frontier Co., Ltd.

As we enter the era of 100-year lifespans, we aim to stay healthy and beautiful forever.

Everyone has a desire to live a fulfilling life.

Frontier Co., Ltd. is committed to "all the people involved"

Giving people dreams, hopes and smiles, and the wonderful power to live that people inherently have.

Our mission is to propose and provide cutting-edge medical care that will inspire you.

We will continue to contribute to everyone.

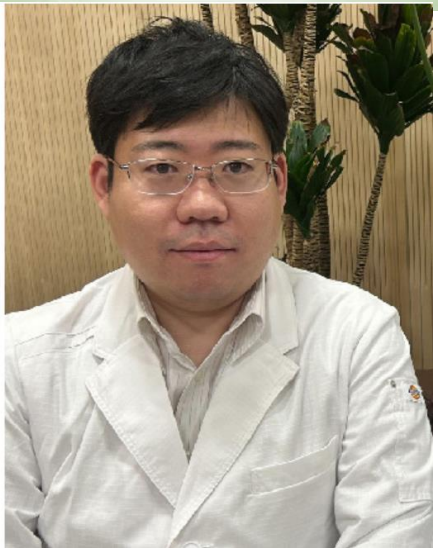
Company Profile

Frontier Co., Ltd.	
Chairman and Representative Director	Seiichi Tobata
Chief Executive Officer	Koutaro Shouji
Director and Chief Technology Officer	Takaaki Ishii (Ph.D.)
R&D Director	Tomoaki Inoue (Ph.D.)
Location (Office)	3-3-5 Kashiihama, Higashiku, Fukuoka, Fukuoka-Pref., 813-0016, Japan
Location (Research Labo.)	Rm. 102, Fukuoka Bio Incubation Center, 1-1 Hyakunenkoen, Kurume, Fukuoka-Pref., 839-0864, Japan
Business Purposes	・Operation of cell culture processing facilities ・Wholesale and sales of stem cell culture supernatant liquid ・Wholesale and sales of exosomes ・Consulting services related to regenerative medicine ・Pharmaceutical business ・Cosmetic raw material development and manufacturing business ・Health food raw material development business ・Stem cell culture for animal regenerative medicine (dogs and cats)

Introduction of researchers

Executive director,
Chief Technology Officer (Ph.D.)

Takaaki Ishii



Introduction of researchers	Department of Applied Life Science, Faculty of Biology, Graduate school of Engineering, Sojo University, Doctor Course Division of Advanced Science and Biotechnology, Graduate School of Engineering, Osaka University. Bio Process Systems Engineering, Graduate School of Engineering, Osaka University, Project Researcher (full time). Start-up Cell Processing Center, Management and Education.
Activities in Academic Societies and Society.	Member of the Japanese Society for Alternative Methods in Animal Experiments. Member of the Japanese Society for Regenerative Medicine. Member of the Japanese Society for Chemical Engineering.

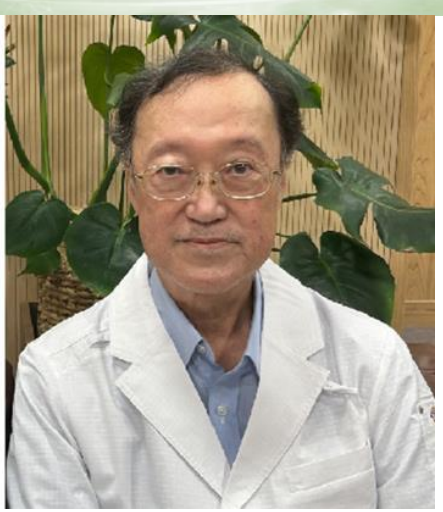
Publications and Patents.

1. T.Ishii, H.Saito, Y.Komizu, R.Tomoshige, and T.Matsushita. Effects of macroporous hydroxyapatite carriers on the growth and funtion of human hepatoblasts derived from fetal hepatocytes.
   J.Biosci Bioeng. 122(2):240-5.(2016)
2. T.Ishii, H.Saito, Y.Komizu, R.Tomoshige, and T.Matsushita. Effects of the use of polyacrylonitrile nanofibers as 3D scaffolds on growth and function of human hepatoblasts derived from fetal hepatocytes. AATEX, 20, 66-72(2015)
3. **International Patent：CELL CULTURE MODULE, WO 2014/034146 A1**

Introduction of researchers

R&D Director (Ph.D.)

Tomoaki Inoue



Introduction of researchers	Department of Biology, Faculty of Science, Kyushu University Hoffman-La Roche Inc. (USA), Investigative Toxicology Principal Scientist, Department of Toxicology, Nippon Roche Co., Ltd. Later, merged with Chugai Pharmaceutical Co., Ltd.
Activities in Academic Societies and Society.	Director of the Japanese Society of Immunotoxicology, Councilor (Former Director) of the Japanese Society for Alternatives to Animal Experiments Councilor of the Japanese Society of Toxicology Member of the Testing Method Evaluation Committee in National Institutes of Health Sciences (Validation Management Team Member) Leader of the Hepatocyte Team in the Consortium for Safety Assessment using Human iPS Cells

Publications and Patents.

1. Human induced pluripotent stem cell-derived hepatocytes and their culturing methods to maintain liver functions for pharmacokinetics and safety evaluation of pharmaceuticals. T. Inoue, N. Iwazaki, T. Araki, H. Hitotsumachi, Curr. Pharm. Biotech., 21 (9), 773-779, 2020.
2. Human induced pluripotent stem cell-derived mast cells useful for in vitro mast cell activation assay exhibiting phenotypes and morphological characteristics of human mast cells. T. Ikuno, S.Ito, T.Inoue,J. Toxicol. Sci.44 (11), 789 – 797, 2019.
3. Requirements for human iPS cell derived hepatocytes as an alternative to primary human hepatocytes for assessing absorption, distribution, metabolism, excretion and toxicity of pharmaceuticals. T. Araki, N. Iwazaki, N. Ishiguro, , A. Sakamoto, K. Nagata, M. Ohbuchi, H. Moriguchi, M. Motoi, R. Shinkyo, T. Homma, S. Sakamoto, Y. Iwase, R. Ise, Y. Nakanishi, M. Uto, T. Inoue, Fund. Toxicol., 3 (3), 89-99, 2016.
4. Electrophysiological characterization of cardiomyocytes derived from human induced pluripotent stem cells. M. Honda, J. Kiyokawa, M. Tabo, T. Inoue, J. Pharmacol. Sci., 117, 149-159, 2011.
5. Application of human iPS cells to preclinical safety evaluatior of drugs – Focusing on cardiotoxicity evaluation system -, T. Inoue, M. Honda, BIO Clinica, 26, 76-81, 2011.
6. Safety evaluation of biopharmaceuticals, T. Inoue, K. Yasugi, Drug Delivery System, 26, 622-627, 2011.
7. International Patent: Method for inducing differentiation of pluripotent stem cells into hepatocytes, PCT WO2019073951A1
8. International Patent: Method for identifying epitope of protein PCT WO2016010002A1

What is regenerative medicine?

Even if the lizard's tail is cut off, it will grow back.
Although not as strong as lizards, humans also have the inherent ability to regenerate.

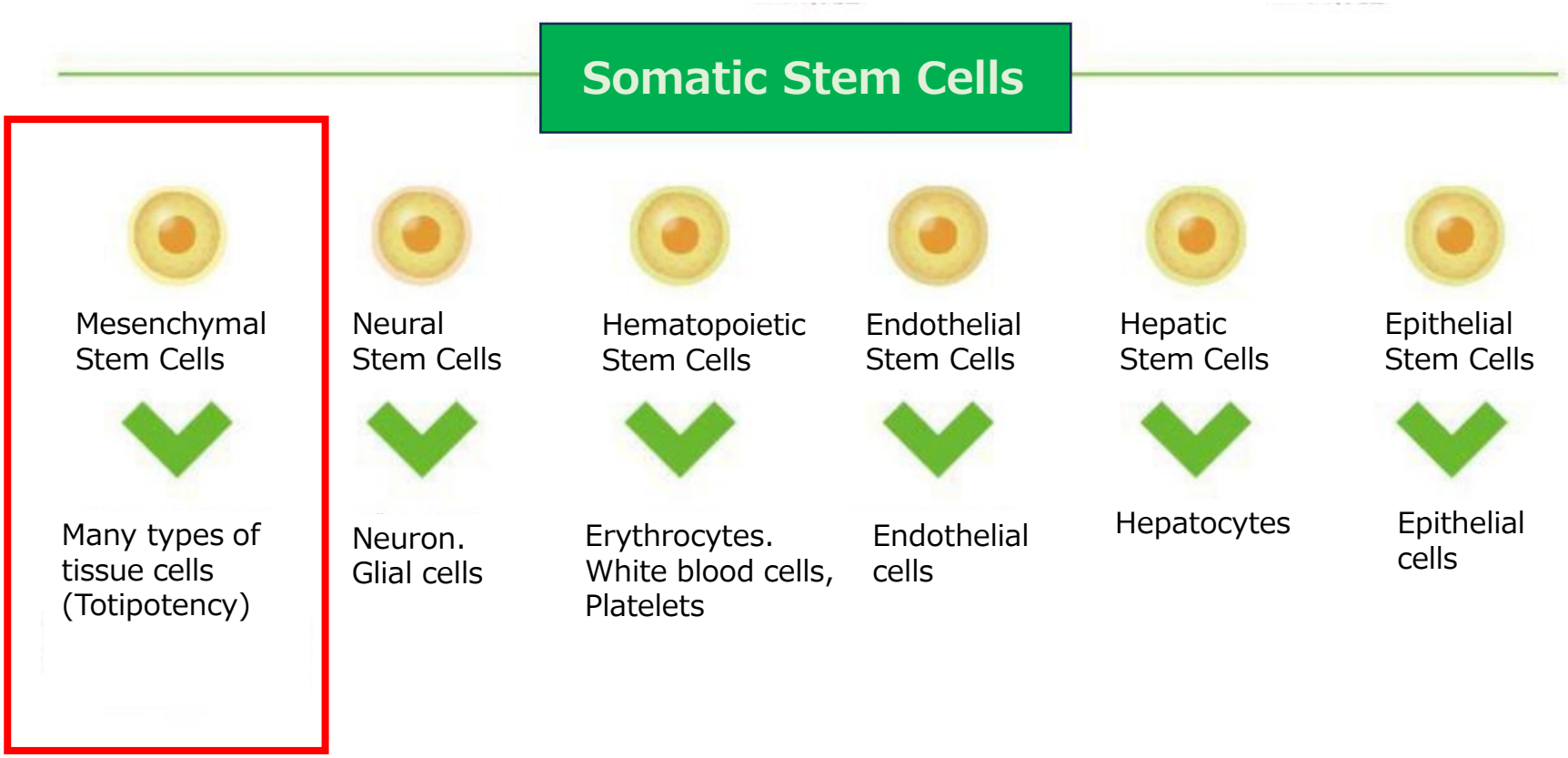
Regenerative medicine aims to regenerate the functions of living tissues and organs that have become dysfunctional by actively using cells. Instead of treating injuries and illnesses with drugs, which are so-called "compounds," the functions that have been lost due to injury or illness can be restored by using the "regenerative power" of the human body. This is the medical care we aim for.

Use of Stem Cells for Regenerative Medicine

	ES cells	Somatic stem cells	iPS cells
Cell source	Fertilized eggs	Adult tissues	Adult tissues
Ethical issues	×	○	△
Characteristics	Pluripotent	Totipotent	Pluripotent
Clinical risks	Carcinogenicity	Limited risks	Carcinogenicity

Stem cells are special cells that have the ability to self-renew and differentiate into various types of cells. Due to these two abilities, cells are thought to play a role in development and tissue regeneration.

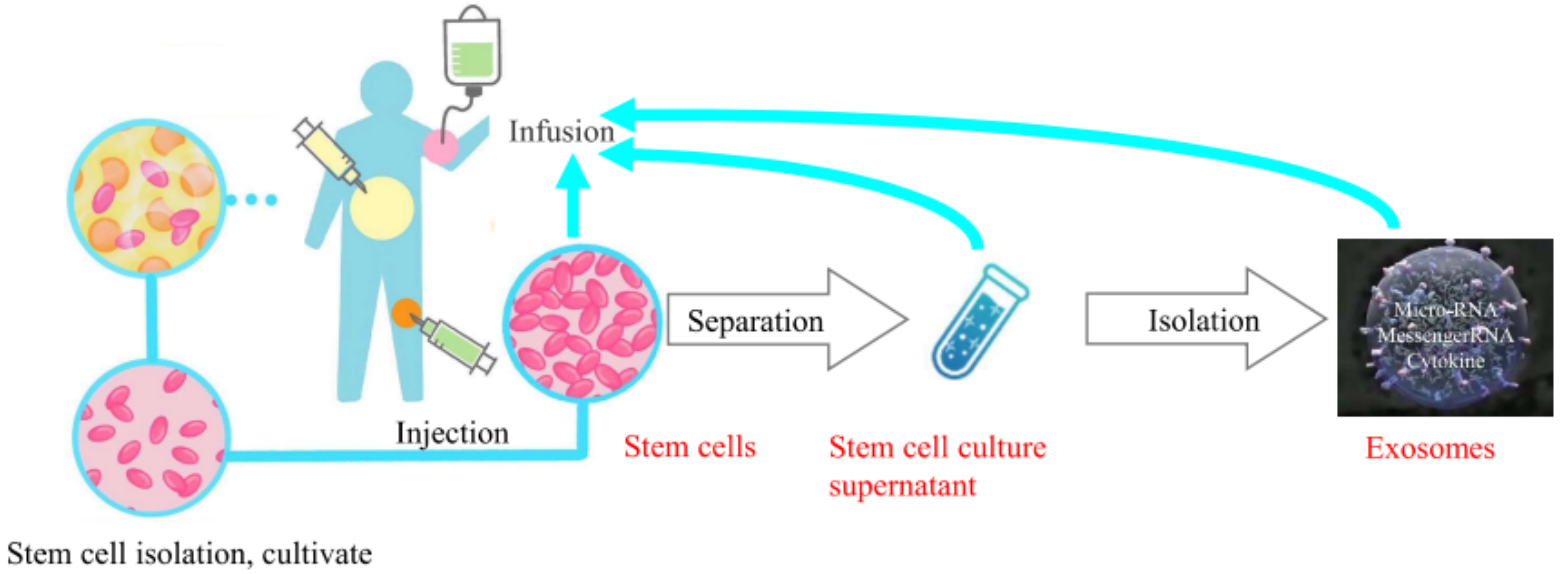
Regenerative Medicine:
Regain tissue function by the power of the existing cells



In general, somatic stem cells differentiate into limited types of tissue cells. However, mesenchymal stem cells (MSCs) differentiate into many types of tissue cells. Though, MSCs are expected to be used for regenerative medicine in many types of diseases.

What is regenerative medicine?

Flow and types of regenerative medicine treatment (Mesenchymal stem cells)



Regenerative medicine using stem cells regenerates damaged organs and tissues by transplanting stem cells, etc. artificially cultured outside the patient's body into the patient's body through intravenous infusion or injection. It is an epoch-making treatment that restores function.
In addition, the stem cell culture supernatant and exosomes obtained in the stem cell culture process are expected to have the same effect as stem cell therapy.

Growth factors and cytokines

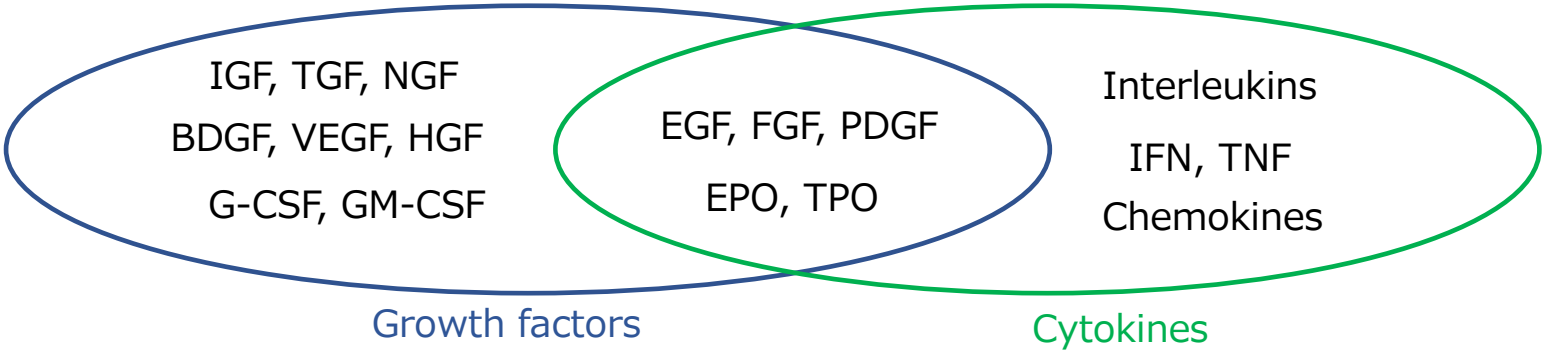
Main growth factors contained in stem cell culture supernatant and their effects

VEGF (vascular endothelial cell growth factor)	・Improving the blood flow environment through angiogenesis ・Creates new cells to improve and prevent wrinkles ・Nourishes hair roots and promotes hair growth
HGF (hepatocyte growth factor)	・Promotes regeneration of nerves and blood vessels ・Proliferates epithelial cells and regenerates skin ・Protects and regenerates tissues and organs such as the liver, kidneys, blood vessels and heart
EGF (epidermal growth factor)	・Creates new skin cells to improve and prevent wrinkles ・Smoothes the skin for a healthy-looking complexion ・It has the effects of promoting metabolism and hasten the recovery of wounds.

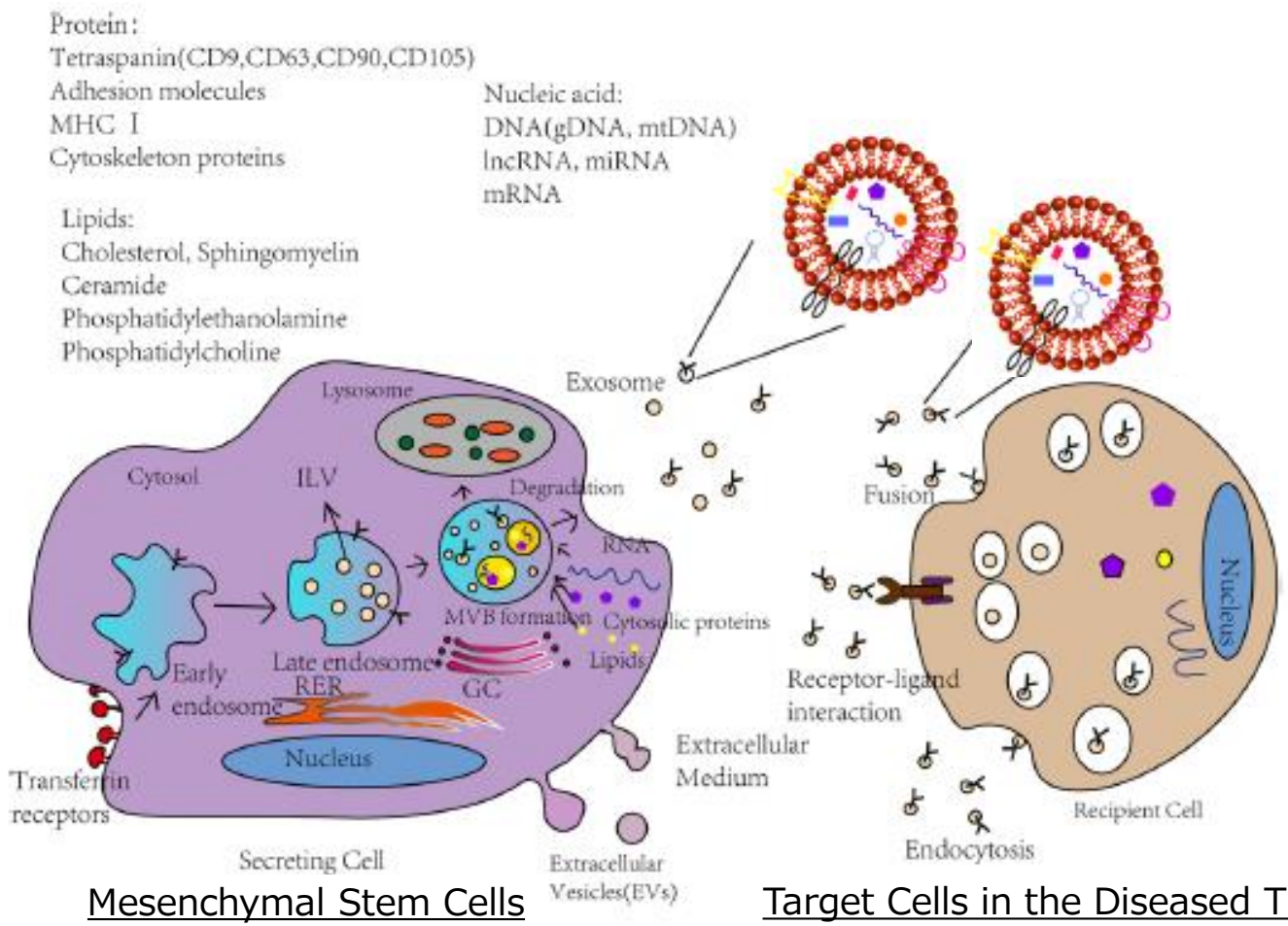
Growth factors：Proteins that promote growth and differentiation of specific cells (in cell biology)

Cytokines：Proteins that work in cell-cell interactions (in immunology)

（Although research has been carried out in different fields, it has become clear that there are common factors. There is a possibility that it will be reclassified based on new findings in future research.）



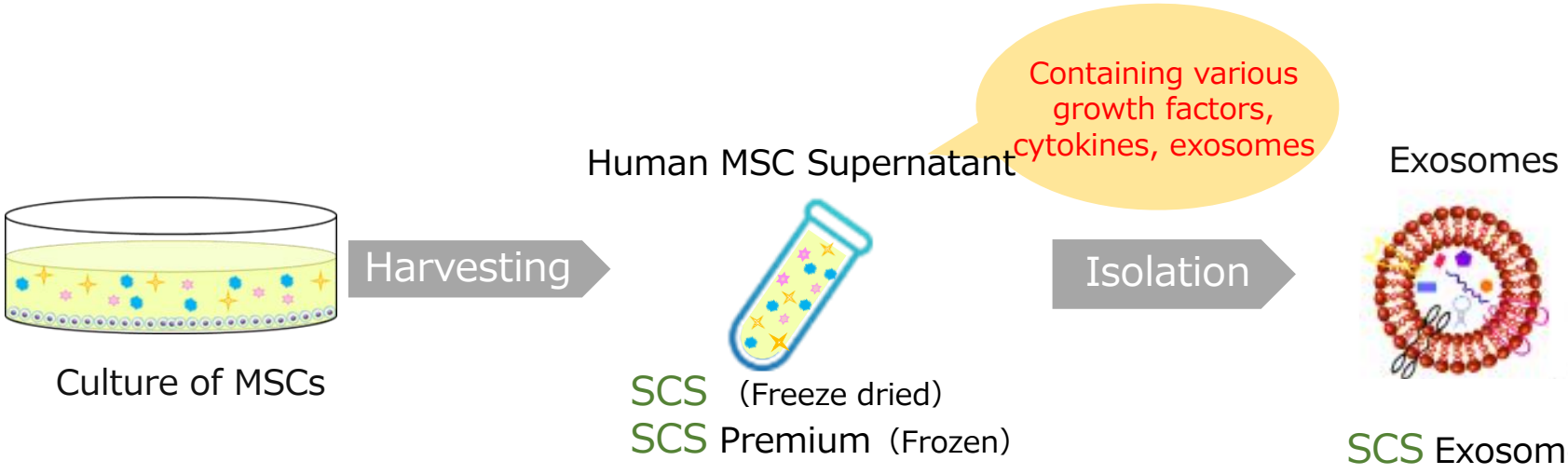
What are exosomes?



Tang *et al. Stem Cell Research & Therapy* (2021) 12:71

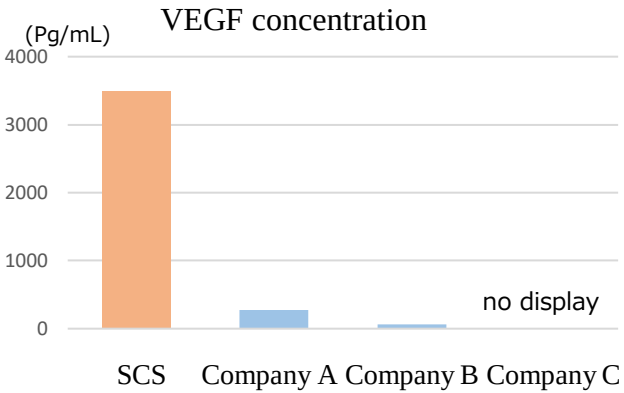
Mesenchymal stem cells secrete exosomes (containing growth factors, miRNA, mRNA etc.). The exosomes selectively reach the target cells by binding specific proteins on the surface of the target cells, and deliver signals for cell activation, proliferation, and differentiation, and result in regeneration of the diseased tissues.

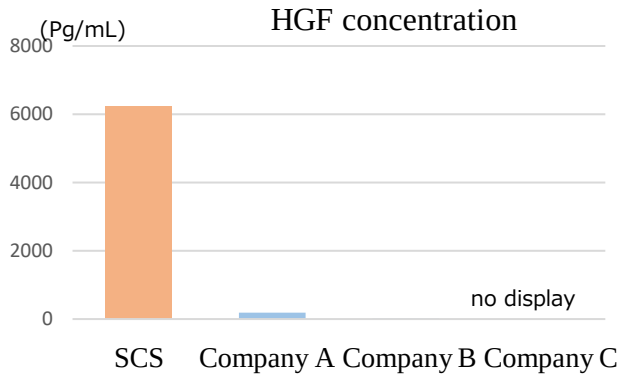
Our products: Supernatant from human mesenchymal stem cells culture SCS 、SCS Premium 、SCS Exosome

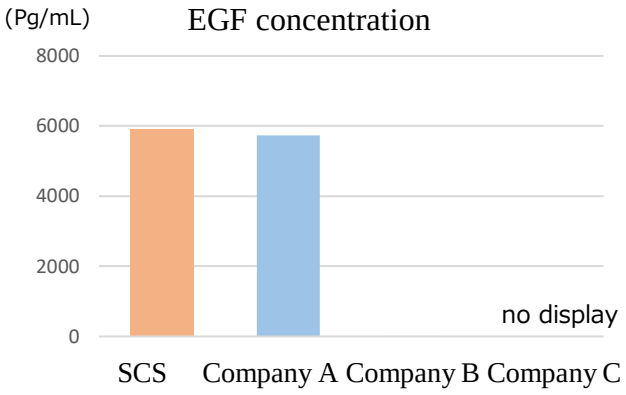


- SCS : Human Stem Cell Supernatant (Freeze dried)
  More than 500 kinds of growth factors and cytokines are included, freeze dried powder. The exosomes may not be functional, because the stability of the exosomes is not proved.
- SCS Premium: Human Stem Cell Supernatant (Frozen)
  More than 500 kinds of growth factors and cytokines, and exosomes are included, frozen liquid. Therapeutic effects of exosomes are expected in addition to growth factors and cytokines.
- SCS Exosome: (Isolated exosomes from human stem cell supernatant, Frozen)
  Isolated exosomes mainly for research purpose.

SCS series comparison with other companies







試 験 成 績 書

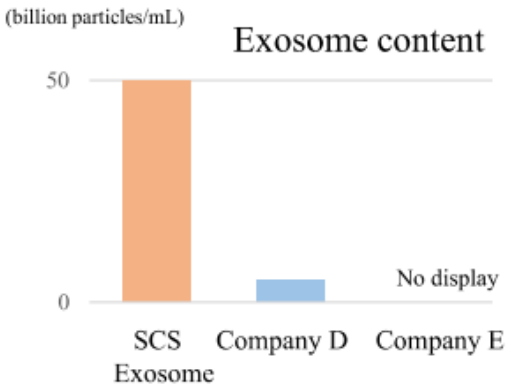
製品コード	：	８２００３７
INCI名（製品名）	：	ヒト脂肪由来幹細胞順化培養液
Ｌｏｔ番号	：	Ｔ２１１０２０２
製造年月日	：	
判定結果	：	合格
判定日	：	

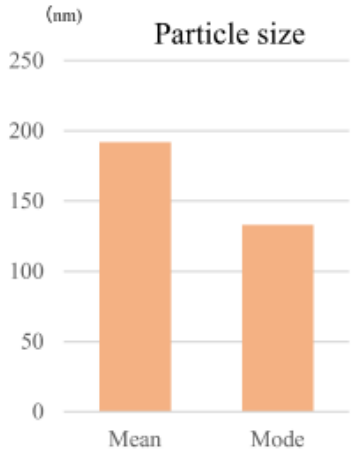
試験項目	規格	試験方法	試験結果
１．性状	白色～淡黄色の粉末	目視評価	適
２．外観検査	容器に破損や汚れがない。異物混入がない。	目視検査	適
３．ｐＨ	実測値（懸濁液100%）	ガラス電極法	7.8
４．生菌試験		メンブレンフィルター法	
細菌	実測値（cfu/10mL）	懸濁液100%	0
真菌	実測値（cfu/10mL）	懸濁液100%	0
５．サイトカイン濃度測定		ＥＬＩＳＡ法	
①ＶＥＧＦ	実測値（pg/mL）		1160
②ＨＧＦ	実測値（pg/mL）		15243
③ＥＧＦ	実測値（pg/mL）		4024

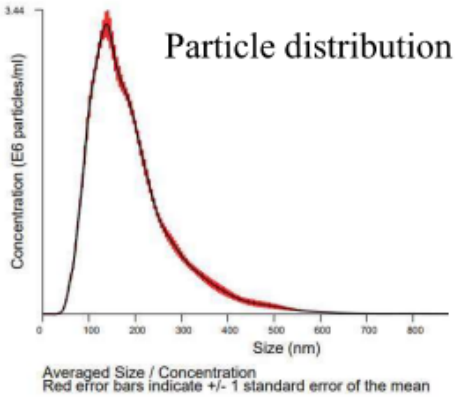
① ヒト脂肪間質細胞順化培養液エキス2000mlをフリーズドライして約20gのFD粉末が得られます。
② 荷姿： 10g ×1、ーGaプラスチックボトル
③ 保存条件： 4℃、遮光保存。
④ 開封後はすみやかにご使用ください。

SCS culture supernatant contains extremely high concentrations of growth factors and cytokines. Proof of more than 1000 pg/mL of VEGF and HGF.

SCS series comparison with other companies







Samples	Dilution of samples	Particle concentration
		Unit 10^{11} particles/mL
Sample1	200	1.03 +/- 0.04

Samples	Dilution	Particle size	
		Mean	Mode
Sample 1	200	192 +/-4.4	133+/-3.3

Exosome content of the sample ： 100 billion particles/mL

SCS Exosome has an exosome content of 50 billion cells/mL as a guaranteed content, and contains an ultra-high concentration of exosomes not found in other companies' products.

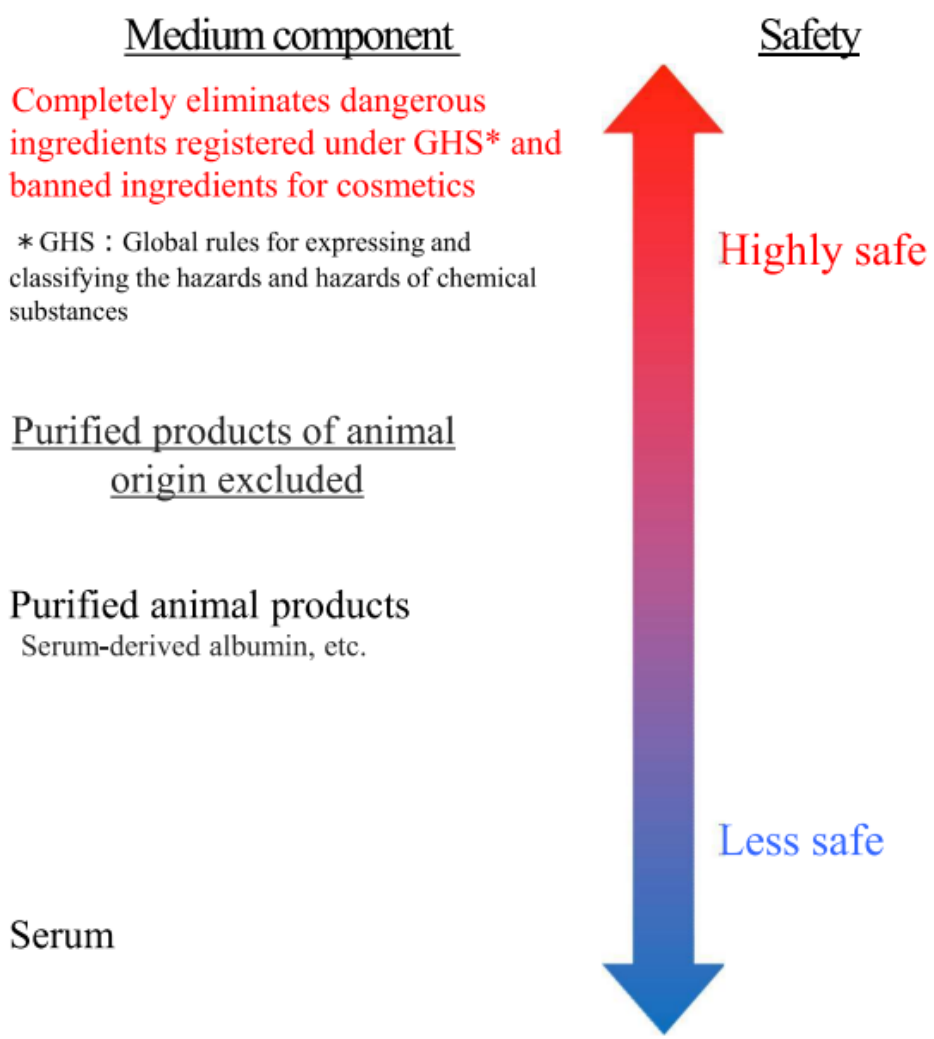
Features of the SCS series (culture medium)

SCS medium
（Elimination of toxic ingredients）
- In addition to the advantages of AOF medium, toxic substances such as heavy metals are eliminated.
- Several types of AOF medium are commercially available, but SCS medium is completely original and extremely safe.

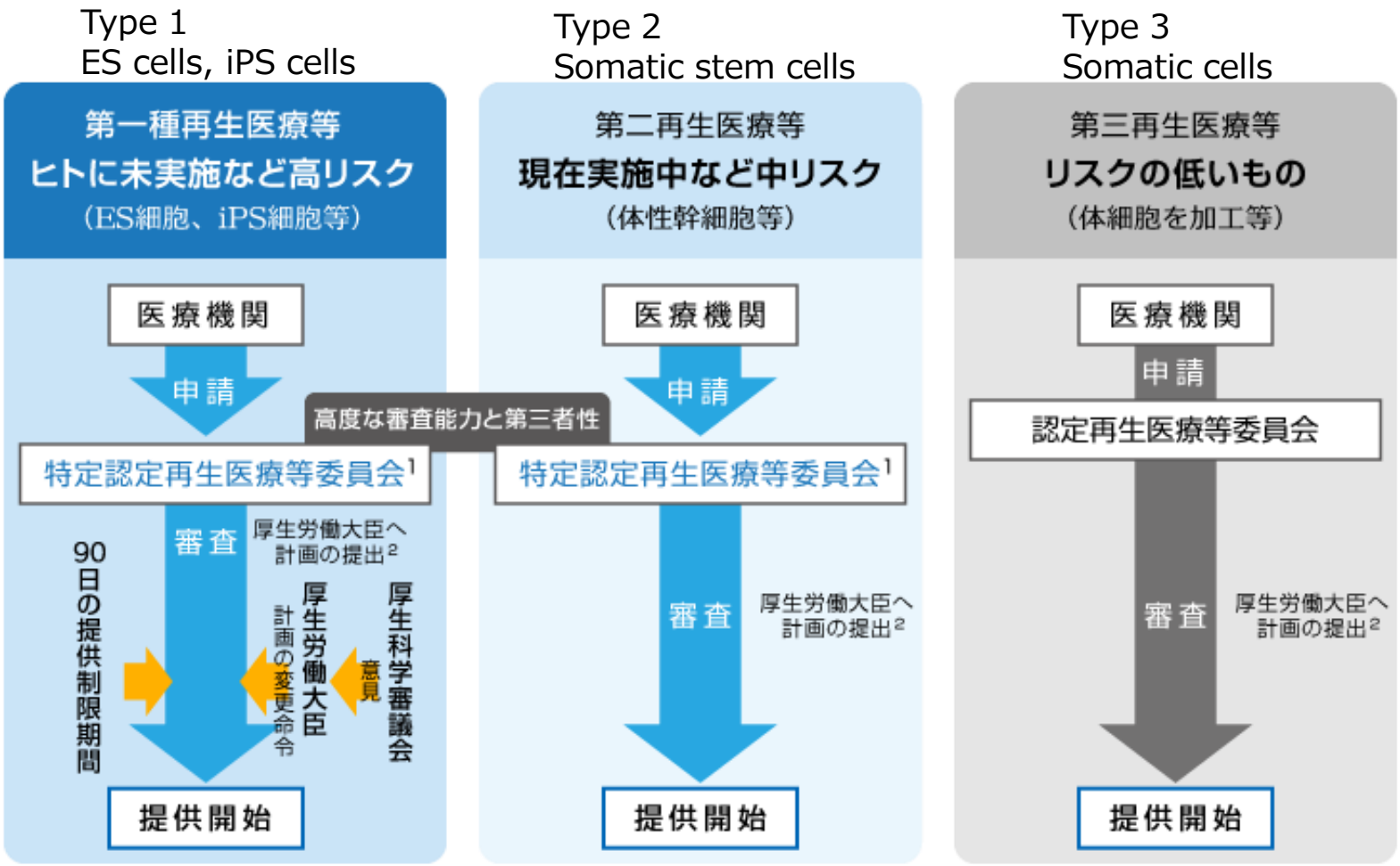
AOF (Animal Origin Free) medium
（Elimination of animal-derived ingredients）
- Uses human-type recombinant proteins
- Maximum elimination of pathogen infection risk. Lot-to-lot variation in performance is small.
- Contains toxic substances such as heavy metals.

Serum-free medium
（General commercially available medium）
- Some contain serum-derived
- Currently, serum is added because it cannot be cultured in a completely serum-free environment. （TSE/BSE risk）
- Lot-to-lot variation is large
- Contains toxic substances such as heavy metals.

Serum medium （basal medium）
- Risk of immune response to foreign antigens.
- Contains toxic substances such as heavy metals. There is a risk of infection due to contamination with pathogens （TSE/BSE risk）
- Lot-to-lot variation is large



Regulation by laws in Japan



According to the Regenerative Medicine Safety Act, Type 2 notification is required for mesenchymal stem cell treatment, but there is currently no law regarding stem cell supernatant liquid. Our company manufactures supernatant liquid with safety standards that comply with the above laws and regulations.

Features of the SCS series (quality tests)

【 Donor screening items 】

- HIV（antigen antibody method ・CLIA method）
- HCV antibody （CLEIA method ）
- HBs antigen （CLIA method ）
- HBe antigen （CLIA method ）
- HTLV-I antibody （CLEIA method ）
- Syphilis （RPR method ）
- Syphilis （TPHA method ）
- Herpes simplex （CF method ）
- Mycoplasma （PA method ）
- Parvovirus B 19（IgM antibody ）

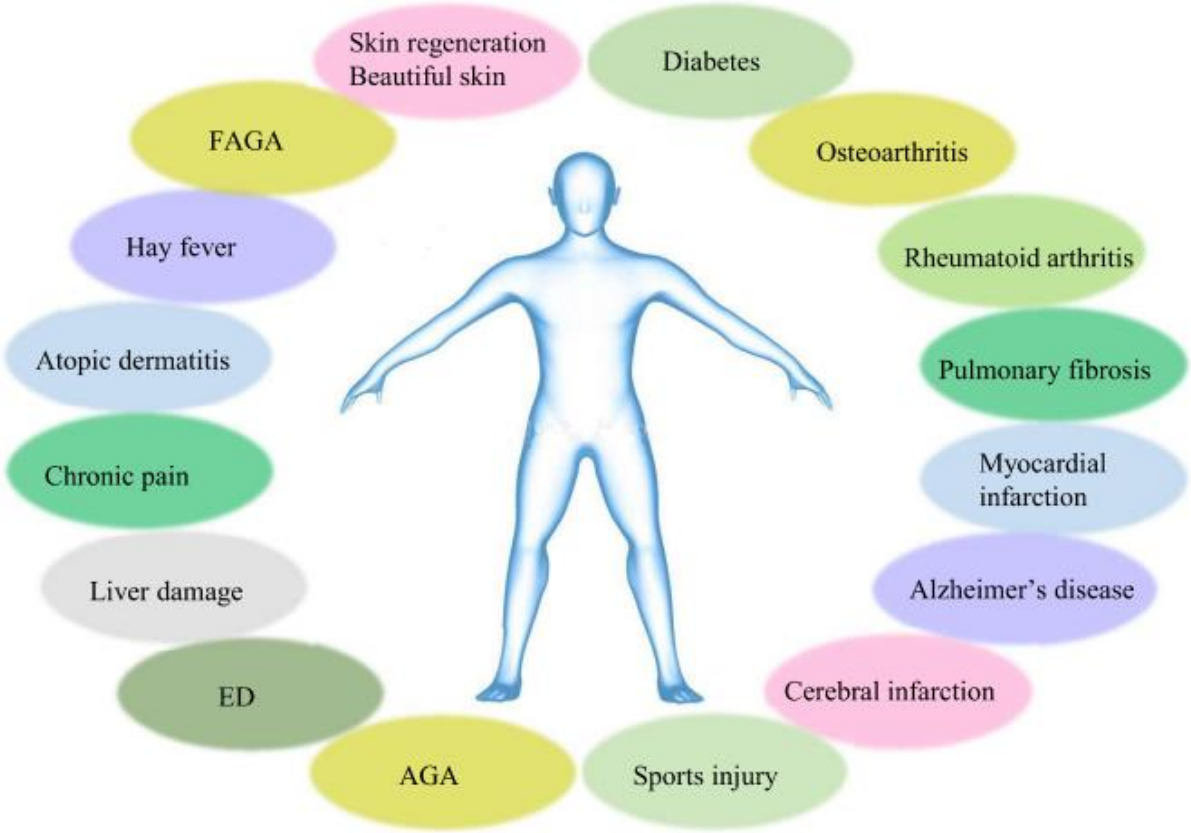
【 Quality control test items 】

- Mycoplasma
- Endotoxin
- Sterility test
- Human immunodeficiency virus type 1 （HIV1）
- Human immunodeficiency virus type 2 （HIV2）
- Human T cell leukemia virus type 1 （HTLV2）
- Human T cell leukemia virus type 2 （HTLV2）
- Hepatitis C virus （HCV）
- Hepatitis B virus （HBV）
- Cytomegalovirus （CMV）
- Human parvovirus B19 （B19）

SCS is produced in a clean room environment controlled by class1000 and class10000. By following the same quality inspection procedures as for stem cell therapy and requesting inspections from a third-party organization, we are confirming safety with stricter standards.

Regenerative medicine treatment

Diseases that can be treated with regenerative medicine (cultured stem cell therapy, culture supernatant, exosomes)



In regenerative medicine, in addition to diseases such as Alzheimer's disease, diabetes, cerebral infarction, cerebrovascular disease, chronic pain, liver damage, atopic dermatitis, skin regeneration, AGA (thinning hair), ED (erectile dysfunction),
It is expected to treat sports injuries and arthrosis of the elbow, knee, and hip joints.

Reported mechanisms of therapeutic effects

Effects	Mechanisms	Examples
Anti-inflammation	Promotes healing of inflamed areas and reduces pain	Effective for joint pain, lower back pain, neck pain, shoulder pain, muscle pain, etc.
Wound healing	Repair damaged cells and heal wounds early	Activates cells from the dermis layer to the skin surface and repairs skin scars and inflammation marks.
Tissue regeneration	The damaged tissues are repaired. Cell division in damaged tissue is activated, Improves tissue regeneration ability and restores function	Effective for liver diseases such as cirrhosis and chronic hepatitis, skin diseases, respiratory disorders, kidney dysfunction, complications of diabetes, etc.
Immune regulation	To prevent allergies from occurring due to abnormal immune reactions, adjust immune function to normal state	Effective for allergic rhinitis and atopic dermatitis
Angiogenesis	When blood flow is disrupted due to arteriosclerosis, etc., blood circulation is restarted through collateral blood circulation angiogenesis.	It is effective as a treatment to prevent the progression of arteriosclerosis, etc.
Anti-oxidation	Helpful in recovering from fatigue and preventing lifestyle-related diseases	
Rejuvenation	Rejuvenation of tissues	Prevents wrinkles and sagging and improves aging
Brain regeneration by nasal administration	Deliver stem cell culture supernatant from the nasal cavity to the capillaries in the brain.	It is indicated for senile Alzheimer's disease, memory decline, and various symptoms after cerebral infarction. It is also effective as a complement to Parkinson's disease.

Regenerative medicine treatment

	Stem cell culture supernatant		Exosomes
Product	SCS	SCS Premium	SCS Exosome
	A culture supernatant containing a high concentration of over 500 types of growth factors and cytokines.	Greatly increase exosomes by using high-quality media.Top quality culture supernatant	Only exosomes are extracted from SCS Premium. Achieved a high concentration of over 50 billion cells/mL
Quantity	2 ml/vial 10 vial/carton	2 ml/vial 10 vial/carton	1 ml/vial 10 vial/carton
Vial	 Glass vial	 Serum tube	 Serum tube
Derived from cells	Adipose-derived dental pulp-derived umbilical cord-derived	Adipose-derived dental pulp-derived umbilical cord-derived	Adipose-derived
Product condition	Freeze drying	Freezing liquid	Freezing liquid
Preservation method	2~8℃ refrigerated storage	Frozen storage below -20 ℃	Frozen storage below -20 ℃
Retention period	2 years	2 years	2 years
Delivery	Refrigerated flight	Frozen flight	Frozen flight

Notes for administration of the supernatant and the exosomes

Contraindications

- Those who are or may be pregnant or breastfeeding
- Those who have a malignant tumor or have been diagnosed with cancer within 2 years
  (Except when there is no problem according to cancer inspection)
- Those who have previously had an allergic reaction due to administration of supernatant fluid or exosomes.
- Others who are deemed unsuitable by a doctor

Possible side effects

- Bleeding at the injection site, subcutaneous bleeding, redness, and mild inflammatory reaction
- Feeling of heat, hypoglycemia, dizziness, ringing in the ears
- Allergic reaction

※For those who have undergone supernatant liquid treatments such as injections, drips, and water light injections, no longer be able to donate blood.

frontier Co., Ltd.