. Cosmetics and Wound healing

<Antioxidation>

- Skin aging is mainly divided into intrinsic aging process and extrinsic aging process. Intrinsic aging process refers to a phenomenon in which physiological functions naturally deteriorate over time, while extrinsic aging process refers to external factors such as ultraviolet rays and pollution. means a phenomenon caused by Among them, reactive oxygen species (ROS) generated through respiration as well as external factors such as ultraviolet rays and stress are considered to be the main cause of skin aging.
- Reactive oxygen means oxygen with free radicals (free radicals), and since it is very reactive, oxidative stress that damages skin cells and tissues occurs. Oxidative stress accelerates skin aging by destroying skin antioxidants, oxidizing proteins, oxidizing DNA, cutting chains of connective tissue components such as collagen and hyaluronic acid, and participating in melanin production. Therefore, when excessive active oxygen is generated in the skin of the human body, the antioxidant defense system is destroyed, ultimately causing skin aging to be accelerated.
- Accordingly, in the functional cosmetics market, DPPH free radical scavenging ability is measured as a representative in vitro test method for measuring antioxidant efficacy that inhibits free radical reactions in vivo. It is a test method to measure the DPPH free radical scavenging ability of a substance by measuring the degree of radical reduction. Therefore, the ‘antioxidant effect measurement test’ was conducted using an in vitro DPPH assay, and can be presented as data to indirectly secure the antioxidant effect evaluation of the test substance.
- It was confirmed that spider silk protein has DPPH free radical scavenging ability and helps antioxidant effect.

→ **test results :** It was confirmed that ‘Spider silk protein’ increased the DPPH free radical scavenging activity by up to 60.50±1.47% compared to the negative control at concentrations of 0.025% or less (0.005%, 0.01%, 0.025%). In particular, it was confirmed that 'Spider silk protein' exhibited higher DPPH free radical scavenging activity than the positive control L-Ascorbic acid (5μg/mL) at a concentration of 0.025%. Through this, 'Spider silk protein' shows DPPH free radical scavenging ability at a concentration of 0.025% or less, and it is judged to be helpful in antioxidant effect.

3. Cosmetics and Wound healing

<Antioxidation>

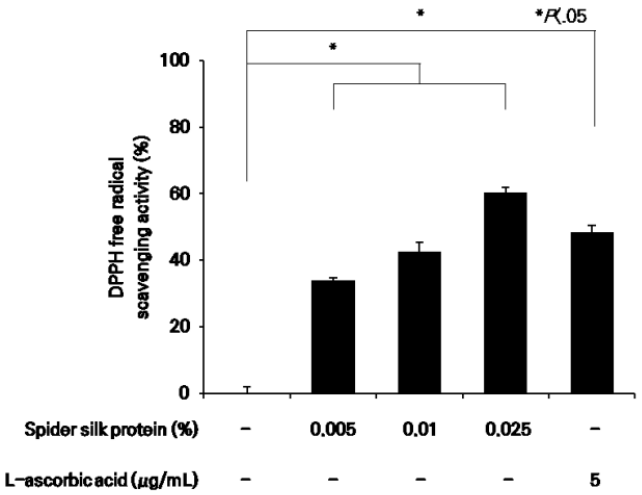


Figure 2. Measurement results of DPPH free radical scavenging ability of test substance Spider silk protein'.

(*P<.05, 음성대조군 대비) Compared to the negative control group)

before reaction

30 minutes after reaction

Figure 3. Color change image of DPPH free radical scavenging ability of test substance Spider silk protein'.

3. Cosmetics and Wound healing

<Hyaluronic acid expression>

- Hyaluronic acid is formed in fibroblasts and keratinocytes of the epidermis and dermis, and it is known that HAS2 among enzymes promoting hyaluronic acid synthesis (Hyaluronic acid synthase, HAS) plays a decisive role in hyaluronic acid synthesis. Hyaluronic acid is involved in the binding and retention of water molecules and has the characteristic of containing water. That is, it binds to water about 1000 times its own weight to regulate skin barrier function, hydrate the extracellular matrix, and maintain the homeostasis of water in tissues. In particular, it is known that the skin contains more than 50% of hyaluronic acid in the body, and they are involved in the stabilization of skin structure such as maintenance of water balance, osmotic pressure and ion flow, as well as wound healing. The decrease in hyaluronic acid in the epidermis is the main phenomenon of skin aging, and it is affected by the increase in age and ultraviolet rays, resulting in loss of moisture and decrease in skin elasticity. In order to prevent this skin aging phenomenon, an ingredient that can restore the structure of the reticular layer of the dermis by activating the function of dermal fibroblasts present in the dermal layer to promote the production of hyaluronic acid enzyme is required. Spider silk protein produces hyaluronic acid enzyme It was confirmed that it helps increase.

→ test results : When 'Spider silk protein' was treated with human dermal fibroblasts at concentrations of 0.025% or less (0.005, 0.01, 0.025%), it was confirmed that the expression of HAS2 mRNA was increased by up to 90.62±2.37% compared to the negative control group. Through this, 'Spider silk protein' is judged to help increase hyaluronic acid enzyme production as HAS2 mRNA expression in human dermal fibroblasts increases at a concentration of 0.025% or less.

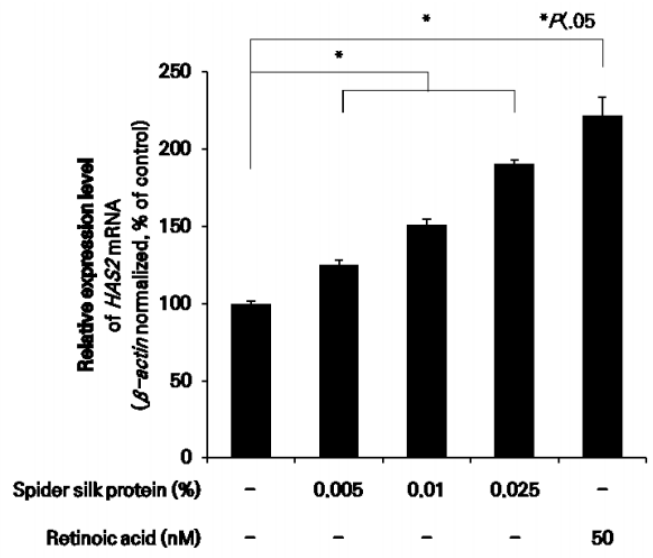


Figure 2. Changes in hyaluronic acid enzyme (Hvaluronan synthase 2. HAS2) gene expression in human dermal fibroblasts (NHDFS) treated with the test substance 'Spider silk protein'

(*P<.05, 음성대조군 대비) Compared to the negative control group)

3. Cosmetics and Wound healing

<Nitric oxide (NO) inhibition >

- Skin diseases are gradually increasing in modern society, and the symptoms are very diverse, from skin lesions such as Atopic dermatitis and Psoriasis caused by the breakdown of skin physiological functions to exacerbation of inflammation by ultraviolet rays. Inflammatory response in the body is one of the immune system's responses to physical and chemical stimuli such as wounds or bacterial infections. Inflammation is induced by the expression of inflammation-related factors through the activation of transcription factors. Cytokine and gene expression in this inflammatory response is regulated by nuclear factor kappa B (NF-κB) transcription factor. When a stimulus such as lipopolysaccharide (LPS) occurs, the production of nitric oxide (NO) is promoted, and NF-κB is activated to activate tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and IL-1β. It induces gene expression of various inflammatory mediating cytokines such as 6. It was confirmed that the spider silk protein inhibited the production of nitric oxide, thereby inhibiting the gene expression of inflammatory mediating cytokines.

→ **test results :** When treated with 'Spider silk protein' at a concentration of 0.025% or less (0.005, 0.01, 0.025%), it was confirmed that NO production in LPS-induced human keratinocytes was reduced by 41.22±3.22% compared to the LPS-only treatment group. . Through this, 'Spider silk protein' is judged to be helpful in inhibiting NO production as the amount of NO production increased by LPS appears to decrease at a concentration of 0.025% or less.

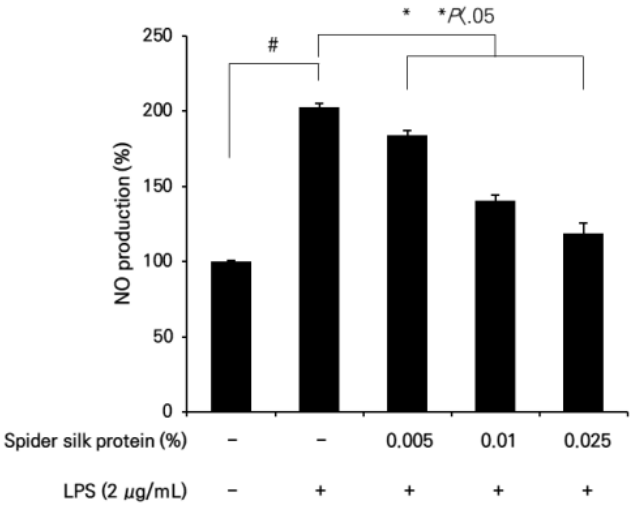


Figure 2. Changes in NO (Nitric oxide) production in human keratinocytes (HaCaT cel) treated with the test substance 'Spider silk protein'. compared to negative control group or compared to LPS alone treatment group)

(#P<.05, 음성대조군 대비 또는 *P<.05, LPS 단독 처리군 대비)

3. Cosmetics and Wound healing

<Two types of whitening (tyrosinase, inhibition of melanin production)>

- Melanin is synthesized in the melanosome and contains specific enzymes required to produce normal melanin. Tyrosinase is an enzyme involved in the most important initial rate-determining step in the melanin production process. It has tyrosine hydroxylase activity that converts L-tyrosine substrate into 3,4-dihydroxyphenylalanine (L-DOPA) and oxidizes DOPA to DOPA-quinone. It has both DOPA oxidase activity. Melanin is produced from DOPA-quinone through DOPA-chrome through auto-oxidation and enzymatic reactions. Causes of excessive melanin production include genetic factors, ultraviolet rays (UV), heat, chemical agents, and inflammation. In particular, ultraviolet rays are known as a trigger that accelerates photoaging, and when exposed to ultraviolet rays for a long time, melanin-promoting factors such as α-melanocyte stimulating hormone (α-MSH), endothelin-1 (ET-1), and nitric oxide (NO) is secreted from keratinocytes. α-MSH, one of the factors regulating melanocytes and skin pigmentation, binds to MC1R (melanocortin 1 receptor), a membrane receptor expressed only in melanocytes, and activates the signal transduction system related to melanin production.
- Through this pathway, melanin synthesis in melanocytes is a complex process involving enzymes such as tyrosinase, tyrosinase related protein (TRP)-1, and tyrosinase related protein (TRP)-2, and the microphthalmia-associated transcription factor (MITF) factor that regulates them. This is done through a process.
- Spider silk protein inhibits the activity of tyrosinase, which plays an important role in melanin production. The effect of the whitening component was confirmed by confirming the inhibition of melanin production.

→ **test results :** When 'Spider silk protein' was treated at a concentration of 0.025% or less (0.005, 0.01, 0.025%), the tyrosinase inhibitory activity against L-tyrosine was inhibited by up to 17.37±1.58% compared to the negative control group, and α–MSH-induced melanogenesis It was confirmed that the amount of melanin produced in the cells was reduced by up to 29.25±1.56% compared to the α–MSH alone treatment group. Through this, 'Spider silk protein' is judged to be helpful in inhibiting in vitro tyrosinase activity and melanin production at a concentration of 0.025% or less.

3. Cosmetics and Wound healing

<Two types of whitening (tyrosinase, inhibition of melanin production)>

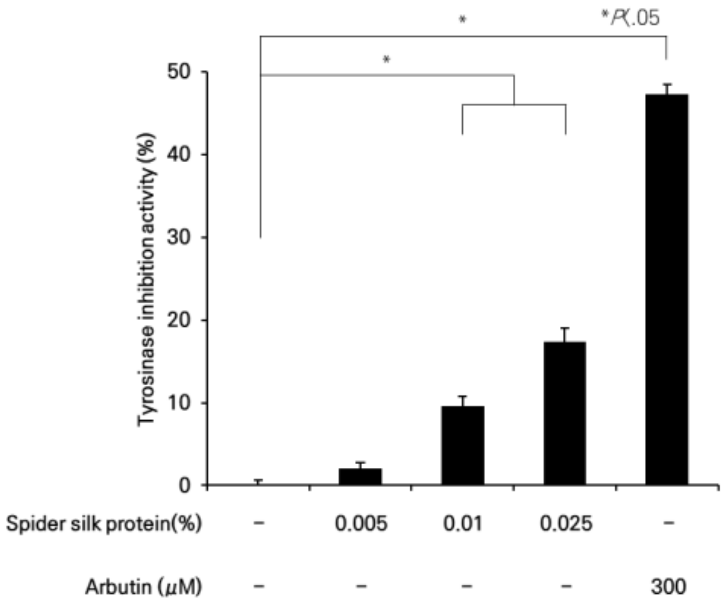


Figure 2. Measurement result of tVroSinase inhibitory activity against L-tosine of 'Spider silk protein' test substance

(*P<.05, 음성대조군 대비)

Compared to the negative control group)

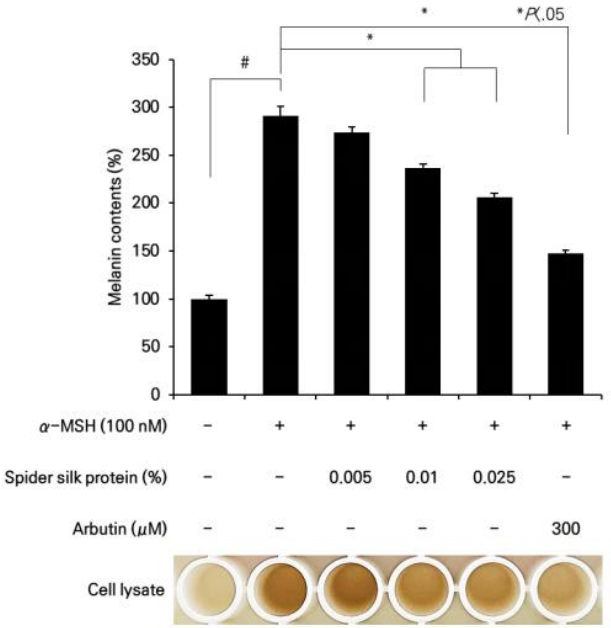


Figure 4. Changes in melanin production in melanocytes (B16F 10 melanorna cells) treated with the test substance 'Spider silk protein'.

(#P<.05, 비처리 대조군 대비 또는 *P<.05, α-MSH 단독 처리군 대비)

(compared to untreated control group or single treatment group)

3. Cosmetics and Wound healing

<Filaggrin Expression>

- Filaggrin is formed in human keratinocytes and is a fine fiber aggregation protein (Filaggrin; Filament aggregation protein). In addition, since filaggrin is decomposed into natural moisturizing factor (NMF) and plays an important role in maintaining moisture in the stratum corneum, it is known to play a decisive role in the differentiation of keratinocytes and maintenance of the skin barrier function. When there is an abnormality in the production of filaggrin, NMF is reduced, and as a result, the amount of moisture in the stratum corneum is reduced and the skin surface pH is increased, causing the skin barrier function to collapse, resulting in skin diseases such as atopic dermatitis. In order to restore such a healthy skin barrier, it is necessary to help maintain the skin barrier function and epidermal homeostasis by smoothly restoring the maintenance and movement of moisture in the epidermal layer by activating the function of keratinocytes to promote the production of filaggrin.
- It was confirmed that the spider silk protein helps to express filaggrin.

→ test results : When human keratinocytes were treated with 'Spider silk protein' at a concentration of 0.025% or less (0.005, 0.01, 0.025%), it was confirmed that filaggrin mRNA expression increased by up to 18.24±4.34% compared to the negative control group. Through this, 'Spider silk protein' is judged to help increase filaggrin production as the expression of filaggrin mRNA in human keratinocytes increases at a concentration of 0.025% or less.

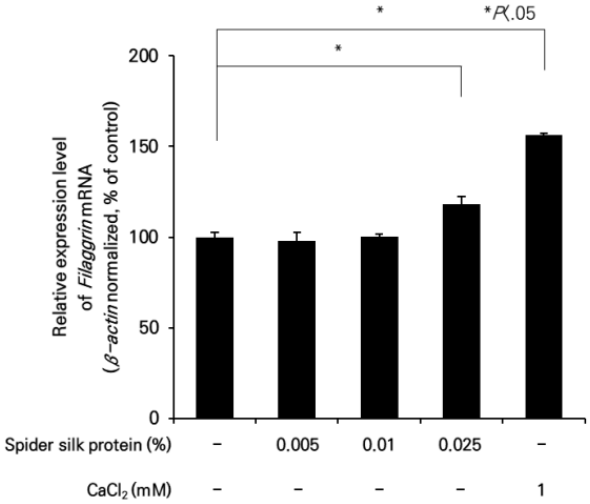


Figure 2. Changes in filaggrin (FLG) gene expression in human keratinocytes (HaCaT cel) treated with the test substance 'Spider silk protein'.

(*P<.05, 음성대조군 대비) Compared to the negative control group)

3. Cosmetics and Wound healing

<3 types of anti-inflammatory (2 types of chemokines (TRAC, MDC), inhibition of NO production)>

Inflammatory response in the body is one of the immune system's responses to physical and chemical stimuli such as wounds or bacterial infections. Inflammation is induced by the expression of inflammation-related genes through the activation of transcription factors. Cytokine and gene expression in this inflammatory response is regulated by nuclear factor kappa B (NF-κB) transcription factor. When a stimulus such as lipopolysaccharide (LPS) occurs, NF-κB is activated and the genes of various inflammatory mediating cytokines such as tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β) and IL-6 induce expression.

- Two types of chemokines (TRAC and MDC) are signal transduction proteins that cause immune responses, and spider silk proteins were confirmed to inhibit the production of TRAC and MDC2 types. In addition, inhibition of nitric oxide production, which inhibits gene expression of inflammatory mediating cytokines, was also confirmed by molecular size.

→ test results : When 'low molecular weight spider silk protein', 'high molecular weight spider silk protein', and 'ultra high molecular weight spider silk protein' were treated at concentrations of 0.025% or less (0.005, 0.01, 0.025%), TARC mRNA expression was significantly higher in the TNF-α alone treatment group. 35.16±4.60%, 35.96±5.00%, and 23.59±0.57% respectively, and MDC mRNA expression decreased by 17.26±2.40%, 8.12±6.08%, and 8.26±6.14 respectively compared to the TNF-α alone treatment group. It was confirmed that NO production was reduced by up to 47.06 ± 3.99%, 38.79 ± 3.00%, and 36.97 ± 1.34%, respectively, compared to the LPS alone treatment group. Through this, 'low molecular weight spider silk protein', 'high molecular weight spider silk protein' and 'ultra high molecular weight spider silk protein' inhibited TARC mRNA, MDC mRNA expression and NO production in human keratinocytes at concentrations of 0.025% or less. It is judged to be helpful in inhibiting the production of two chemokines and inhibiting NO production.

3. Cosmetics and Wound healing

<3 types of anti-inflammatory (2 types of chemokines (TRAC, MDC), inhibition of NO production)>

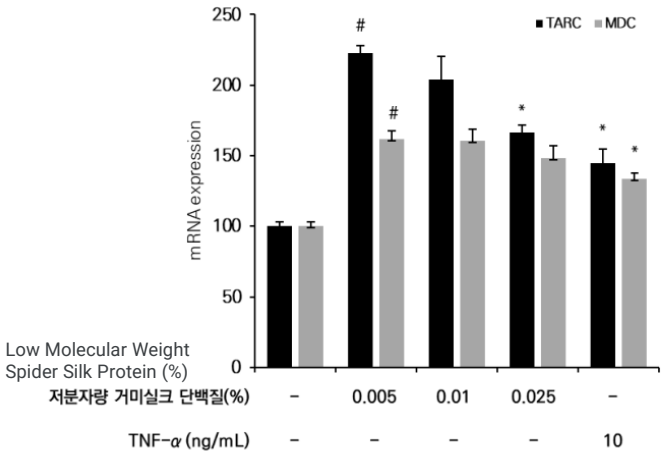


그림 4. '저분자량 거미실크 단백질'을 처리한
인간각질형성세포(HaCaT cell)의 케모카인 2 종(*TARC* 및 *MDC*) 유전자 발현 변화.
(#*P*<.05, 음성대조군 대비 또는 *P<.05, TNF-α 단독 처리군 대비)

Figure 4. Expression of two chemokines (TARC and MDC) in human keratinocytes (HaCaT cel) treated with 'low molecular weight spider silk protein'.

(Compared to negative control group or single treatment group)

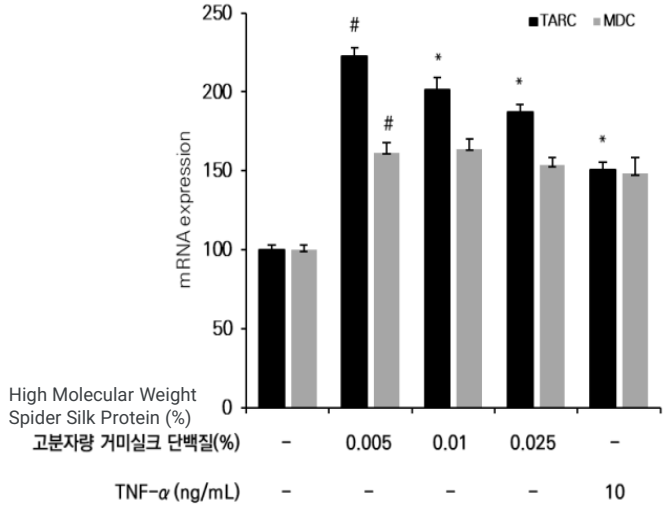


그림 5. '고분자량 거미실크 단백질'을 처리한
인간각질형성세포(HaCaT cell)의 케모카인 2 종(*TARC* 및 *MDC*) 유전자 발현 변화.
(#*P*<.05, 음성대조군 대비 또는 *P<.05, TNF-α 단독 처리군 대비)

Figure 5. Changes in the gene expression of two chemokines (TAAC and MDC) in human keratinocytes (HaCaT cal) treated with high molecular weight and spider silk protein.

(Compared to negative control group or single treatment group)

3. Cosmetics and Wound healing

<3 types of anti-inflammatory (2 types of chemokines (TRAC, MDC), inhibition of NO production)>

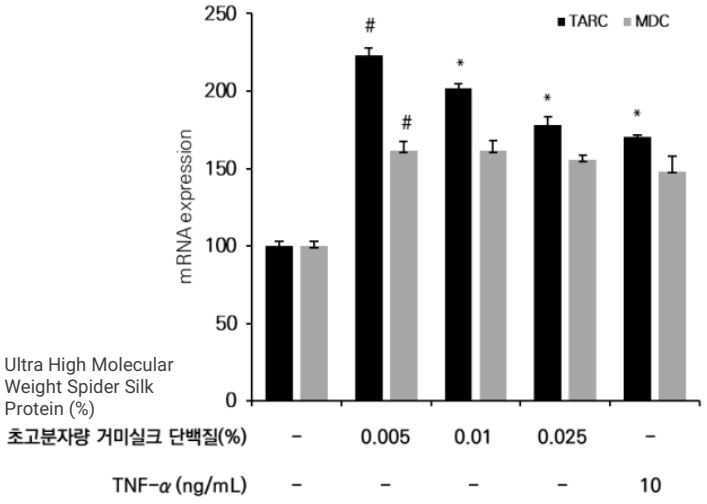


그림 6. '초고분자량 거미실크 단백질'을 처리한 인간각질형성세포(HaCaT cell)의 케모카인 2 종(*TARC* 및 *MDC*) 유전자 발현 변화.
(#*P*<.05, 음성대조군 대비 또는 **P*<.05, TNF-α 단독 처리군 대비)

Figure 6. Changes in the gene expression of two chemokines (TARC and MDC) in human keratinocytes (HaCaT cel) treated with 'ultra-high molecular weight spider silk protein'.

(Compared to negative control group or single treatment group)

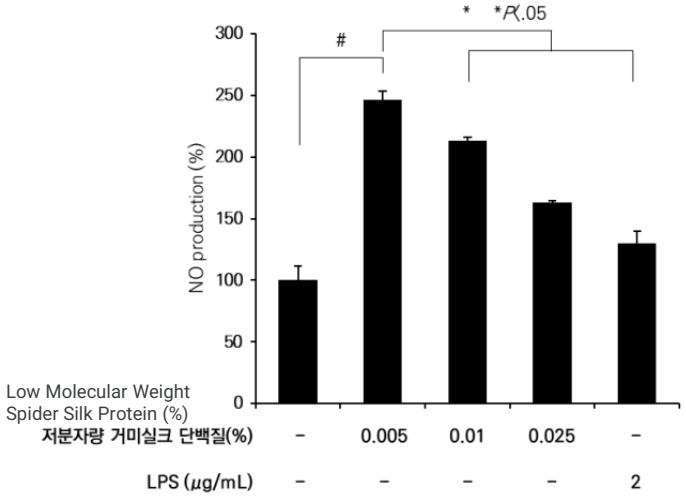


그림 7. '저분자량 거미실크 단백질'을 처리한 인간각질형성세포(HaCaT cell)의 NO (Nitric oxide) 생성량 변화.
(#*P*<.05, 음성대조군 대비 또는 **P*<.05, LPS 단독 처리군 대비)

Figure 7. Changes in NO (Nitric oxide) production in human keratinocytes (HaCaT cel) treated with 'low molecular weight spider silk protein'.

(Compared to negative control group or single treatment group)

3. Cosmetics and Wound healing

<3 types of anti-inflammatory (2 types of chemokines (TRAC, MDC), inhibition of NO production)>

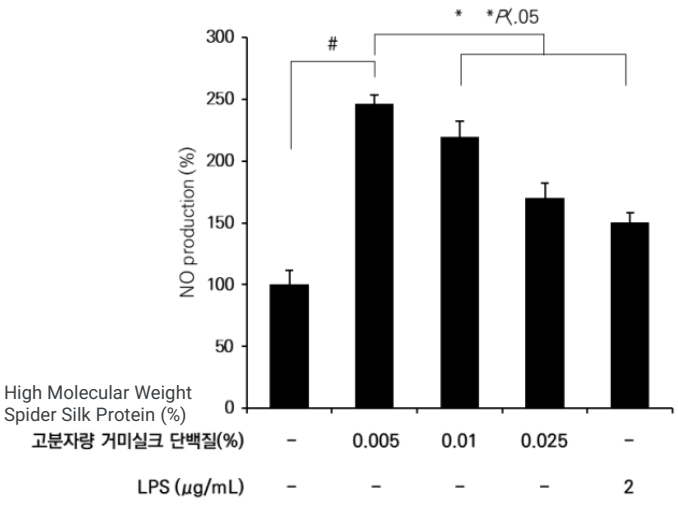


그림 8. '고분자량 거미실크 단백질'을 처리한
인간각질형성세포(HaCaT cell)의 NO (Nitric oxide) 생성량 변화.
(#P<.05, 음성대조군 대비 또는 *P<.05, LPS 단독 처리군 대비)

Figure 8. NO (Nitric oxide) production change in human keratinocytes (HaCaT cells) treated with high molecular weight spider silk protein.

(Compared to negative control group or single treatment group)

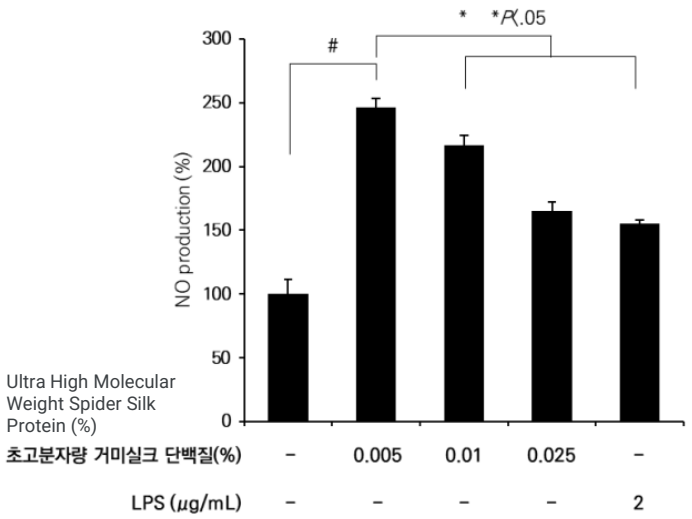


그림 9. '초고분자량 거미실크 단백질'을 처리한
인간각질형성세포(HaCaT cell)의 NO (Nitric oxide) 생성량 변화.
(#P<.05, 음성대조군 대비 또는 *P<.05, LPS 단독 처리군 대비)

Figure 9. Changes in NO (Nitric oxide) production in human keratinocytes (HaCaT cel) treated with 'ultra-high molecular weight spider silk protein'.

(Compared to negative control group or single treatment group)

Techonology Overview

3. Cosmetics and Wound healing

In this market where hair loss products and functional skin cosmetics products applied with MCB Spider silk raw materials are highly competitive, the basis for what the comparative advantage is.

- As can be seen by comparing the positive control of the attached experimental results, we show that Spider Silk Protein, such as whitening, anti-oxidation, and anti-aging, is not a single-functional raw material, but a multi-functional raw material.
- Although there are many single ingredients with functions such as whitening, wrinkle improvement, and moisturizing ingredients, spider silk protein is a multifunctional raw material and helps to prevent and manage abnormalities that may occur on the scalp and skin, such as inhibiting inflammation.
- In addition, hair loss due to physical damage (friction, combing, etc.) and chemical damage (product use, perm or dyeing, etc.) is lost when using a wash-off type product containing spider silk protein. It was also confirmed in other papers that the damaged cortex was restored. (Refer to the photo below)
- (A: normal hair, B: bleached hair without silk treatment, C: bleached hair treated with silk) According to the U2021/0113446A1 patent, it is possible to confirm that the hair shaft is improved when bleached hair is treated with spider silk protein (the arrow indicates that the hair shaft is damaged). It was confirmed that the spider silk protein is absorbed into the hair and helps to improve the hair texture.

(19) **United States**

(12) **Patent Application Publication**
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(54) **COSMETIC COMPOSITION FOR TREATING KERATIN FIBERS**

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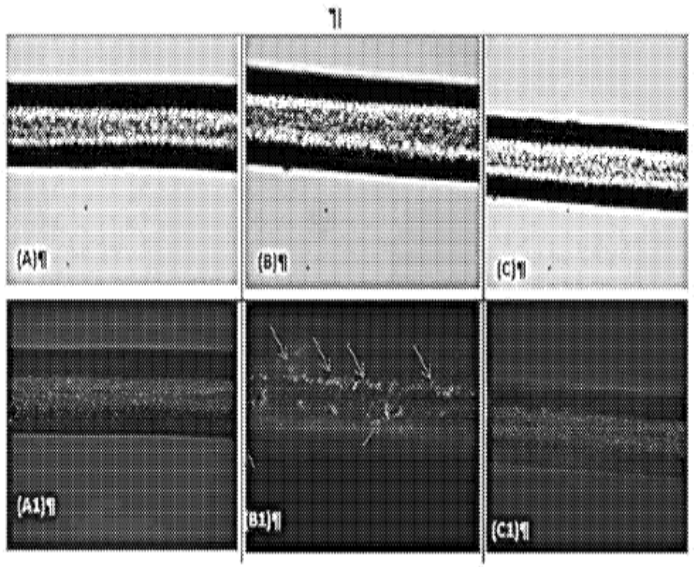
A61Q 5/06	(2006.01)
A61Q 5/12	(2006.01)

(52) **U.S. Cl.**
CPC *A61K 8/64* (2013.01); *A61K 8/042* (2013.01); *A61Q 5/12* (2013.01); *A61Q 5/02* (2013.01); *A61Q 5/065* (2013.01); *A61Q 1/10* (2013.01)

(57) **ABSTRACT**

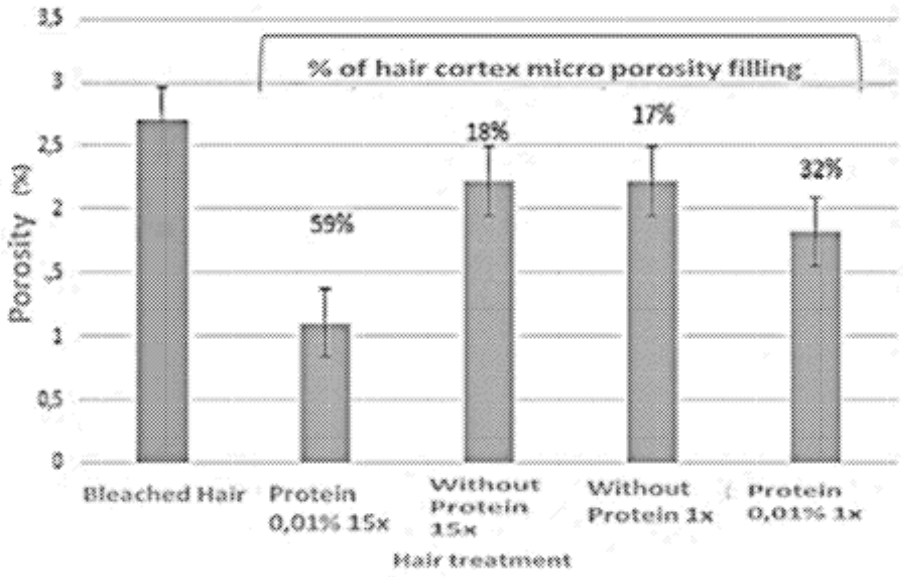
A cosmetic composition for treating keratin fibers is provided. The cosmetic composition comprises about 0.06 to about 0.008% of ADF-4 recombinant silk protein based on the total weight of the composition, and cosmetic acceptable vehicles.



3. Cosmetics and Wound healing

In this market where hair loss products and functional skin cosmetics products applied with MCB Spider silk raw materials are highly competitive, the basis for what the comparative advantage is.

- Trendy multi-functional and high-functional raw materials have issues with irritation and skin reactions, but spider silk protein is excellent in biocompatibility and biodegradability, so it can be used without worrying about irritation or allergy to problematic skin caused by hair loss.
- Spider silk proteins are cationic (hydrophobic). Cationic property has the property of adsorbing to hair.
- Porosity comparison experiment using wash-off spider silk protein product on bleached hair in a patent
- When treated with spider silk protein, porosity was reduced by 59% and 32% compared to when not treated
- It was confirmed that the spider silk protein is adsorbed to the hair and helps to restore damaged hair due to bleaching.



Techonology Overview

3. Cosmetics and Wound healing

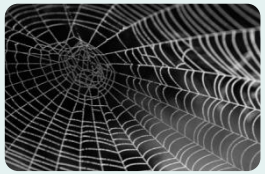
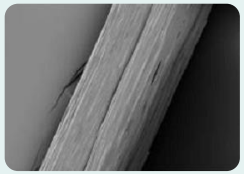
How MCB spider silk protein improved skin collagen and tissue regeneration

- The mechanism by which spider silk protein enhances cell and tissue regeneration and collagen regeneration, the mechanism of action for promoting the Nf-kb canical pathway that spider silk protein promotes cell regeneration was demonstrated in Figure 6, and cell regeneration through this was confirmed. In the wound healing assay, it was confirmed that the expression of col1a1 protein was improved in the group treated with spider silk protein. Furthermore, as a result of the non-clinical efficacy test of the wound dressing, when using the wound dressing containing spider silk protein, it was confirmed by H&E staining that tissue regeneration was achieved compared to the existing wound dressing through tissue staining, In this process, smooth collagen regeneration was confirmed through MCT (Masson's trichrome) staining. Also, it can be seen that the spider silk protein solution increases the collagen enzyme.
- In this data, the negative control group (G1), which was not treated with anything after wound induction, the coating material applied by spraying spider silk protein in the form of a spray (G2), and the group coating the surface of the coating material by dissolving spider silk protein in hydrogel (G3), commercially available wound dressings are classified as (G4), the wound width is indicated by a red arrow, the area where re-epithelialization occurs is indicated by a black dotted line, and the area where collagen regeneration is measured is indicated by a black box.
- Through in-vitro experiments, ROS inhibition, collagen expression, antioxidant, hyaluronic acid expression, NO inhibition, whitening 2 types, filaggrin expression, inflammation 3 types, and positive effects on cell growth were confirmed.
- **Moisturizing :** When treated with human dermal fibroblasts at a concentration of 0.025%, it was confirmed that HAS2 mRNA expression increased by 90.62±2.37% compared to the negative control group.
- **Wrinkle improvement :** When treated at a concentration of 0.025%, it was confirmed that the production of reactive oxygen species (ROS) in human keratinocytes induced by UVB was reduced by up to 52.73±0.77% compared to the group treated with UVB alone.
- When treated with human dermal fibroblasts at a concentration of 0.025%, COL1A1 mRNA expression was confirmed to increase by up to 60.09±2.55% compared to the negative control group.
- At 0.025% concentration, DPPH free radical scavenging activity was confirmed to increase by up to 60.50±1.47% compared to the negative control group. In particular, it was confirmed that 'Spider silk protein' showed higher DPPH free radical scavenging activity than L-Ascorbic acid (5μg/mL), a positive control, at a concentration of 0.025%.
- Experimental results compared with other raw materials can be compared with the in-vitro positive control of answer 23.
- **Breathable :** Spider silk is of great interest as a naturally degradable natural material with excellent strength and elasticity. These properties suggest that spider silk proteins can be utilized to form semi-occlusive films. Spider silk protein has a beta-sheet conformation structure similar to type 2 collagen, enabling strong binding between proteins. Due to this, high molecular weight spider silk proteins can be used to form semi-occlusive films. Based on this, nano- and micro-scale semi-occlusive films are being developed, and if commercialized, they can be used in various fields such as medical materials, food packaging, sensors, and coatings. (doi: 10.1073/pnas.1109420109.)

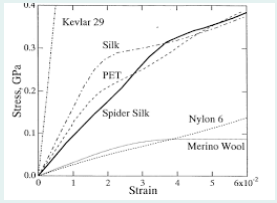
1.Core Technology

High-efficiency, high-productivity spider silk expression platform and mass production technology

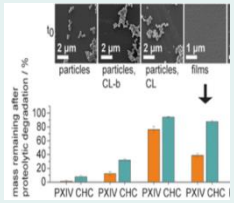
SPIDER SILK PROTEIN

- 5X stronger than steel when equal mass
- Higher elasticity than man-made fiber, Kevlar
- High biocompatibility and biodegradability (Eco-friendly material)



Mechanical properties

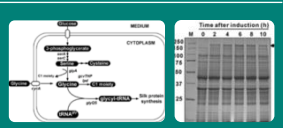


Biological properties

World Innovative top-class spider silk protein technology secured

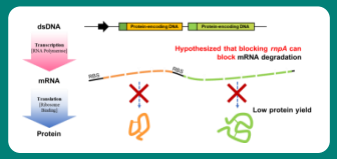
Development of spider silk protein expressing platform using DNA manipulation

Application of metabolic engineering for higher production

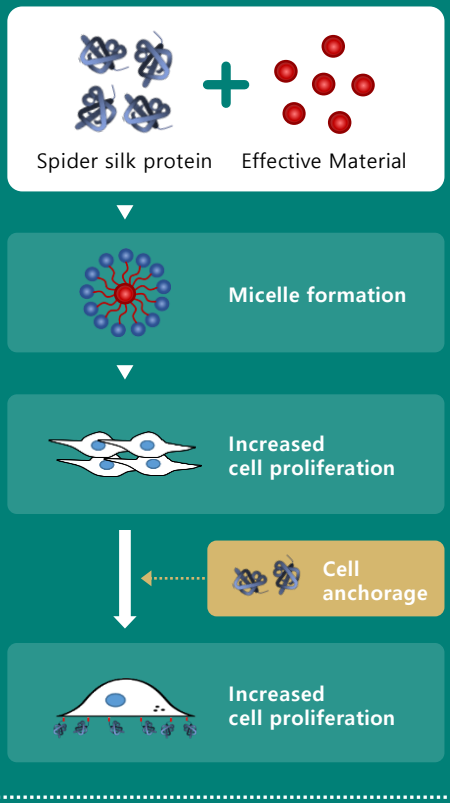


Application of synthetic biology for mass production

특허청



Enhanced drug delivery effect



1.Core Technology

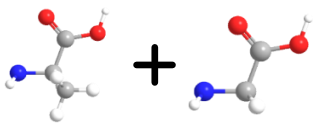
Medicos Biotech

Spider silk with excellent properties with the possibility to expand to various industries

Highly efficient bio-fiber, (Eco-friendly material)
able to replace existing petrochemical products

- High strength
- High elasticity
- Biodegradability
- Biocompatibility

Repeating units of glycine and alanine



Alanine + Glycine

1.Core Technology

7 times higher productivity than global 4 competitors

Incomparable global competitiveness secured based on outstanding technological competence

7 times productivity compared to other companies

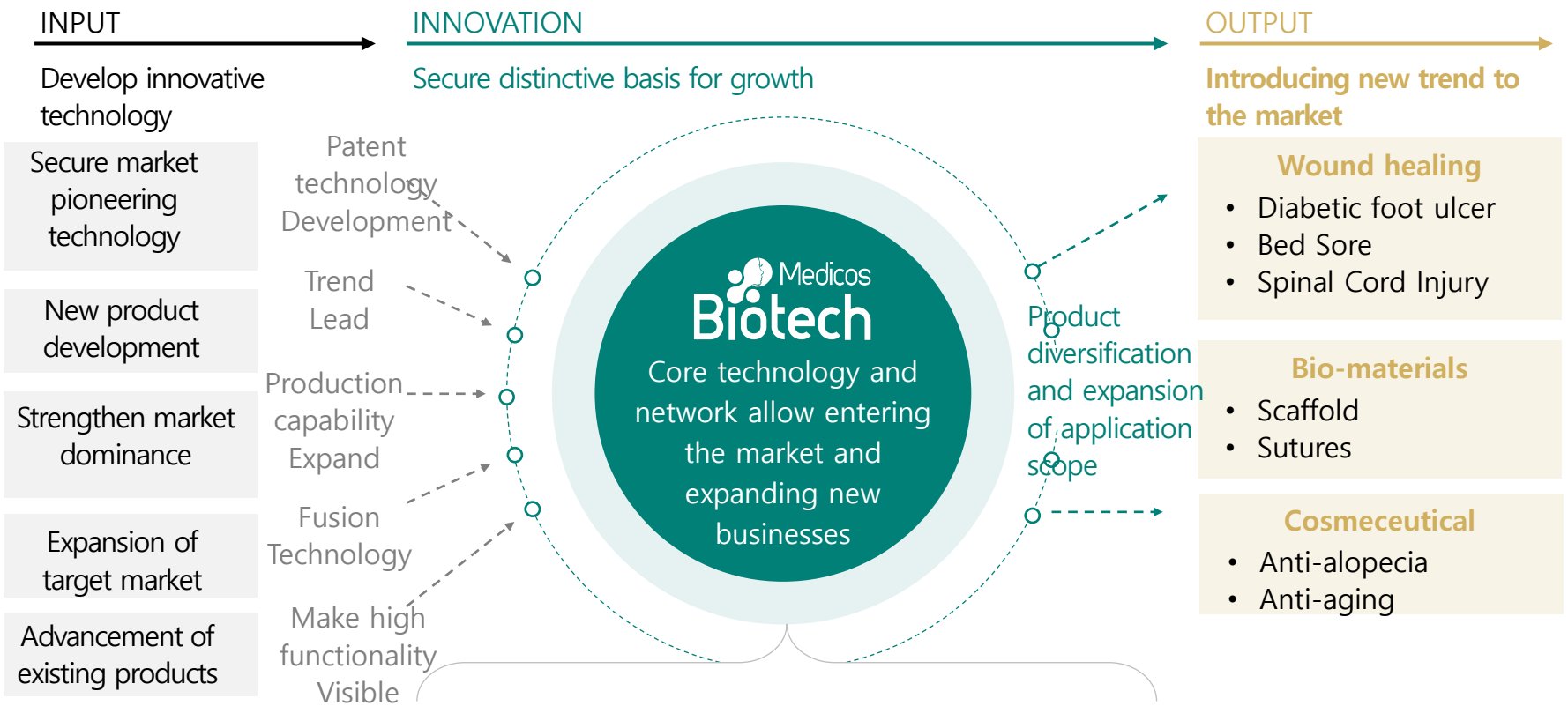
Production of ultra high-molecular weight spider silk protein than others

Application of metabolic engineering possible (Core technology for production of bio-based chemical and substance)

Category		Kraig Biocraft	AMSilk	Spiber	Bolt Threads	MCB
Time of development		2012	2008	2007	2009	2020
Accumulated Investment		$5M	$42.3M	$910.9M	$218.1M	$26.8 M (Corporate Valuation)
Technology platform		Silkworm	Colon Bacillus	Colon Bacillus	Yeast	Colon Bacillus
Technology development team		University of Wyoming	University of Bayreuth	Keio University	MIT	KAIST
Core technology	Maximum protein size produced (kDa)	15	50	200	100	370
	Production capability	-	0.36 g/L	1 g/L	0.5 g/L	~7 g/L
Applied technology	Production platform	Low	High	Middle	Middle	**High**
	Application of metabolic engineering	-	-	Available	-	Available

1.Core Technology

Pipeline of market friendly field established based on core technology



2.Biomedical Applications of Spider Silk

Biomedical Application

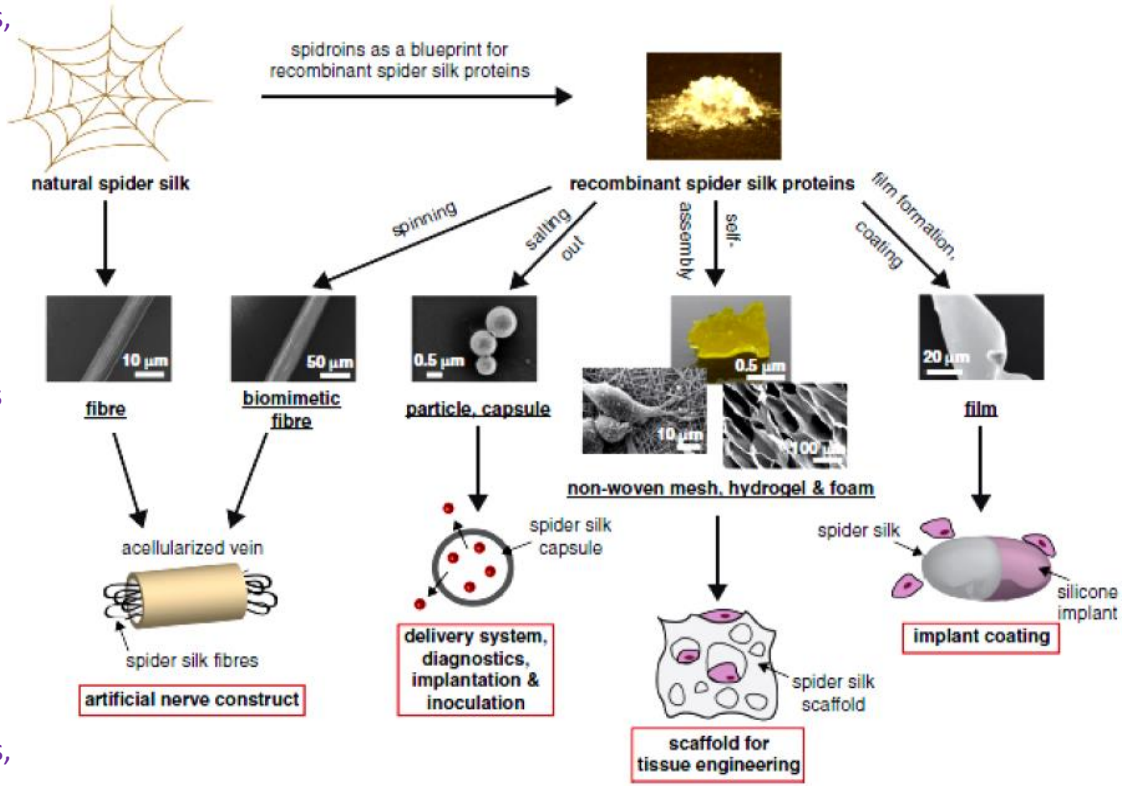
- Spider silk show excellent mechanical properties, high tensile strength and elasticity as well as biocompatibility, making it an attractive item in the biomedical industry
- As a coating material, spider silk's high biocompatibility characteristics allow reduction of inflammation and lower the rejection of silicon-based implants
- It can also be used as encapsulation materials for drug, protein, gene, cell delivery and analysis

- Can be applied to gene carrier, transplantation and inoculation related to cancer

- **Mash, hydrogel form of spider silk protein can be used as scaffold material in tissue engineering**

- Has been used as surgical sutures for many years, while non-woven form has large surface area – which is excellent for cell adhesion

- From studies, endothelial cells show higher proliferation when cultured with spider silk fibers



< Various biomedical applications of spider silk >

* Source : Arshdeep Kaur et al., Spider Silk: an excellent candidate as toughest biomaterial, 2019

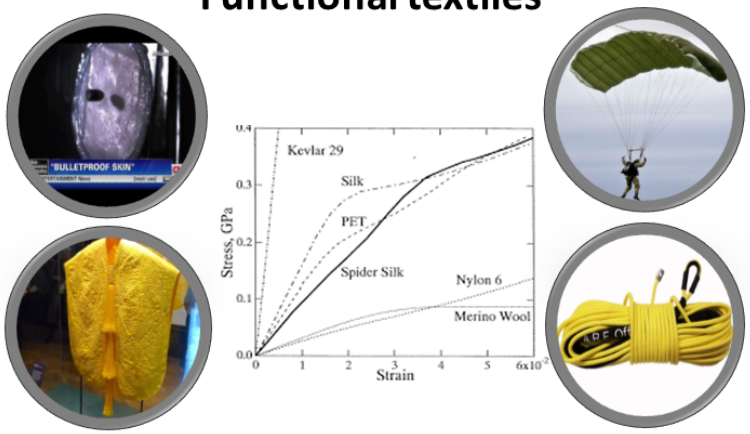
3.Industrial Applications of Spider Silk

Spider silk protein as an advanced biomaterials

Mechanical properties

Balanced Strength & Extensibility

Functional textiles

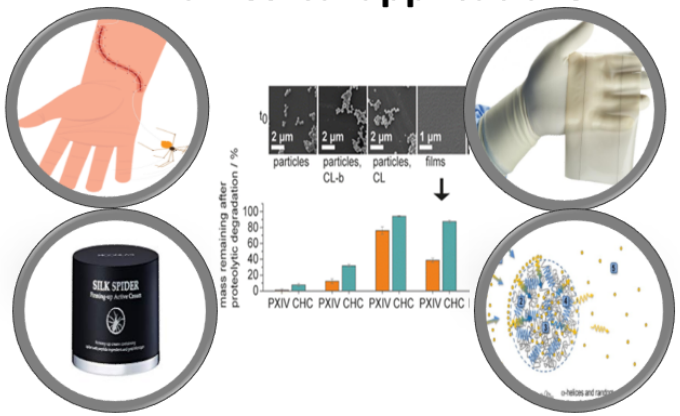


Tensile strength stronger than Kevlar

Biological properties

Biodegradability & Biocompatibility

Biomedical applications



Biocompatibility
Biodegradability

Material	Strength (N m^{-2})	Elongation (%)	Energy to break (J kg^{-1})
Spider Dragline Silk Protein	**4x10^9**	**35**	**4x10^5**
Flagelliform silk	1x10^9	>200	4x10^5
Kevlar	4x10^9	5	3x10
Rubber	1x10^6	600	8x10^4

Ko, Frank K., and Lynn Y. Wan. "Engineering properties of spider silk." *Handbook of Properties of Textile and Technical Fibres*. Woodhead Publishing, 2018. 185-220.

4.Medicosbiotech Business domain

Medicos Biotech

Core Tech: **Spidersilk protein FIRST & ONLY**

1 MEDICAL

MCB1-Wound Healing, MCB2-Spinal Cord

- **MCB-WH**
  - Licensing out to global pharmaceutical companies possible
- **MCB-SC**
  - Spinal cord injury recovery possible using in-house product

2 COSMETIC

MCB 3_Dr. Graft Spi Derma

- **Dr. Graft**
  - Use of specialized MCB-GF formula and MCB-Spider silk protein for anti-hair loss
- **Spi-Derma**
  - Spider silk protein as a cosmetic ingredients

3 BIO

MCB4_Spider Silk Protein Scaffold

- **Spidersilk protein**
  - **FIRST & ONLY** production of native-sized spider silk protein in the World
- **Scaffold**
  - Superb efficacy to be used as scaffold material

4.Medicosbiotech Business domain

A. MCB001 Spider silk wound dressing

Limitation of previous wound dressing

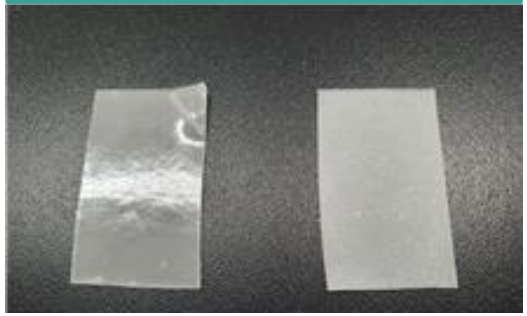
· The need for wound dressings and wound healing agents that minimize healing scars are rapidly increasing.

· The current wound dressing merely absorbs the ooze from the wound and prevents the formation of blood clots.

· Previous wound dressing has a limitation that it leaves a scar depending on the type and size of the wound and it needs quite long recovery time.

→ Development of advanced wound dressing containing spider silk protein with curing properties

Application of spider silk in powder form



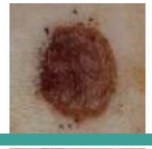
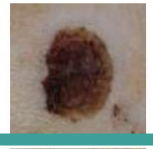
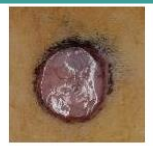
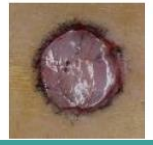
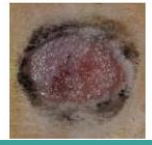
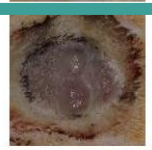
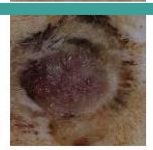
Application of film-type spider silk in CMC+PEG hydrogel

Prototype based on hydrocolloid wound dressing

Wound healing effect of spider silk wound dressing

- Confirmation of **improved recovery ability** in G2 and G3 groups (reduced wound area)

Photograph 1. Wound Area

	Group	Day 0	Day 2	Day 5
G1	Negative control			
G2	Experimental Group 1			
G3	Experimental Group 2			
G4	Comparison group			

G1: negative control
G2: Test substance 1 treated group,
G3: Test substance 2 treated group
G4: existing wound dressing treated group

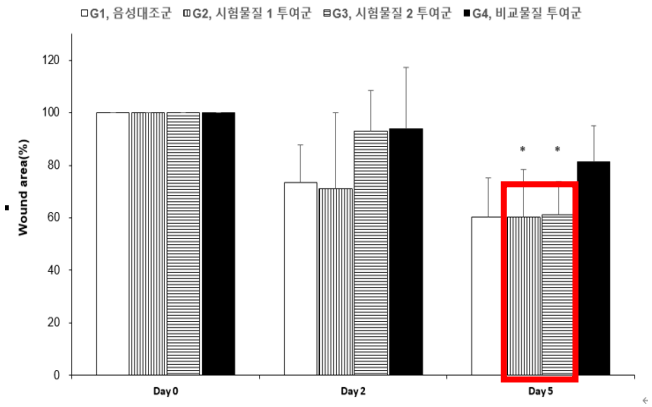


Figure 1. Wound Area

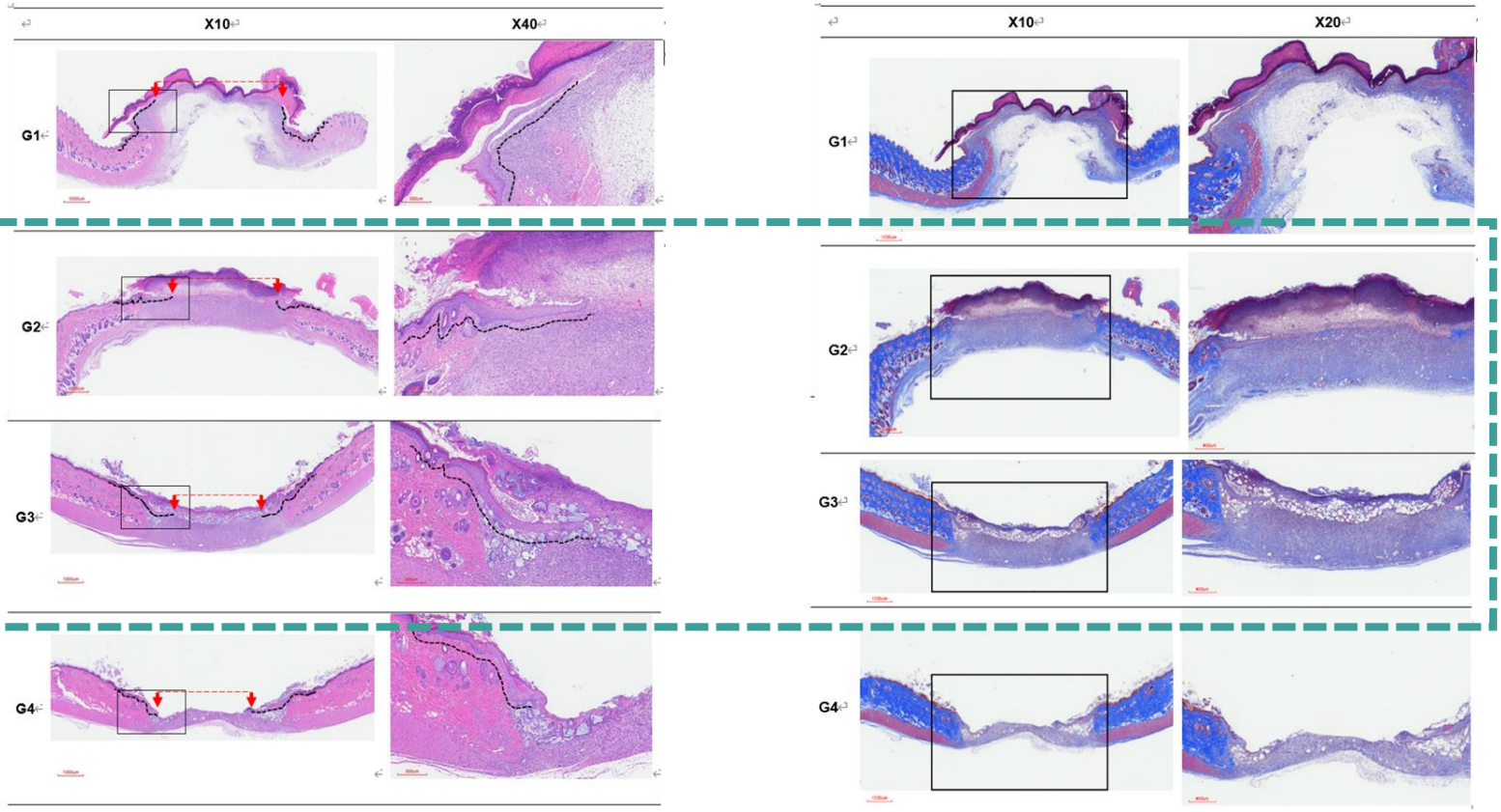
Each data expressed mean + S.D. (n=6)
* p<0.05, Significant differences was noted in the substance groups from the comparative substance control (G4) by Student T-test.

- Reduction in wound area when compared to negative control (G1), comparison group (G4) and experimental groups (G2, G3)
- Negative control (G1) show higher reduction of the wound area due to scab formation

Wound healing effect of spider silk wound dressing

- Confirmation of improved collagen and tissue regeneration

G1: negative control
G2: Test substance 1 treated group,
G3: Test substance 2 treated group
G4: existing wound dressing treated group
Red arrow: Wound width
Black dot line: re-epithelialization
Black box: Collagen measurement site



4.Medicosbiotech Business domain

A. MCB001 Spider silk wound dressing

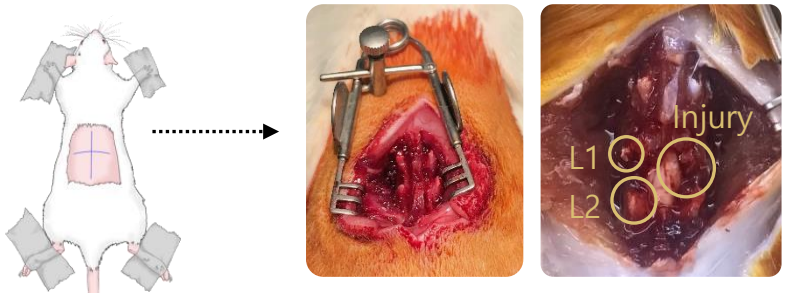
- **Possible market entry through differentiated mechanism and material**
  - Compared to existing products, superiority in wound protection and regeneration performance was confirmed
  - Securing competitiveness through self-production of materials and possession of source technology

-	Foam type patch	Device containing stem cell	Patch with growth factors	Spider silk protein patch
Antibacterial ingredient	X	X	X	V
Anti-inflammatory	X	X	X	V
Easy handling	V	X	X	V
Biocompatible	V	V	V	V
Price	$	$$$$	$$	$ ~ $$

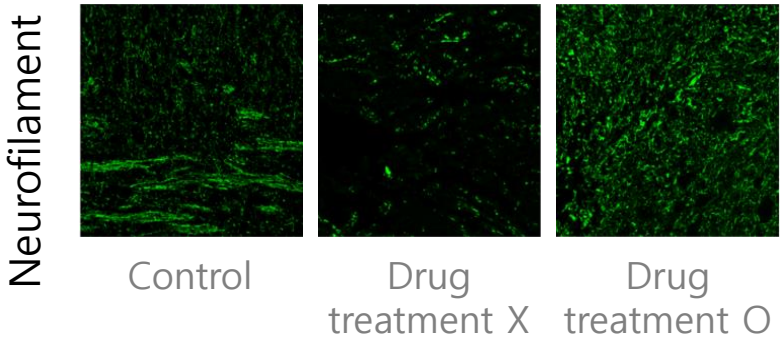
4.Medicosbiotech Business domain

B. MCB002 Efficient neurofilament regeneration (Spinal cord injury recovery)

- Verification through in-vivo experiments

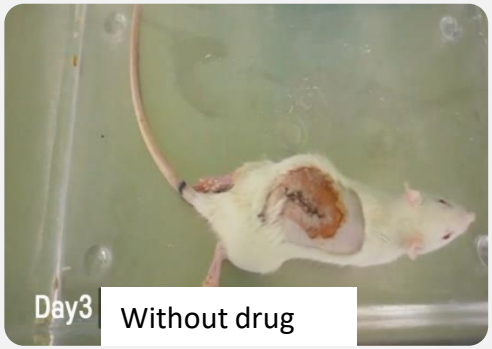


- Neurofilament regeneration efficacy confirmed

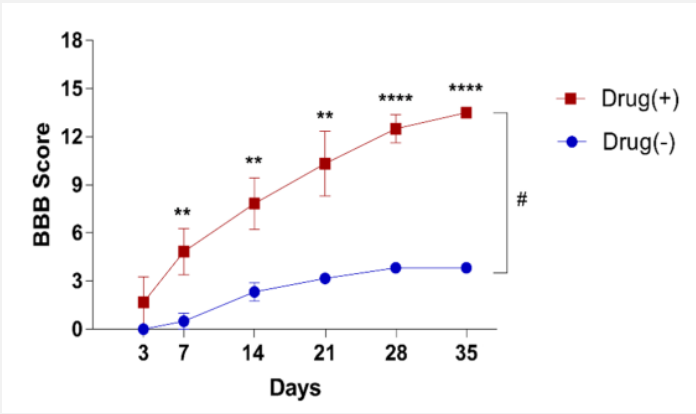


Recovery speed change check on Day28

▶ No drug treated

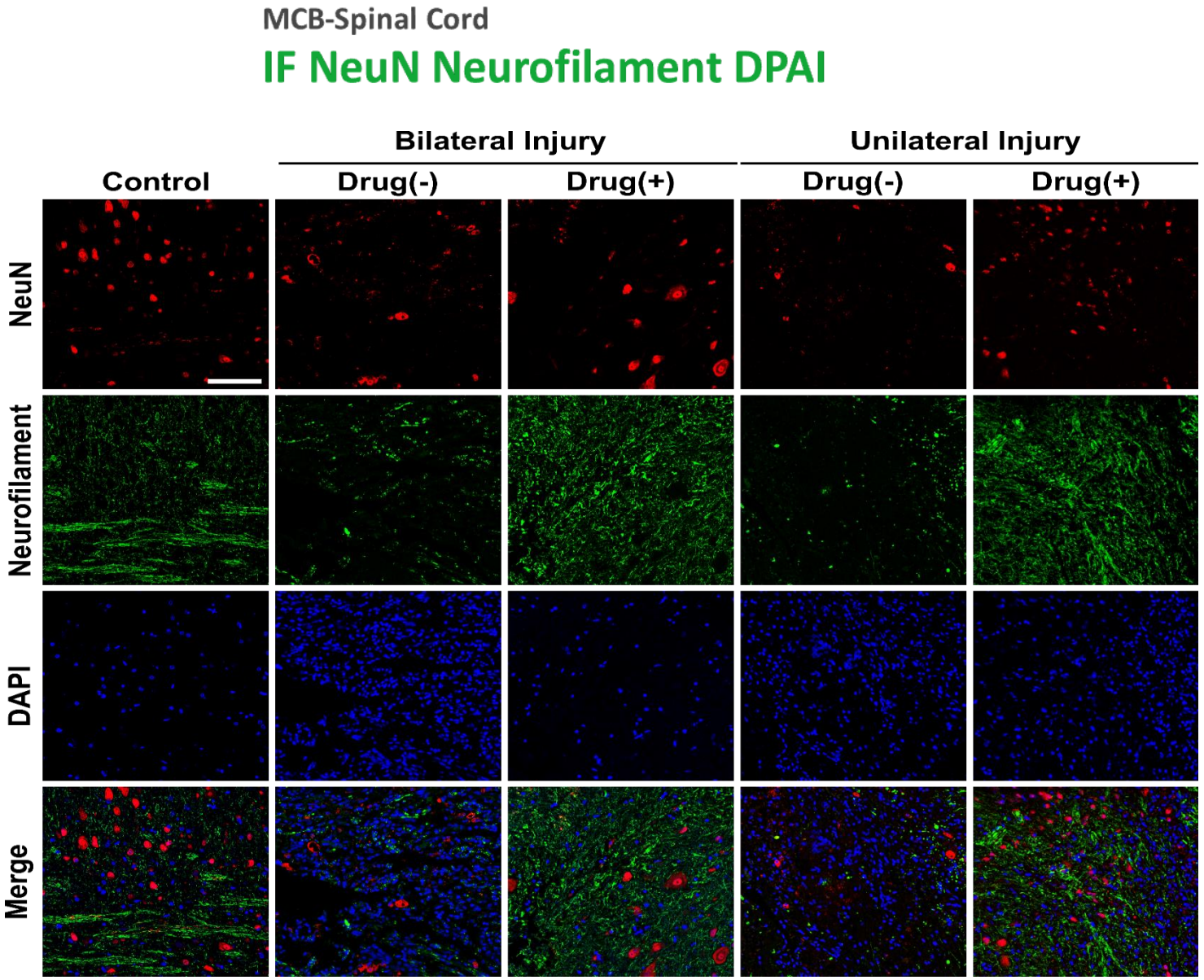


▶ When treated with MCB-002



4.Medicosbiotech Business domain

B. MCB002 Efficient neurofilament regeneration (Spinal cord injury recovery)



4.Medicosbiotech Business domain

C. MCB003 Spider Silk Protein as Cosmetic Ingredients

The outstanding advantage of using Spider silk protein as a cosmetic ingredient… ?

A protein component derived from nature (Spider web) and has excellent biocompatibility and biodegradability.

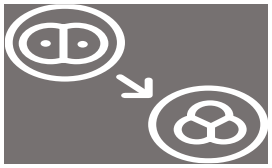
Very high tensile strength and physical properties due to its repeating sequence and protein structure.
(5 times harder than iron and more resilient than nylon and Kevula)

A skin protection effect by improving cell regeneration and forming a closed film.

Excellent moisturizing and anti-wrinkle effect.
Excellent breathability and lotion softening properties.

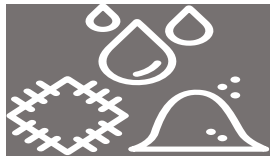
Manufactured as an aqueous solution, so it is very easy to store and add to products.

biodegradable



cell proliferation

biocompatibility



various formulations

Optimal biomaterial and cosmetic raw material for regeneration and recovery!!!

4.Medicosbiotech Business domain

C. MCB003 Spider Silk Protein as Cosmetic Ingredients

MCB003_Anti hair loss hair products contain Spider Silk Protein

Dr.GRAFT Scalp line(since 2019)

Shampoo

- Scalp Shampoo
- 300ml

Tonic

- Scalp Tonic
- 100ml

Dr.GRAFT Aranea line(since 2021)

Shampoo

- Aranea Shampoo
- 500ml

Treatment

- Aranea Treatment
- 200ml

■ Oversea's Certificate

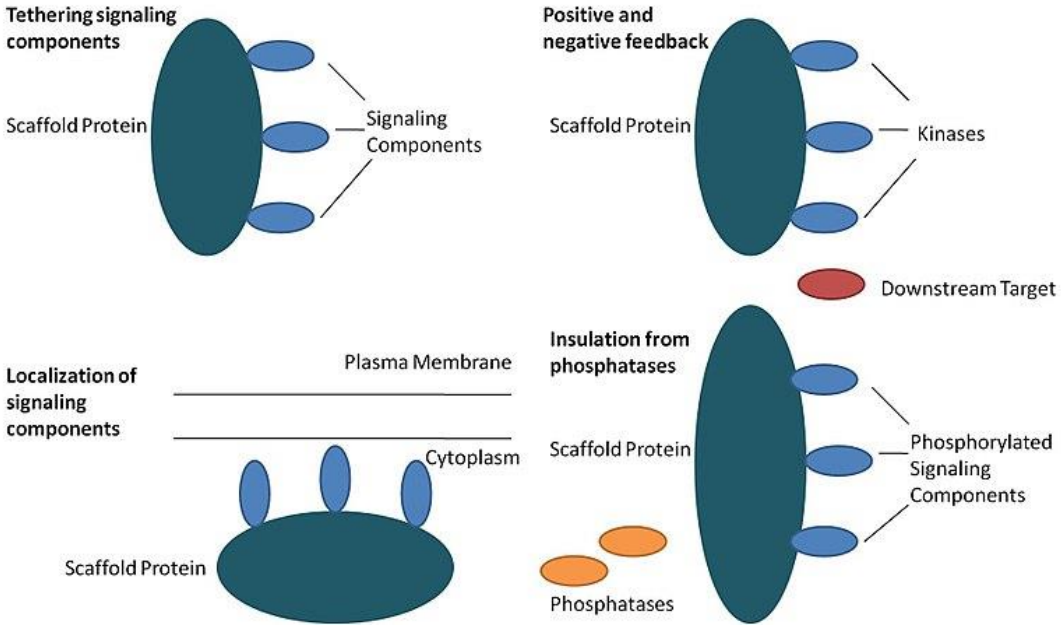
■ Anti Hair loss Patents

4.Medicosbiotech Business domain

D. MCB004 Spider silk protein scaffold (Bio materials)

● Scaffold : Artificial ECM

Artificially made for transplantation and treatment of damaged tissues from diseases and injuries



Essential criteria of scaffold

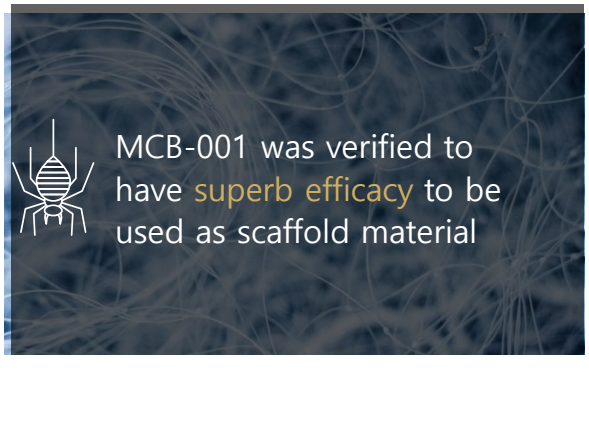
- Must be able to attach and deliver cells
- Must induce cell proliferation and accelerate growth
- Must stimulate cellular response
- Must be quick and efficient with wound healing
- Must be biocompatible and biodegradable, etc

● Verification of Scaffold's Properties

MCB-Spidersilk + Polyethylene glycol diacrylate (PEGDA)

- PEGDA-Spider Silk Cryogel -

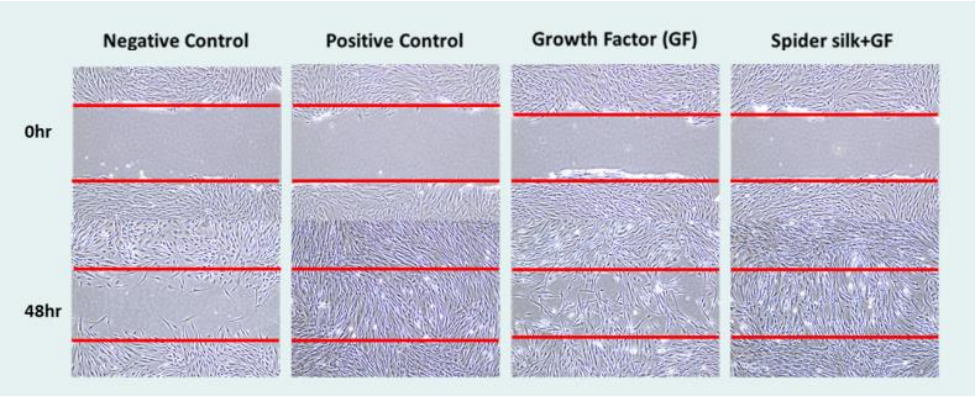
Verified to be useful as scaffold due to its excellent swelling potential



4.Medicosbiotech Business domain

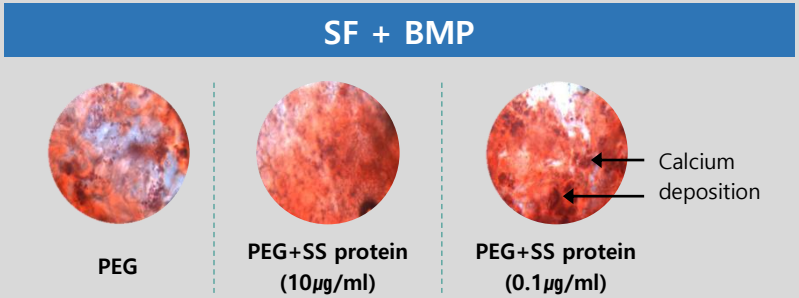
D. MCB004 Spider silk protein scaffold (Bio materials)

● ***In – vitro*** **wound-healing assay**



- Excellent cell regeneration ability confirmed in the test group containing spider silk protein through scratch assay

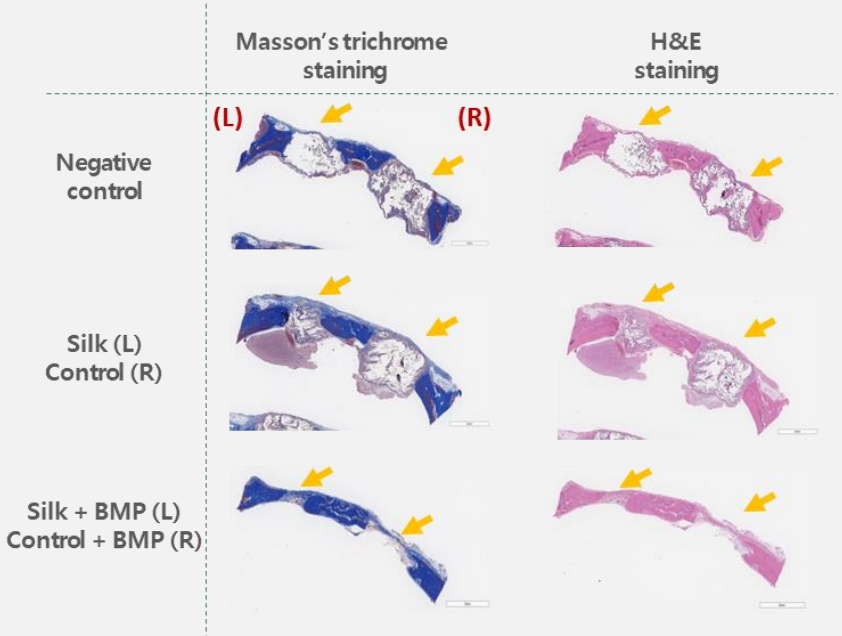
● **Calcium deposition assay – Alizarin red S staining**



- The highest calcium deposition was confirmed in the PEG+spider silk protein group

● ***In – vivo*** **bone regeneration**

· **Active bone, collagen and tissue regeneration**



Rat calvarial defect model

- Confirmation of bone and collagen regeneration through Masson's trichrome staining
- Confirmation of tissue regeneration through H&E staining

5.Medicosbiotech Business domain

Cancer Marker, G-CSF mutein - Background

MCB-CM1

Cancer Marker

Class	Brand	Company	Molecule	Launch Date
G-CSFs	Neupogen	Amgen	Filgrastim	1991
	Neulasta	Amgen	Pegfilgrastim	2002
	Granocyte	Kyowa Hakko Kirin	Filgrastim	1991 (Japan)
	Neu-up	Kyowa Hakko Kirin	Natograstim	1994 (Japan)
	Neutrogin/Granocyte	Chugai	Lenograstim	1991 (Japan) 1994 (Europe)
	Lonquex	Teva	Lipegfilgrastim	2014
GM-CSFs	Leukine	Genzyme	Sargramostim	1991
	Leucomax	Novartis	Molgramostim	1991

- Execution

- Promotes the differentiation and activity of callus cells and induces immune enhancing effect
- Helps to control white blood cell count by preventing or treating neutropenia

- **Target**

  - Cancer patients under chemotherapy, AIDS patients, etc.

- **Kinds**

- Granulocyte-CSF (G-CSF): Increases neutrophil production in the bone marrow
- Granulocyte Macrophage-CSF (GM-CSF): Increases production of eosinophils, macrophages and neutrophils

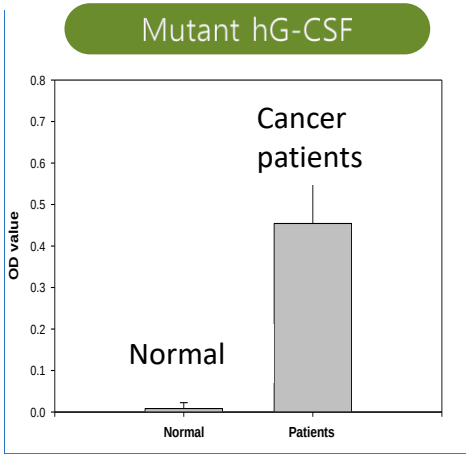
5.Medicosbiotech Business domain

Cancer Marker, G-CSF mutein - Background

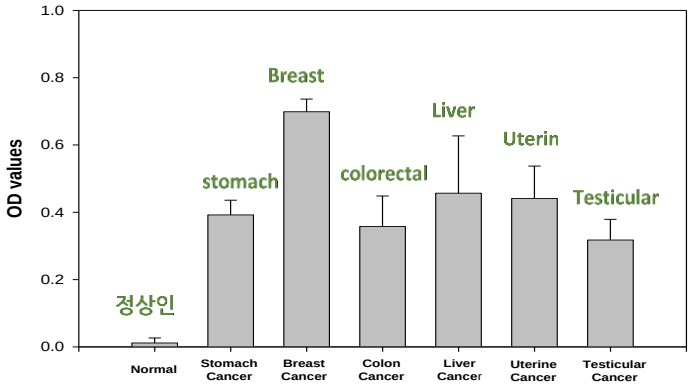
MCB-CM1

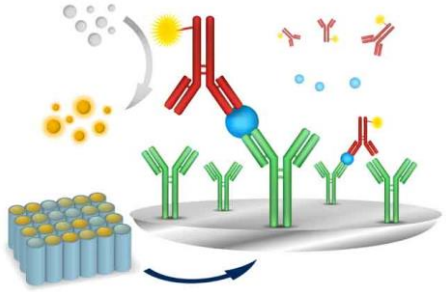
Diagnostic kit using ELISA

Mutant hG-CSF



Mutant hG-CSF





- An ELISA-based kit that can diagnose the fluorescence emitted when the antibody reacts with a sample having an antigen is prepared
- 4-times higher values in cancer patient samples with mutant G-CSF
- As a result of the experiment with the samples obtained from various cancer patients, the diagnosis of each cancer can be confirmed

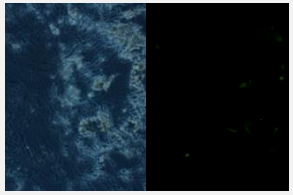
5.Medicosbiotech Business domain

Cancer Marker, G-CSF mutein - Background

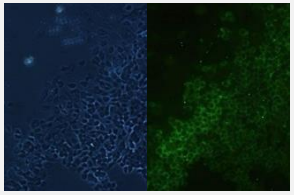
MCB-CM1

MCB-mGCSF

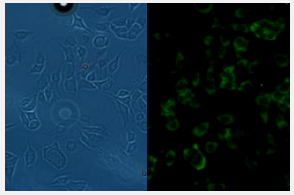
Normal



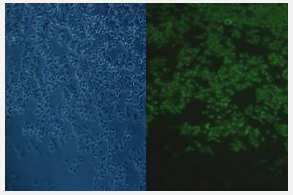
Prostate Cancer (PC3)

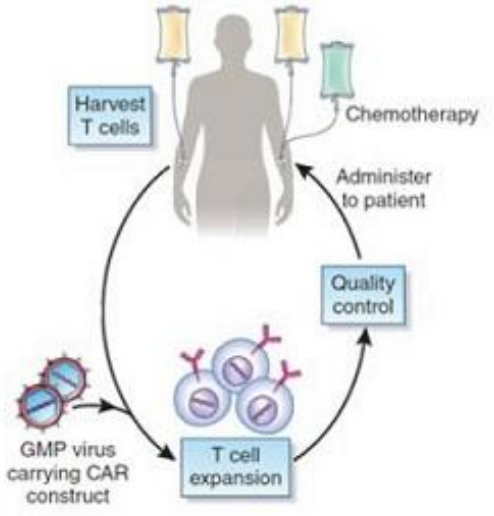


Lung Cancer (NCI1793)



Breast Cancer (MCF7)





- CAR-T Therapeutic Therapy, a cancer treatment, is targeted to cancer cells to kill cancer cells
- The efficiency of CAR-T is low due to immunosuppressive microenvironment including T-cell deactivation factors secreted by tumor tissues
- Because there is no clear antigen for solid tumors, there is no specific targeting for cancer cells,

MedicosBiotech's m-GCSF is a technology that can be treated using mutations found in various cancer cells

5.Medicosbiotech Business domain

Cancer Marker, G-CSF mutein - Background

Granulocyte Colony Stimulating Factor (G-CSF)

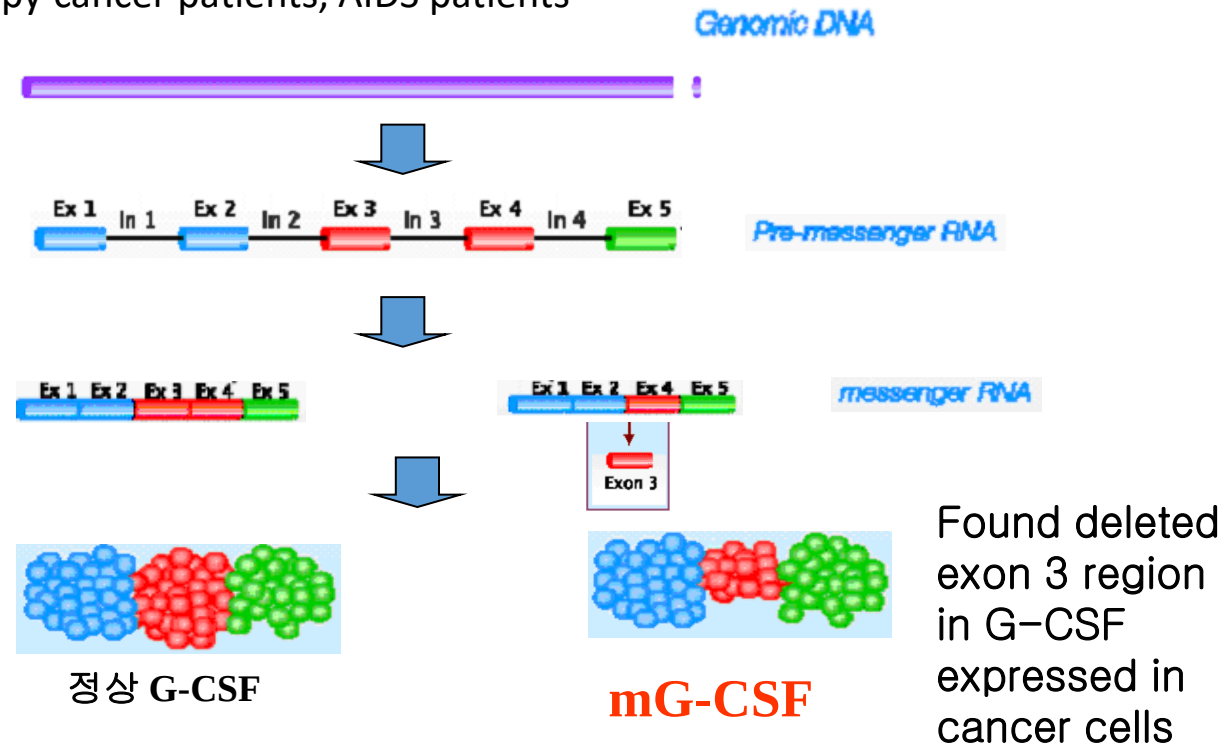
- Glycoprotein known to stimulate bone marrow to produce granulocyte and stem cells
- Treated for chemotherapy cancer patients, AIDS patients

G-CSF Gene

hnRNA expression

Selected exon expressed mRNA

G-CSF protein expression



Found deleted exon 3 region in G-CSF expressed in cancer cells

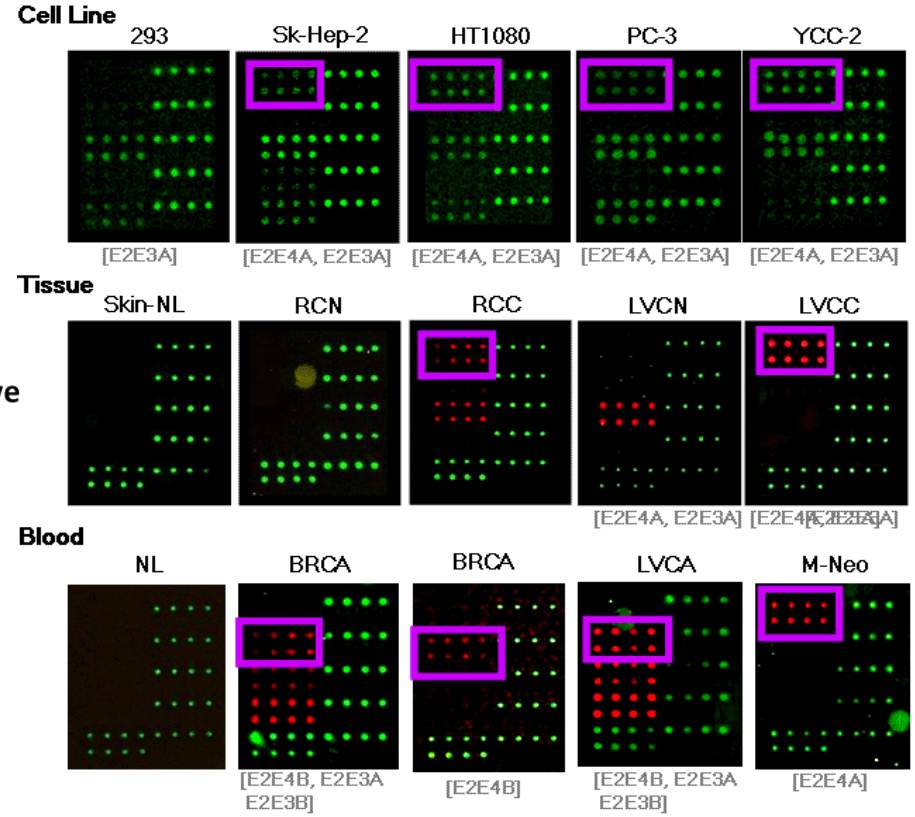
Hypothesized to target exon 3 deleted G-CSF to specifically treat cancer

5.Medicosbiotech Business domain

Cancer Marker, G-CSF mutein - Background

- Production of DNA chip using DNA probe capable of detecting mutant protein in cancer originated samples
- As a result of experiment with various samples, it is confirmed that it can be diagnosed with high frequency
- Melanoma, pancreas, and prostate cancer are 100% diagnosed
- Stomach 89%, liver, lung, kidney, sarcoma more than 70% more accurate diagnosis

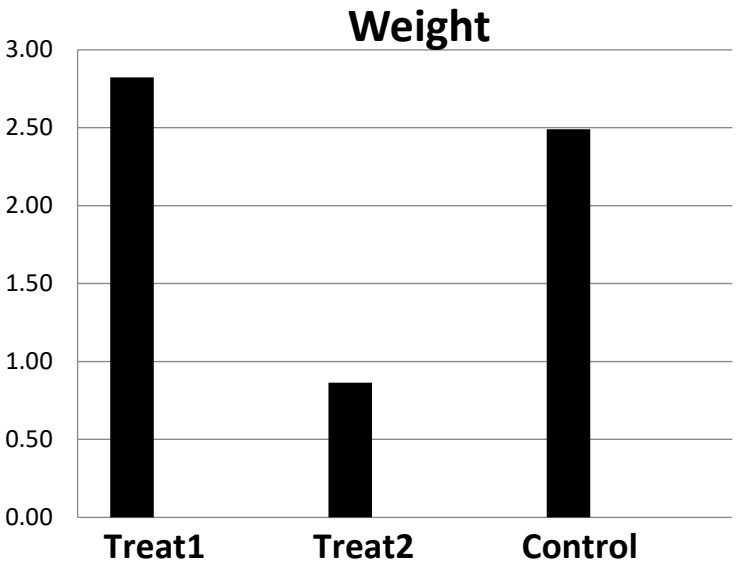
I. G-CSF mutein (Previous results)

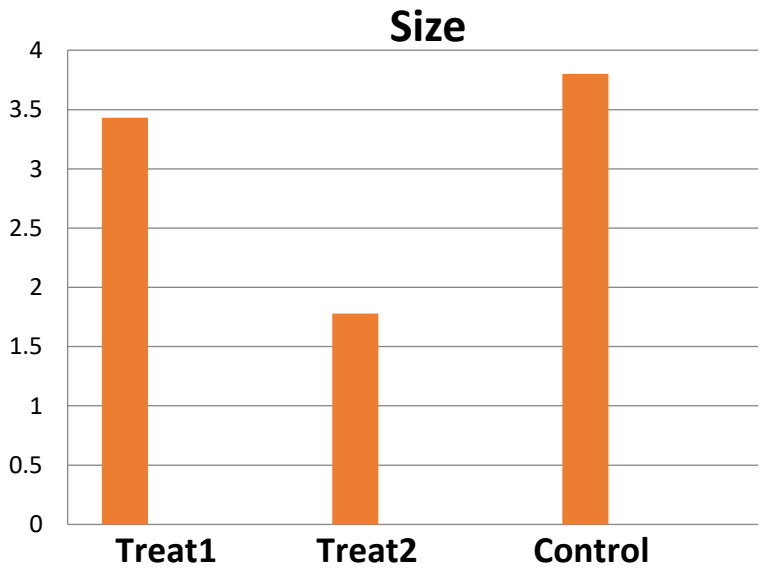


III. G-CSF mutein – Possibility of cancer vaccine

Pilot study for possibility of cancer vaccine development

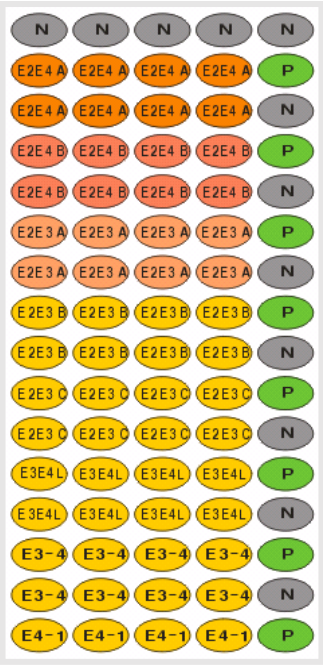
- Confirmation of cancer cell growth inhibition after injection of cancer cells into mice
- Size of the cancer cells decreased when antibody was injected after 1 week compared to those injected with cancer cells and antibody simultaneously
- Expect the target to be further develop into cancer vaccine





5.Medicosbiotech Business domain

Cancer Marker, G-CSF mutein - Background



Splice junction region (exon 2-4)

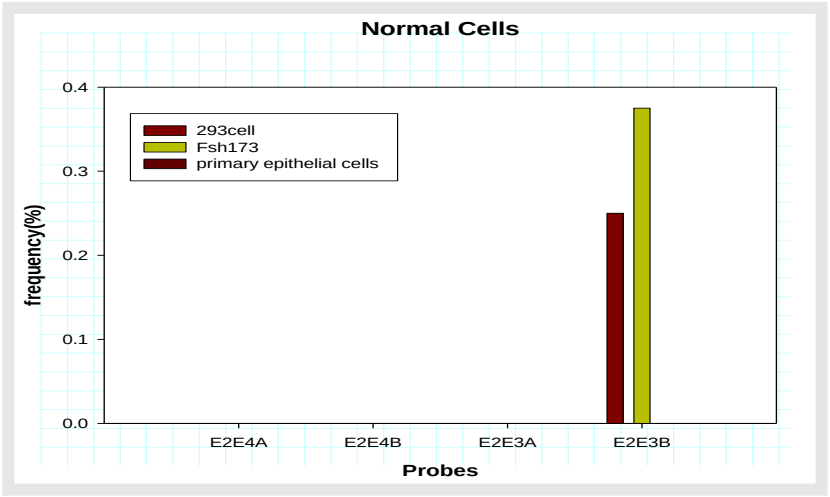
Exon 2-3 junction region

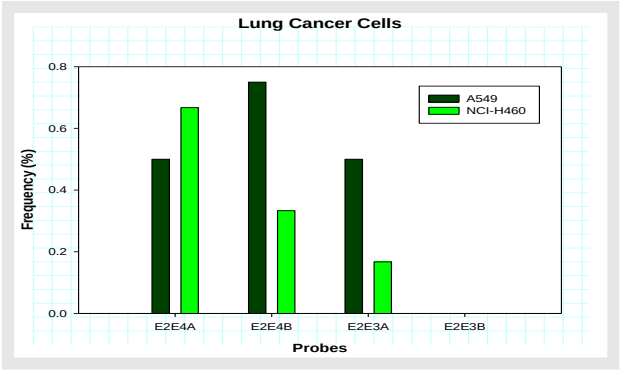
Exon 3-4 junction region

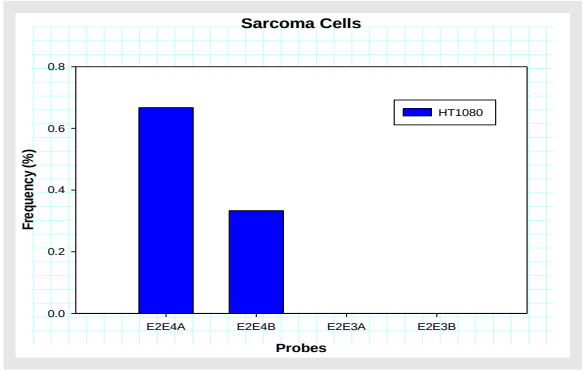
Exon 3 region

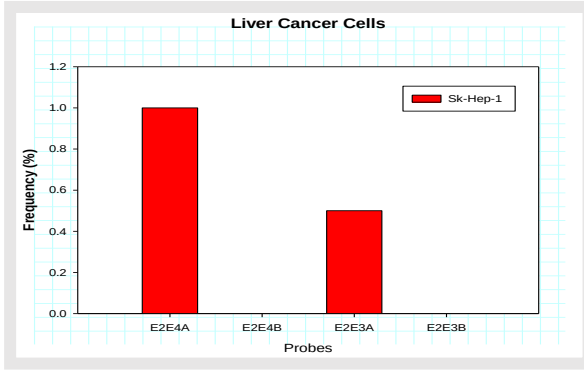
Exon 4 region

I. G-CSF mutein (Previous results)









Designed DNA chip probe to detect specific region of G-CSF

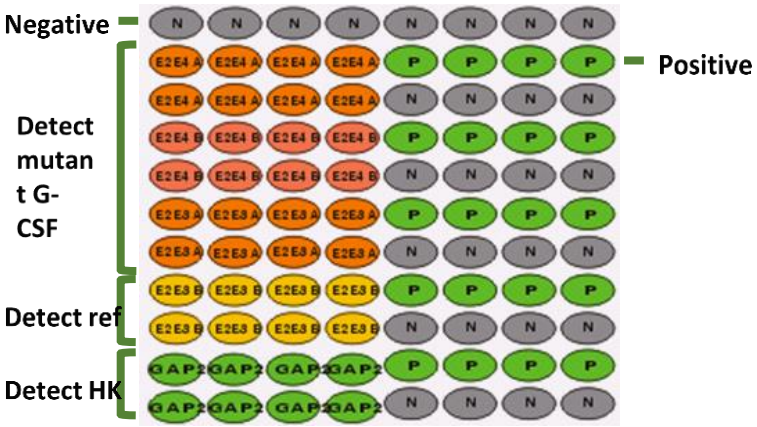
→ Found over 95% detection rate for liver, sarcoma, lung and over 80% detection rate for colon and stomach

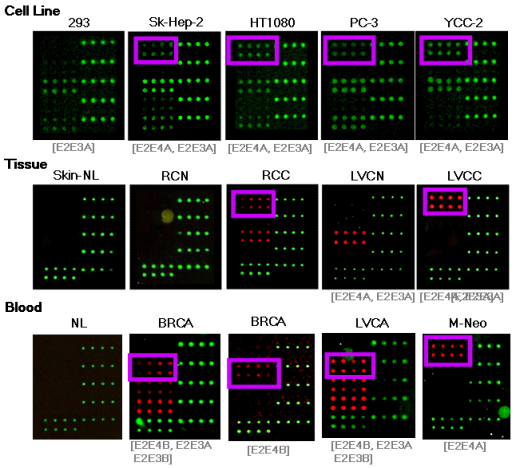
5.Medicosbiotech Business domain

Cancer Marker, G-CSF mutein - Background

MCB-CM1

Diagnostic kit using DNA chip





- Production of DNA chip using DNA probe capable of detecting Native G-CSF and mutant G-CSF
- As a result of experiment with various samples, it is confirmed that it can be diagnosed with high frequency
- Melanoma, pancreas, and prostate cancer are 100% diagnosed
- Stomach 89%, liver, lung, kidney, sarcoma more than 70% more accurate diagnosis

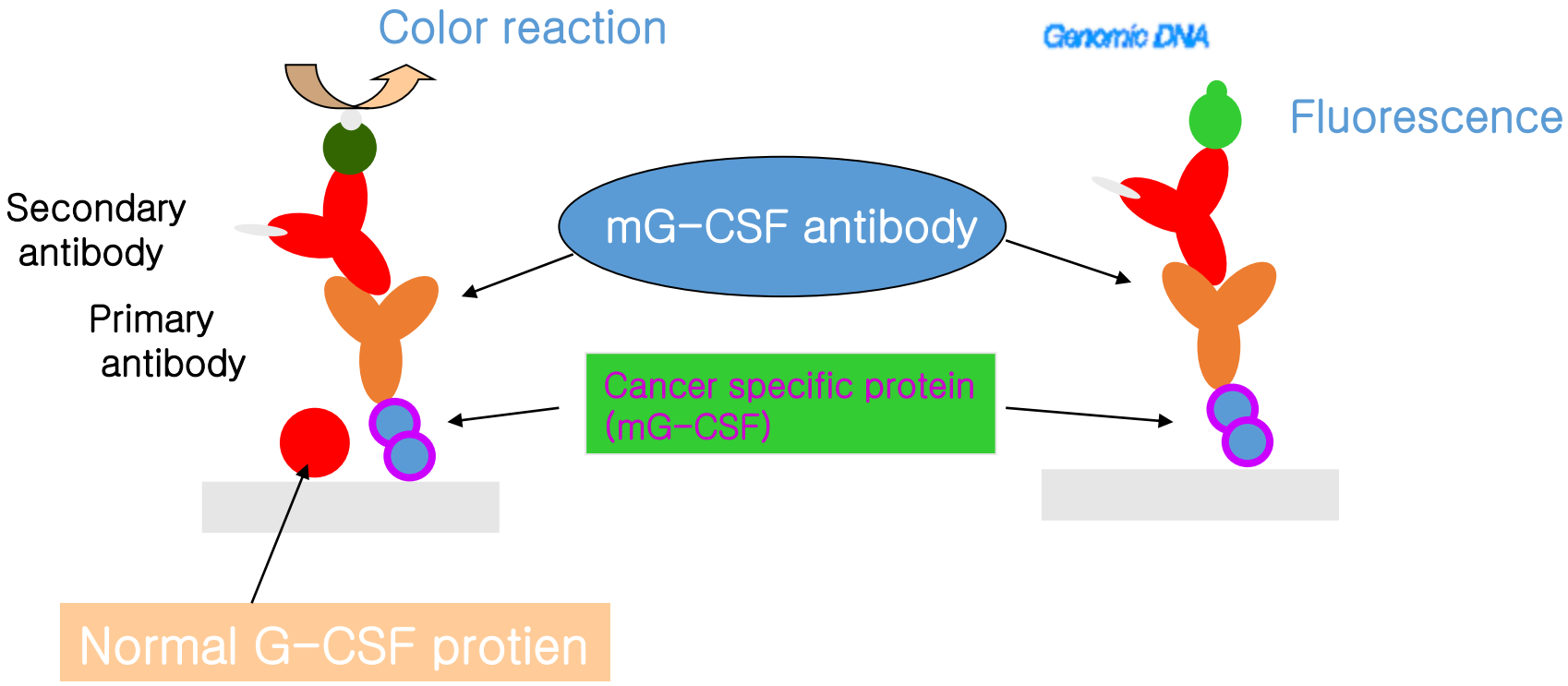
5.Medicosbiotech Business domain

Cancer Marker, G-CSF mutein - Background

I. G-CSF mutein (Previous results)

Blood test through ELISA

- ELISA detection using G-CSF targeting antibody to confirm DNA chip data

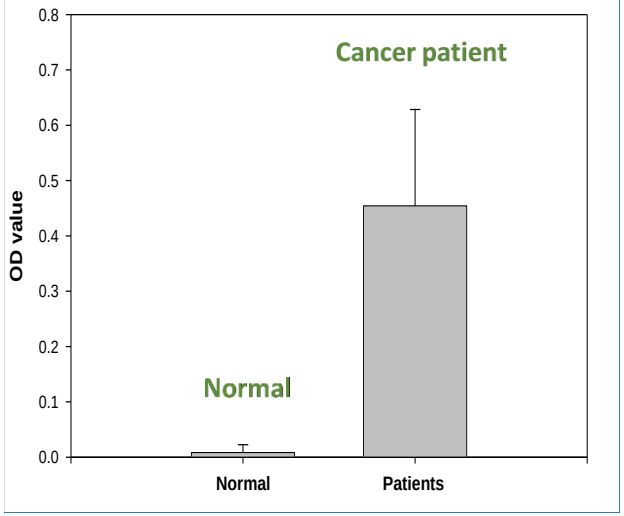


5.Medicosbiotech Business domain

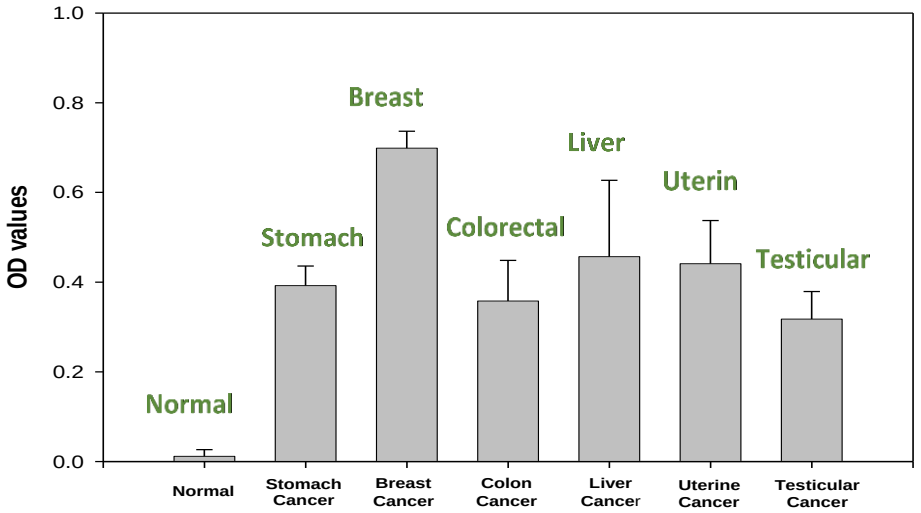
Cancer Marker, G-CSF mutein - Background

I. G-CSF mutein (Previous results - ELISA)

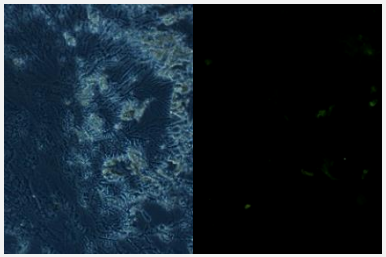
Mutant Protein



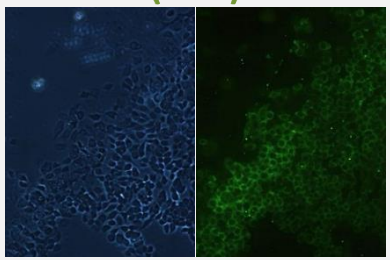
Mutant Protein



Normal



Prostate Cancer (PC3)



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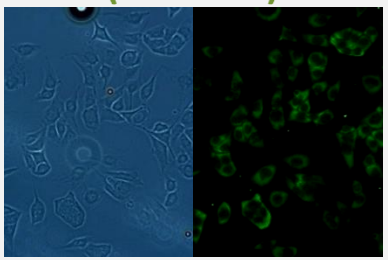
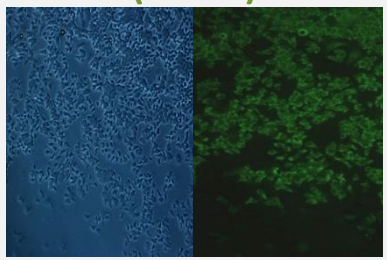


Breast Cancer (MCF7)

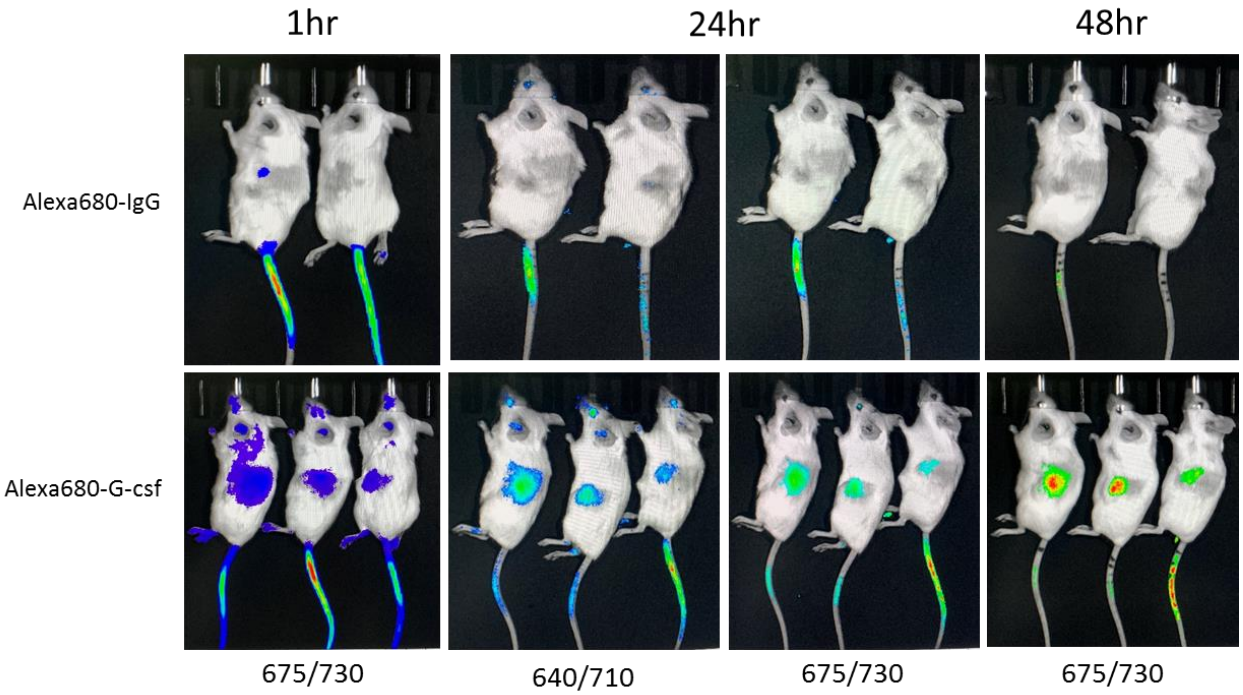


Cancer diagnosis possible through various cancer tissues from patients

II. G-CSF mutein – Current Results

In-vivo experiment through G-CSF mutein specific antibody

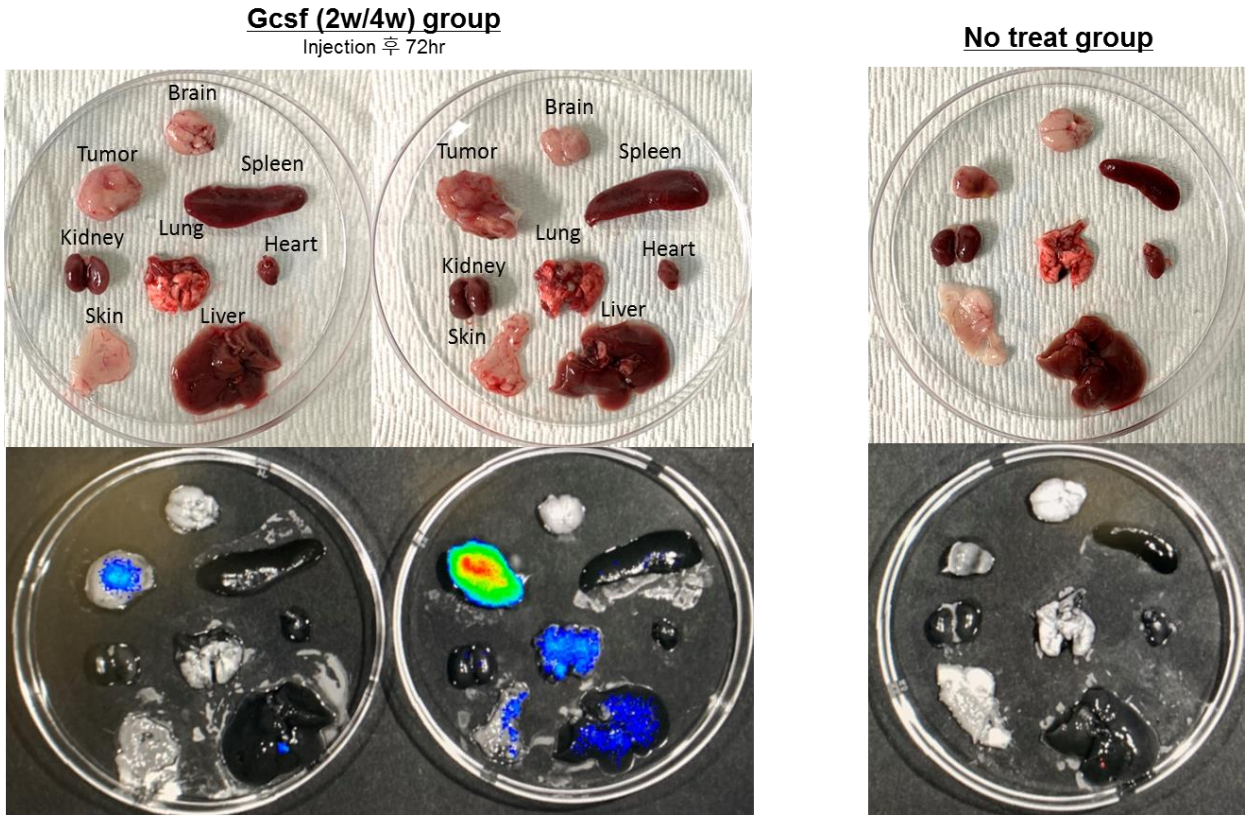
- Created polyclonal antibody using G-CSF protein (exon 3 deleted)
- Inserted antibody to mouse model with breast cancer (4T1 cell) to confirm detection
- Used Alexa680 fluorescence marker to localize the detection



II. G-CSF mutein – Current Results

In-vivo experiment through G-CSF mutein specific antibody

- Confirmed additional metastasis after 72 hrs of antibody injection
- Fluorescence detected in other metastasized tissues as well

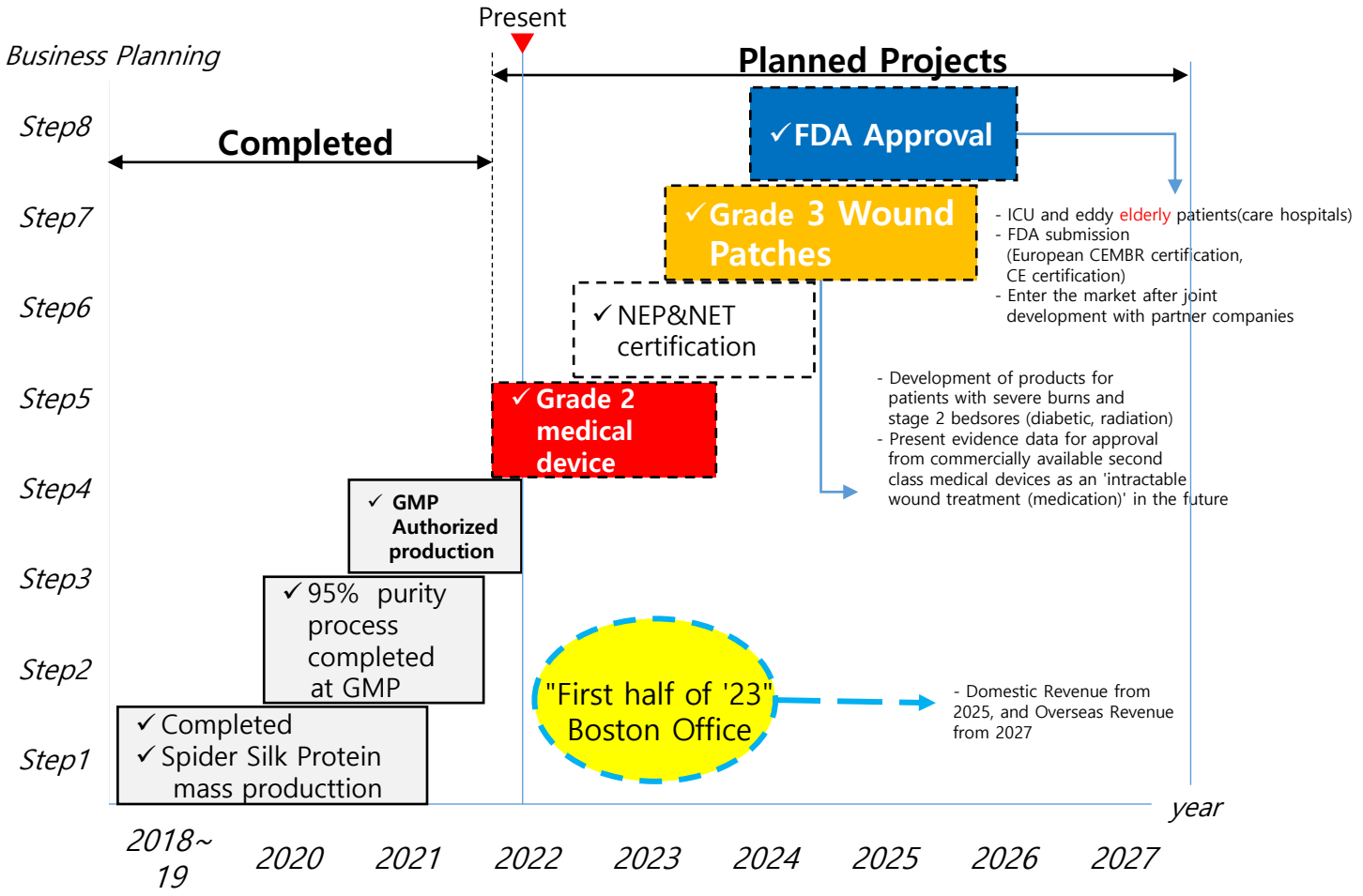


6. Commercialization Schedule

Wound Healing Conservative Schedule

Medicos Biotech

Wound Healing **Roadmap**



6. Commercialization Schedule

Wound Healing Conservative Schedule

Medicos Biotech

Wound Healing **Roadmap**

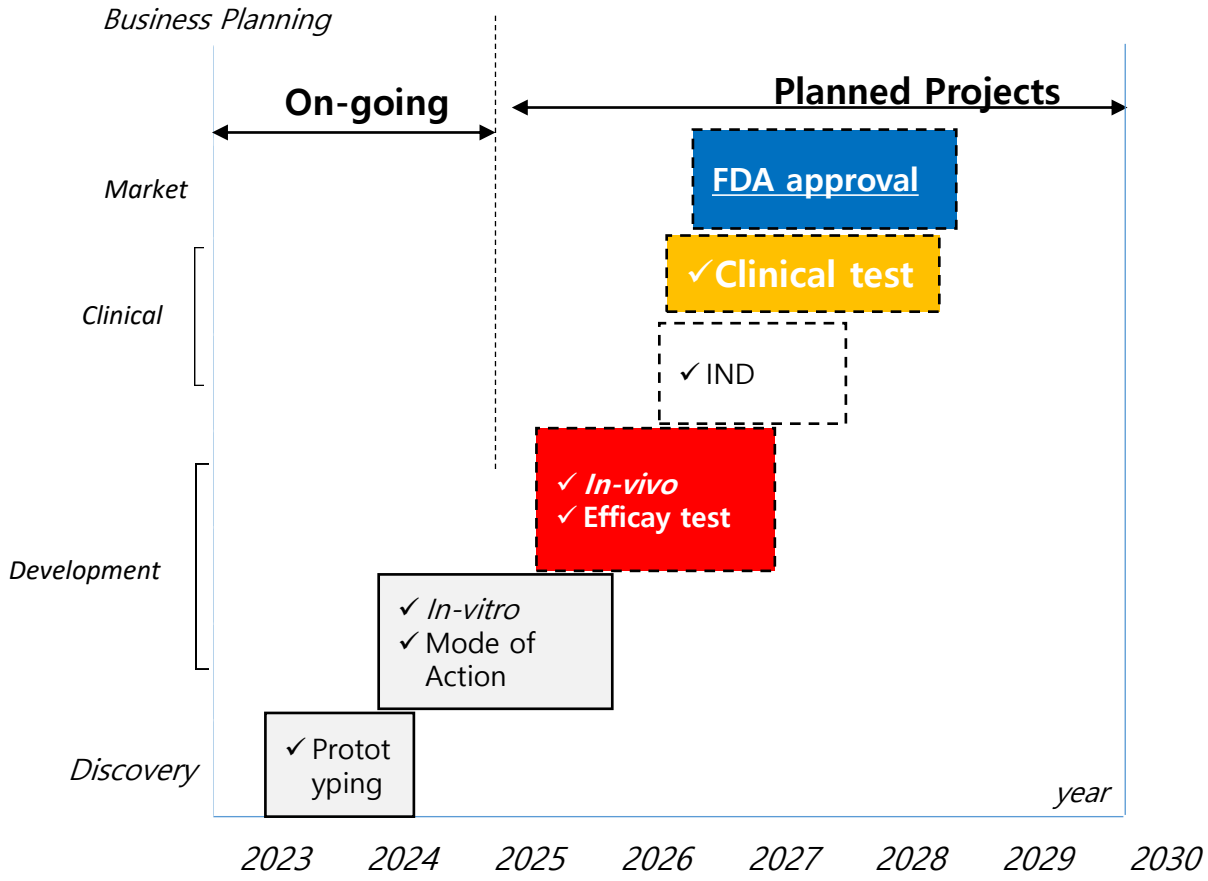
Program`	Indication	Discovery	Development		Clinical Test for FDA	Market	Collaborator
			Class 2	Class 3			
Chronic Wound **Healing Patch**	Spider Silk Protein	Proto type 6 months	Schedule to Release 2nd half of 2023	Clinical test required to have class 3	Single clinical test : 2 years	Release Product in 6 months after FDA	

	Basic cost	Time	USD_Mil
Lab Operation	2 Mil / Year	5 year	10
Proto typing	0.5 Mil		0,5
test for Class 2	1 Mil		1
Clinical Test for class 3 in Korea	2 Mil	2 year	4
US Operation	5	3 Years	15
Clinical Test	10 Mil	1	10
CRO/FDA	3 Mil	1	3
Total Cost USD Mil			43

6. Commercialization Schedule

Cancer Marker Conservative Schedule – Detection Kit

Cancer peptide **Roadmap**



6. Commercialization Schedule

Cancer Marker Conservative Schedule – Detection Kit

Medicos Biotech

Cancer peptide **Roadmap**

Program`	Indication	Discovery	Development		Clinical Test	Market	Collaborator
			In-vitro	In-vivo			
Cancer peptide	Contrast agent	Proto type 6 months	Identification of MoA 6 months	Preclinical efficacy test, Preparing technical documents 1 year	Phase 1 : 1 years Phase 2 : 2 years Phase 3 : 2 years	Release Product in 6 months after FDA	

	Basic cost	Time	USD_Mil
Lab Operation	2 Mil / Year	5year	20
Proto typing	0.5 Mil		0,5
Efficacy test	1 Mil		1
IND/CRO	2 Mil	3 year	10
Clinical Test 1	2 Mil		2
Clinical Test 2	5 Mil		5
Clinical Test 3	10 Mil		10
Total Cost_Mil USD			48

6. Commercialization Schedule

6 product Conservative Schedule

Medicos Biotech

Spider Silk Product **Roadmap (Conservative)**

Product		Year to local Commercialization	Year to Global(US) Commercialization	Total Cost(USD) to Commercialization
Chronic Wound Patch	Medical/ Bio materials	1 year	4year	43 Mil
Spinal Cord		8 Years	11 Years	200 Mil
Scaff Fold		5 years	6 years	5 Mil
Cosmetic Ingredient	**Skin care/ Hair**	**Commercialized confirmed**	**Commercialized confirmed**	Marketing Investment 5 Mil
Cosmetic		**Commercialized confirmed**	**Commercialized confirmed**	Marketing Investment 5 Mil
Cancer Marker	-	8	10	48 Mil
Fabric/Textile	Textile engineering	8	10	100 Mil

*As it is a situation where US impressions are made after clinical trials in Korea, Year to Global includes the domestic development period. This is a conservative estimation period, and if large-scale funding is available in the beginning, the commercialization period can be shortened by proceeding with the US FDA.

*Cosmetics and raw materials have been commercialized already, so hair products (Dr.Graft) are scheduled to be sold starting this year, and mass production and sales of skin care cosmetics are possible from the second half of this year or next year if marketing costs are met.

*Fabric It is not an exact figure, but it was written with reference to Spiber information details. It is also considered that the commercialization schedule can be shortened depending on the funding schedule.

State of raw materials for **each Applications**

Recombinant spider silk protein is produced through environmentally friendly process using bacterial fermentation. No animal farming or use of animal related sources are involved in the process, but only use plant derived glucose as the sole carbon source during its production.
In addition, raw materials used during protein purification are environmentally friendly, especially ammonium sulfate is used as a fertilizers for nutrient source to plants.

Application	Form of spider silk protein applied
Chronic wound healing	**Liquid form**
Spinal cord injury treatment	**Fabricated gel form**
Biomaterial (Scaffold)	**Fabricated gel form**
Cosmetics	**Powder form**
Fabric/textile engineering	**Powder form**

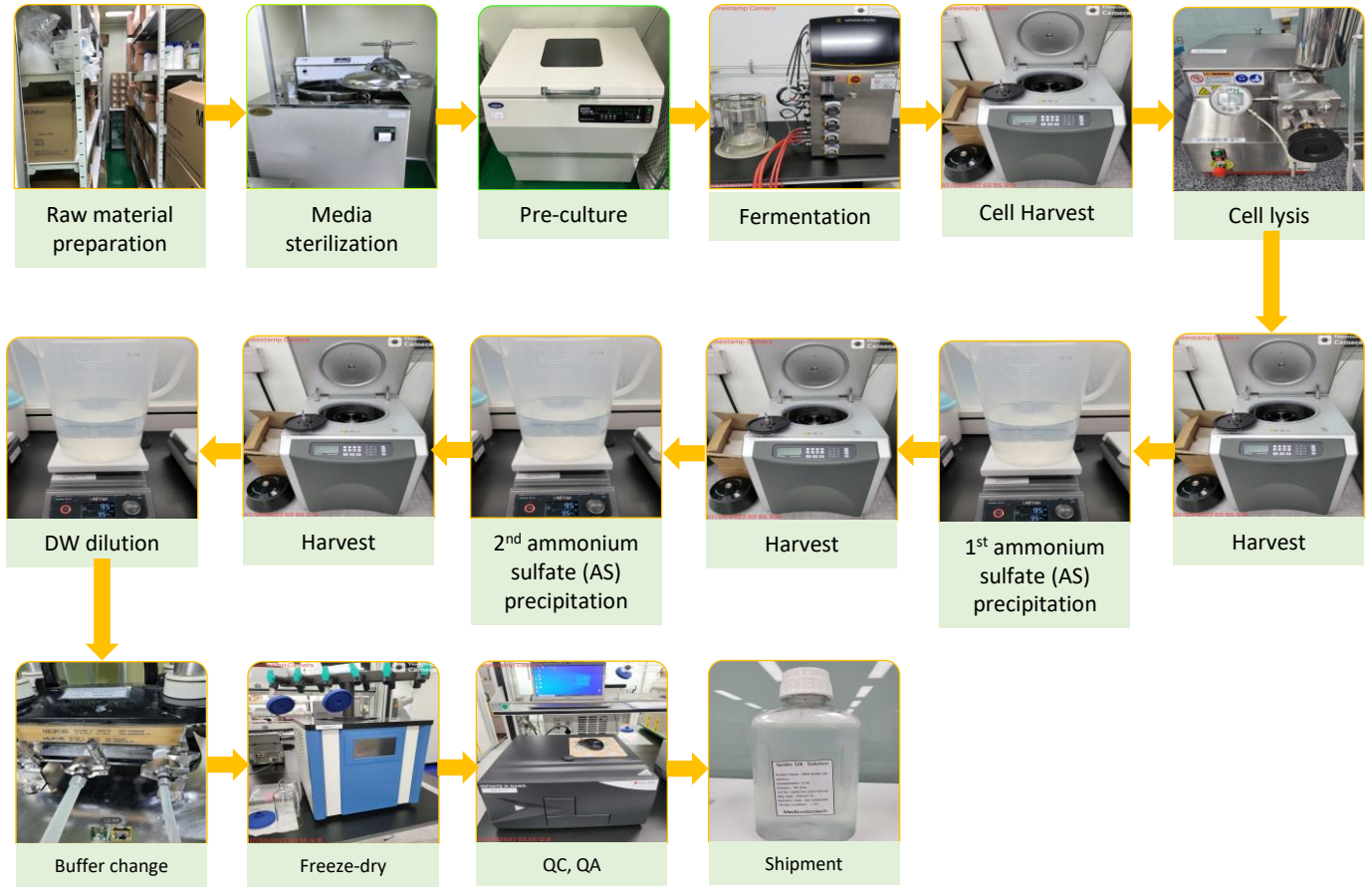
6. Commercialization Schedule

Types of raw materials for manufacturing flow chart

Medicos Biotech

State of raw materials for **Manufacturing flow**

Manufacturing flow chart



6. Commercialization Schedule

ESG Agenda (Environment)

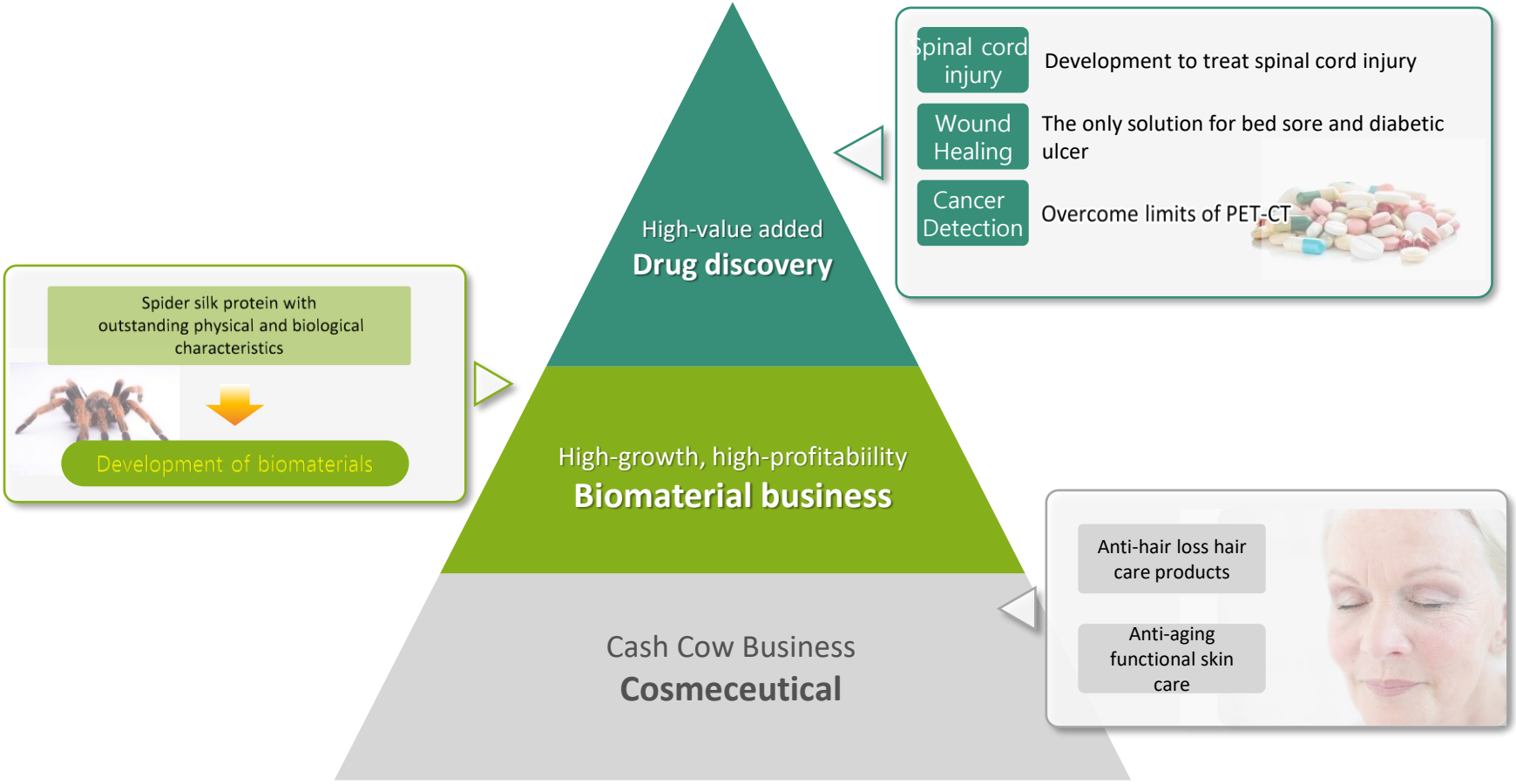
Medicos Biotech

The product meets eco-friendly requirements in the entire process from raw material production to manufacturing and disposal.

Product	In Detailed
Chronic Wound Patch **Spinal Cord** **Scaff Fold**	In medical applications such as wound treatment, biomaterials, and spinal injury treatment, spider silk has **excellent biocompatibility**, making it a suitable fiber for making surgical threads and artificial organs such as artificial hearts and artificial blood vessels.
Cosmetic Ingredient/Cosmetic	Compared to cosmetic competitors, if you look at the ingredients of the product, less chemical additives are used due to the use of spider silk raw materials.
Fabric/Textile	• In particular, in the case of textiles for industrial/apparel use and petrochemicals where **synthetic resins** such as nylon and polyester are used, raw materials themselves are derived from petrochemicals. • It consumes **enormous heat, electricity and water required** for melting in the manufacturing and production process. It causes a large amount of carbon emissions in the manufacturing process, such as the yarn process. • When consumers discard the product, there is a problem **that petrochemical yarn does not rot well.** ➔ **Using eco-friendly spider silk raw materials, heat and electricity are hardly needed, so only water is required, so carbon emissions are absolutely low in the manufacturing process.** In other words, the entire process of production, manufacturing is much closer to eco-friendly requirements. ➔ Since spider silk is a fiber obtained from natural ingredients, it has eco-friendly characteristics because it is **easily decomposed by microorganisms when buried in the ground after use.**

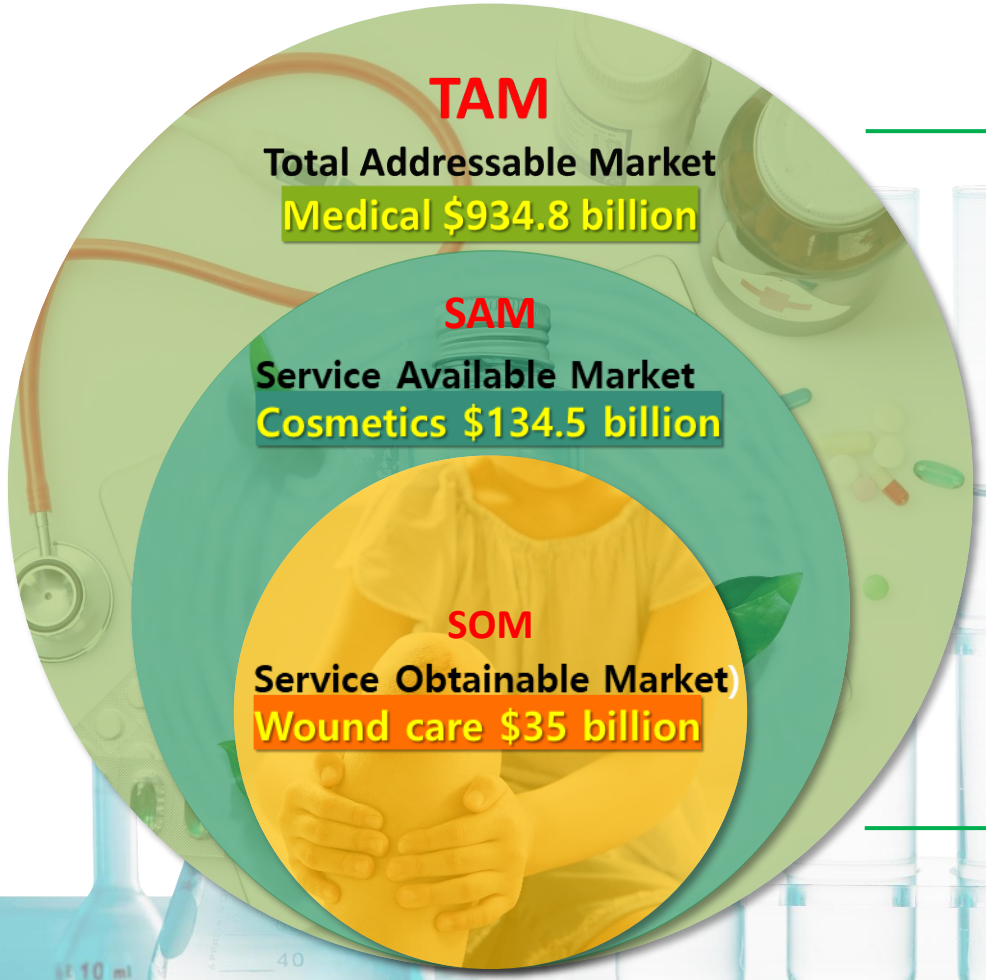
Medical Cure to Care
Technology applicable to various fields

We focus on providing efficient medical services to spinal patients and patients requiring wound care, and solving the public's demand for diagnostic services for early cancer prevention.



7. Company Organization

Market Size, and How big we can be!



(Spinal cord injury, Biomaterial, Cosmeceutical, Cancer related peptide, BBB penetration)
Excluding the eco-friendly textile market in the past, the total size of the remaining 5 markets is 139.5B, and our future value is considered to be at least 1/10, 13.9 B USD.

Total Addressable Market

SPAC Listing in USA/ Hongkong/ Singapore

- **Clinical test (Wound healing and Cancer marker) and R&D**
- **Eco-textile engineering entering study**

Served Available Market

Pre-IPO Investment

- **Governance restructuring**
- **R&D Improvement**
- **Marketing of Cosmetic application**

Serviceable Obtainable Market

7. Company Organization

Business Area and Specific Market Size

Medicos Biotech

Business area regarding specific R&D project

-	Spinal cord injury	Biomaterial	Cosmeceutical	Cancer related peptide	BBB penetration
Core competitive-ness and development status	· Treatment for spinal cord injury · Non-clinical testing showed outstanding results within 28 days · Neurofilament regeneration confirmed	· Spider silk protein possess outstanding physical characteristics · Also, biodegradable and biocompatible material · Development of scaffold, suture, bone regeneration scaffold possible using spider silk protein	· Releases hair-care product for scalp regeneration (anti-hair loss shampoo and tonic) · Functional cosmetics for anti-aging under development	· Common sequence found in cancer cells and peptide to control cancer cell growth discovered · Non-clinical testing showed control of cancer cells using the peptide · Development of cancer detection kit possible using the peptide/antibody	· Discovered BBB penetration possible drug (opening of BBB) · Non-clinical testing showed albumin passing through the BBB with found drug
Target market size (world)	**$2.3 billion** (2017)	**$83.9 billion** (2018)	**$49.5 billion** (2018)	**$4.1 billion** (2018)	**$500 million** (2016)
CAGR	**3.7 %**	**14.7 %**	**7.5 %**	**6.7 %**	**25.0 %**

-	Size of the eco-friendly textile market (Definition and scope of eco-friendly textiles
Core competitive-ness and development status	Eco-friendly fibers, a core material of the low-carbon Green New Deal, are recycled fibers, biodegradable/biomass fibers, natural fibers, and minimization of environmental pollution in order to minimize global environmental destruction such as resource depletion, environmental pollution, and global warming. It refers to sustainable textile materials and products that include manufacturing processes and lead to neutrality.
Target market size	**$69.4 billion** (Potential World Market, 2025)
CAGR	**9.2 %**

7. Company Organization

Team & Advisory (Mr. Sang Yup, Lee - **Co-founder** of Medicos-biotech, KAIST)

Distinguished Professor, Senior Vice President for Research, KAIST
Dept. of Chemical & Biomolecular Engineering, KAIST
•Head, Metabolic and Biomolecular Engineering National Research Laboratory, Director of BioProcess Engineering Research Center, Director. Bionformatics Research Center (Dept. Chemical & Biomolecular Engineering, KAIST)

Research Interest
•Metabolic Engineering, Systems biology/biotechnology, Synthetic biology, Biochemical engineering, Nanobiotechnology, Industrial biotechnology

He is a world-renowned scholar in the field of intestinal microbiome.

Academy Membership/Fellowship
2005 Fellow of the American Academy of Microbiology, USA
2007 Fellow of the Korean Academy of Science and Technology, Korea
2007 Fellow of the American Association for the Advancement of Science, USA
2010 Fellow of the Society for Industrial Microbiology, USA
2010 International Member of the National Academy of Engineering, USA
2011 Fellow of the National Academy of Engineering Korea, Korea
2012 Fellow of the American Institute of Chemical Engineers, USA
2013 Fellow of the American Institute of Medical and Biological Engineering, USA
2013 Fellow of the World Academy of Sciences (TWAS), Italy
2017 International Member of the National Academy of Sciences, USA
2017 Fellow of the National Academy of Inventors, USA
2021 Foreign Member of the Royal Society, UK
2023 Fellow of the Asia-Pacific Artificial Intelligence Association (AAIA)

EDUCATION
1986 (B.S.) Dept. of Chemical Engineering, Seoul National University, Seoul, Korea
1987 (M.S.) Dept. of Chemical Engineering, Northwestern Univ., Evanston, IL, U.S.A
1991 (Ph.D.) Dept. of Chemical Engineering, Northwestern Univ., Evanston, IL, U.S.A.

7. Company Organization

Team & Advisory (Mr. Sang Yup, Lee - Co-founder of Medicos-biotech, KAIST)

Academic Position

1994-1996, Assistant Professor, Dept. Chemical Engineering, KAIST
1997-2002, Associate Professor, Dept. Chemical Engineering, KAIST
2000-present, Director, BioProcess Engineering Research Center, KAIST
2001-present, Director, BioInformatics Research Center, KAIST
2002-present, Professor, Dept. Chemical & Biomolecular Engineering, KAIST
2003-2013, Adjunct Professor, Dept. Bio and Brain Engineering, KAIST
2004-2010, LG Chem Chair Professor
2004-present, Honorary Professor of University of Queensland
2005-present, Adjunct Professor, Australian Institute of Bioengineering and Nanotehnology
2005-2012, Special Advisor, Bioprocessing Technology Institute, Biopolis, Singapore
2006-2012, Co-director, KI for the BioCentury, KAIST
2007-present, KAIST Distinguished Professor
2007-present, Director, Center for Systems and Synthetic Biotechnology, KAIST
2008-2013, Adjunct Professor, Dept. of Biological Sciences, KAIST
2008-2013, Dean (Founding Dean), College of Life Science and Bioengineering, KAIST
2012-present, Honorary Professor, Institute of Microbiology, Chinese Academy of Sciences, China
2013-2015, Dean, KAIST Institutes, KAIST
2013-present, Scientific Director, New Bioactive Compounds Section, Novo Nordisk Center for Biosustainability, Technical University of Denmark
2013-present, Advisory Professor, Shanghai Jiao Tong University (SJTU), China
2013-present, Professor, Moon Soul Graduate School of Future Strategy, KAIST
2014.9-present, Honorary Professor, Wuhan University, Wuhan, China
2014.9-present, Honorary Professor, Hubei University of Technology, Wuhan, China
2014.10-present, Honorary Professor, Beijing University of Chemical Technology, Beijing, China
2017.3-2021.2, Dean, KAIST Institutes, KAIST
2017.3-present, Director, KI-Space, KAIST
2017.7-2021, Director, the Fourth Industrial Revolution Intelligence Center, KAIST
2017.10-present, Honorary Professor, Jiangnan University, China
2017.10-present, Honorary Professor, Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences, China.

7. Company Organization

Team & Advisory (Mr. Sang Yup, Lee – KAIST. Co-founder of Medicos-biotech Co.)

Academic Position

2019.3-present, Honorary Professor, Ocean University of China, China
2019-2020, Honorary Chair Professor, National Tsing Hua University, Hsinchu, Taiwan
2019-present, Director, Korea Policy Center for the Fourth Industrial Revolution, KAIST
2020, Vice President, Korean Society for Biotechnology and Bioengineering, Korea
2021.3-present, Senior Vice President for Research, KAIST, Korea
2023, President, Korean Society for Biotechnology and Bioengineering, Korea
2023.4-present, Chairman, Board of Trustees, KAIST MG Community Credit Cooperatives, Korea

Research and Skill HIGHLIGHTS

Research Activity (as of June, 2023)

Journal paper: 727 papers published
Proceedings paper: 156 papers published
Conference presentations/ Abstracts: 2827 papers
Patents : 802 including 545 international patents
Books/Books Edited : 91 books
Essays and Editorials: 163 essays
Plenary/Keynote/Invited Lectures/Seminars : 625 presentations
Newspaper/TV/Scientific News/Magazine: 5391 times

7. Company Organization

Team & Advisory (Mr. Won-Min, YOO – MD Phd. **Co-founder** of Medicos-biotech Co.)

SUMMARY OF CAREER
［2008 ~ Present］ DM plastic surgery clinic
［2003 ~ 2004］ Visiting Professor Research Scholar in Cancer Center of Yale Medical School in US
［2002 ~ 2008］ Chief Professor of Plastic Surgery Dept. of Gangnam Severance Hospital
［1996 ~ 2008］ Professor of the Department of Plastic Surgery of Medical School of Yonsei University
［2000］ Foreign Young Surgeon Scholarship of American Society of Plastic and Reconstructive Surgeons

He is one of Korea's leading surgeons (Surgical operations).

Research and Skill HIGHLIGHTS

◈ Wound Healing: Incurable wound (high grade pressure sore. DM foot ulcer, venous ulcer)
Scarless wound healing(keloid)
◈ Spinal cord injury: paralysis
◈ Cancer: Cancer marker and Cancer vaccine
◈ Brain: BBB(blood brain barrier) and Alzheimer Tx
◈［2003-2004］ Visiting professor of Cancer Center of Medical School of Yale University in US
- Cancer marker and Scarless Wound Healing research
◈Operated Reconstruction of Incurable Wound: Pressure sore, DM foot ulcer and venous ulcer etc over 1000 cases
◈Operated Antiaging: facelifts over 5000 cases for 10 years

EDUCATION

［1984-1988］ Yonsei Medical School graduate
［1988-1989］ Yonsei Severance Hospital Medical Gangnam medical practitioners
［1992-1996］ Yonsei Gangnam Severance Hospital Plastic Surgery Dept. Residents

7. Company Organization

Team & Advisory (Mr. Yoo, Won-Min. Co-founder of Medicos-biotech, MD Phd)

PROFESSIONAL EXPERIENCES

Regular member at The Korean Society of Plastic and Reconstructive Surgeons,
Regular member at the Korean Society for Aesthetic Plastic Surgery,
Regular member at Korean Cleft Palate-Craniofacial Association,
Member of Korean skull base society, Member of Jaw facial contour research society,
Member of facial trauma research society,
Member of Fat Surgery research society

Articles of Journals

J Craniofac Surg. 2009 “Gossypiboma after mandibular contouring surgery.”
Wound Repair Regen. 2009 “The effect of botulinum toxin A on skin flap survival in rats.”
Mol Cell Probes. 2009 “High-throughput identification of clinically important bacterial pathogens using DNA microarray.”
J Plast Reconstr Aesthet Surg. 2010 “Palmar Crease-plasty.”
Plast Reconstr Surg. 2008 “Infrabrow excision blepharoplasty: applications and outcomes in upper blepharoplasty in Asian women.”
Plast Reconstr Surg. 2009 “Inferior gluteal artery perforator flap: a viable alternative for ischial pressure sores.”
Plast Reconstr Surg. 2007 “Medial epicanthoplasty using the skin redraping method.”
Br J Ophthalmol. 2007 “Development of a DNA chip for the diagnosis of the most common corneal dystrophies caused by mutations in the betaigh3 gene.”
J Plast Reconstr Aesthet Surg. 2006 “Endoscopy-assisted ultrasonic surgical aspiration of axillary osmidrosis: a retrospective review of 896 consecutive patients from 1998 to 2004.”
Mol Cell Probes. 2006 “DNA microarray-based detection of nosocomial pathogenic Pseudomonas aeruginosa and Acinetobacter baumannii.”
Protein Expr Purif. 2004 “Constitutive production of human leptin by fed-batch culture of recombinant rpoS- Escherichia coli.”
Plast Reconstr Surg. 2004 “Minimally invasive localization technique: needle fixation of subcutaneous lipoma.”
Plast Reconstr Surg. 2002 “Root z-epicanthoplasty in asian eyelids.”
Br J Plast Surg. 2000 “Ultrasonic surgical aspiration with endoscopic confirmation for osmidrosis.”
Plast Reconstr Surg. 1999 “An analysis of 123 temporoparietal fascial flaps: anatomic and clinical considerations in total auricular reconstruction.”

7. Company Organization

Team & Advisory (KAIST, Medical Doctors)

Medicos Biotech

The Team

Pic	Name		Carrier
	**JiYoung Park, Ph.D**	Researcher	• BA, Seoul National Univ • PhD, KAIST • Scaffold
	**Hemoon Woo**	Researcher	• KAIST research Institution • Cha Meditech • Prestigebio
	**Deok Hyun Na**	Researcher	• Dong Kook University (M.S.) • CEFO Bio Researcher
	**Sung Hoon Park**	Researcher	• CJ Cheiljedang Researcher • KAIST Global Frontier Researcher • Korea Institute of Industrial Technology
	**KiYul Park**	**Admin**	• BA, Dankook Univ • Yellow Bloon Travel • Online Tour • TideSquare
	**HyungSeung Park**	**Admin**	• BA, Jangang Univ • Eland Finance team

Advisory Board

Pic	Name	Carrier
	**Sang Yup Lee**	• Northwestern University, Chemical Engineering (Ph.D) • KAIST Distinguished professorKAIST Research Center Director • Research field: Metabolic engineering, synthetic biology
	**Won Jae Lee**	• Yonsei Medical School (M.D.) • Professor at Yonsei Medical School, Plastic Surgery • Research field: wound healing, fibrosis mechanism
	**Seung Yong Song**	• Yonsei Medical School (M.D., Ph.D) • Professor at Cha Medical Hospital • Professor at Yonsei Medical School, Plastic Surgery • Research field: Stem cell, wound healing
	**Seung Joo Song**	• Inaje University Medical School(M.D., Ph.D) • KAIST Ph.D • Professor at Seoul Asan Hospital • Research field: spinal cord injury, brain-blood nerve system
	**Phil Hue Lee**	• Yonsei Medical School (M.D., Ph.D) • Professor at Ajou University Medical School • Professor at Severance Hospital • Research field: Parkinson's disease, Alzheimer's disease, stem cell
	**Hee-Joong Ryu**	• Yonsei Medical School (M.D.) • Chief of Mega Graft Hospital • Research field: hair transplantation, cosmetic surgery

7. Company Organization

Team & Advisory (KAIST, Medical Doctors)

Management

Won Min Yoo CEO

- M.D., Ph.D
- Professor at Yonsei Severance Hospital
- Chief of The M Plastic Surgery Hospital

Daniel Kim CEO

- BA, NYU, MS, StonyBrook
- GlaxoSmithKlein
- Fujitsu Korea
- IBM Korea

Hannah Chung CTO

- B.A., M.S., Ph.D from KAIST
- Major in Chemical & Biomolecular Engineering
- Specialized in metabolic engineering and protein engineering

Company chronicle

2021	03	• Daejeon City Government support programs selected
	07	• ARANEA Brand Launched
	08	• Additional Tech transferred from KAIST
	09	• Export promising company selected
2020	03	• US office open (Delaware)
	07	• HQ & Lab expanded
2019	07	• Certified Venture company • Patents applied in the US
	09	• Dr. Graft Copyright applied
	10	• MCB-003 functional cosmetic released
2018	05	• Medicosbiotech
	06	• Tech transferred from KAIST
	10	• TIPS selected

Name	Medicosbiotech Inc
CEO	Won Min Yoo, Sooncheol Kim
Foundation date	8 May 2018
Paid In capital	1 Mil USD
Employees	13
Address	Yooseong Gu, Daejeon City
Business	Bio new material & New Drug development

7. Company Organization

Intellectual Property

NO	Patents	Country	Status	Application, Registration No.	Date of Application, Registration	Etc.
1	Method for Preparing Recombinant Proteins Through Reduced Expression of rnpA	Korea	Registered	10-1765255-0000	2017.07.31	Tech transfer complete (KAIST)
2		PCT	Applied	PCT/KR2015/013419	2015.12.09	
3		United States	Registered	10351890	2019.07.16	
4			Applied	16027478	2018.07.05	
5		China	Applied	201580072798	2017.07.07	
6	Composition for Treating Alopecia or Stimulating Hair Growth	Korea	Registered	10-2018-0146288	2022.02.10	
7		PCT	Applied	PCT/KR2019/016012	2019.11.21	
8		United States		17/296310	2021.05.24	
9		Australia		2019384462	2021.06.16	
10		China		201980086222	2021.06.23	
11		Japan		2021-529142	2021.05.21	
12		Europe		19886811.9	2021.06.22	
13		Singapore		11202105242T	2021.05.19	
14	Pharmaceutical Composition for Treatment of Wounds	Korea	Applied	10-2018-0146287	2018.11.23	
15		PCT		PCT/KR2019/016011	2019.11.21	
16		United States		17/296301	2021.05.24	
17		Australia		2019383263	2021.06.16	
18		China		201980083434.3	2021.06.16	
19		Japan		2021-529098	2021.05.21	
20		Europe		19888039.5	2021.06.22	
21		Singapore		1120210523U	2021.05.19	

7. Company Organization

Intellectual Property

NO	Patents	Country	Status	Application, Registration No.	Date of Application, Registration	Etc.
22	G-CSF Exon 3-Deleted Protein and Antibody thereof, and Producing Method thereof	Korea	Registered	10-0716014-0000	2007.05.02	
23	Composition for Treating Alopecia or Stimulating Hair Growth Containing Growth Factor	Korea	Applied	10-2020-0029994	2020.03.11	
24		PCT		PCT/KR2021/002969	2021.03.10	
25		Japan		2021544890	2021.07.29	
26		Singapore		11202108253P	2021.07.28	
27		United States		17/427,082	2021.07.29	
28		Europe		21742294.8	2021.07.27	
29		China		202180002250.7	2021.08.27	
30		Australia		2021209267	2021.07.29	
31	Compositions for bone and tissue regeneration containing recombinant silk proteins and porous scaffolds containing the same	Korea	Applied	10-2021-0143632	2021.10.26	
32	Method for Preparing Protein Having High Specific Amino Acid Content Through Co-expression of tRNA of Specific Amino Acid	Germany	Registered	2330186	2014.12.31	Tech transfer complete (KAIST)
33		United Kingdom				
34	Recombinant microorganism with improved recombinant silk protein production capacity and method of producing high molecular weight recombinant silk protein using the same	Korea	Applied	10-2020-0169583	2020.12.02	
35	High Molecular Weight Recombinant Silk or Silk-like Proteins and Micro or Nano-spider Silk or Silk-like Fibres Manufactured by Using the Same	Japan	Registered	5858936	2015. 12. 25	
36		China	Registered	102906107B	2015. 05. 20	

7. Company Organization

Intellectual Property

NO	Patents	Country	Status	Application, Registration No.	Date of Application, Registration	Etc.
1	Dr.Graft 닥터 그라프트	Korea	Registered	4015297530000	2019.10.08	
2	Dr.GRAFT		Applied	4020190138870	2019.09.06	
			Registered	4020200097027	2020.10.26	
3	Dr.GRAFT	Madrid	Registered	4020190138870	2020.10.26	
4	Aranea 아라네아	Korea		40-2020-0185606	2020.10.20	
				40-2021-0130680	2021.06.25	
6	Aranea	Madrid		KR-2021-001319	2021..07.13	

Dr.Graft 닥터그라프트 (Korea)	Dr.GRAFT (Korea)		Dr.GRAFT (Madrid)	Aranea 아라네아 (Korea)	Aranea (Madrid)
Dr. Graft 닥터 그라프트	Dr.GRAFT	Dr.GRAFT	Dr.GRAFT	Aranea 아라네아	Aranea

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