CAREGEN CO., LTD.

Revolution Beyond Innovation

:Total Health Care Solution from Injectables to Topicals with Noble Peptides

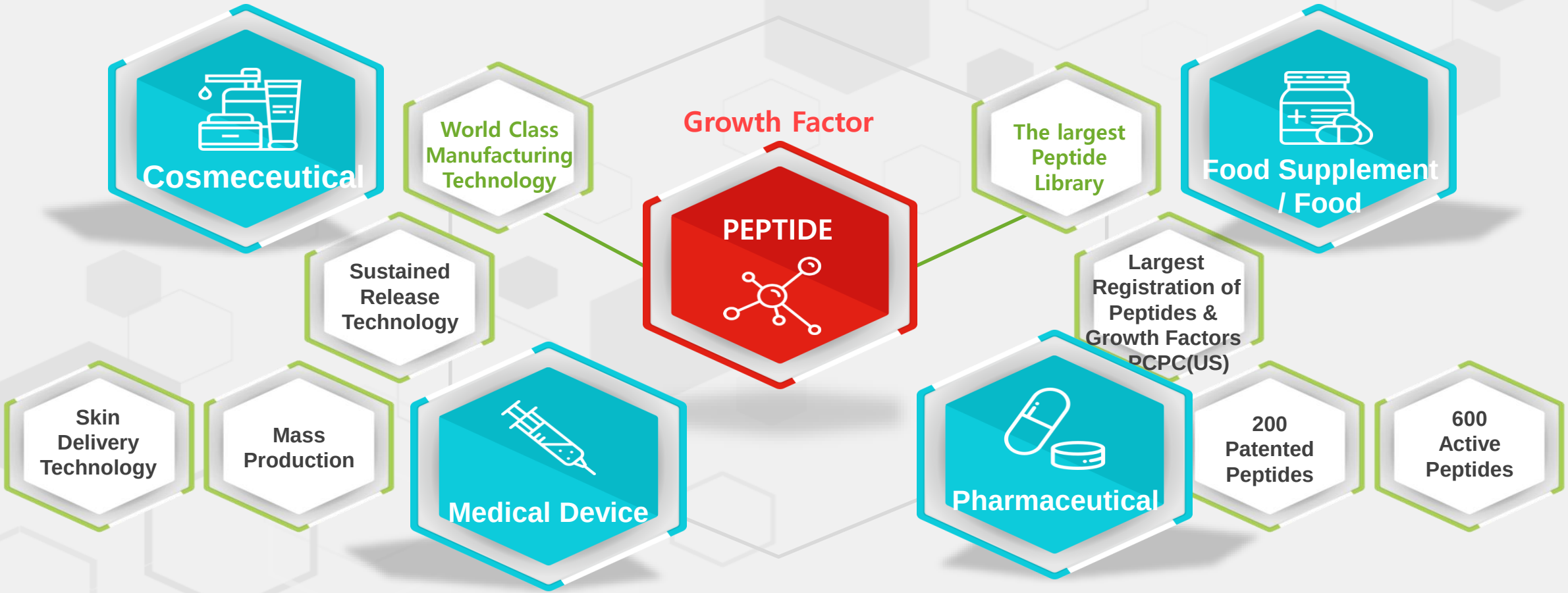
Growth Factors and
Biomimetic Peptides

CAREGEN CO., LTD.

01 Introduction of Caregen

Platform Technology

Caregen is a global leading company with a specialty in biomimetic peptides
Caregen has developed a variety of applications based on platform technology



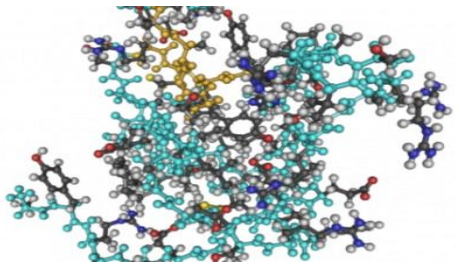
Growth Factor & Biomimetic Peptide

Growth Factor is crucial for healthy life

Caregen has molecular remodeling technology

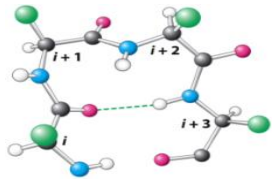
to make Big size of Growth Factors to Smaller size of Biomimetic Peptides

Growth Factor

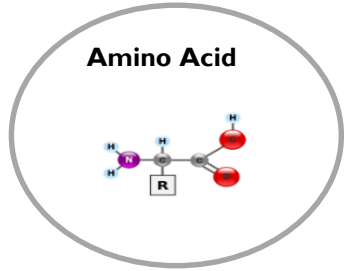


Growth factor is a naturally occurring substance capable of stimulating cellular growth, proliferation, healing and cellular differentiation

Peptide



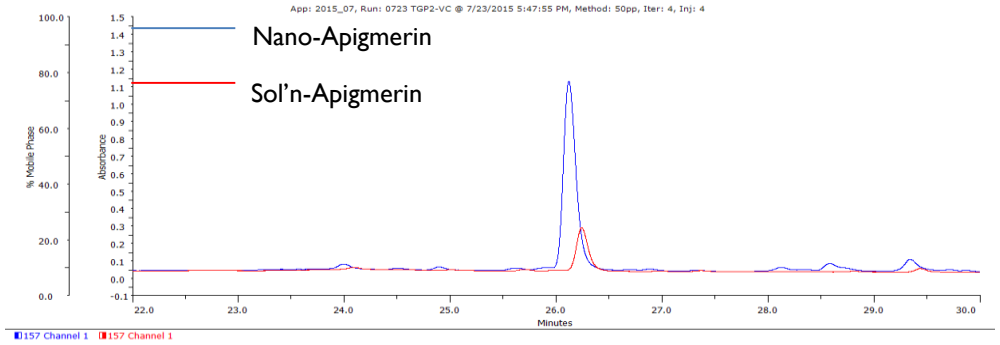
short chains of amino acid monomers

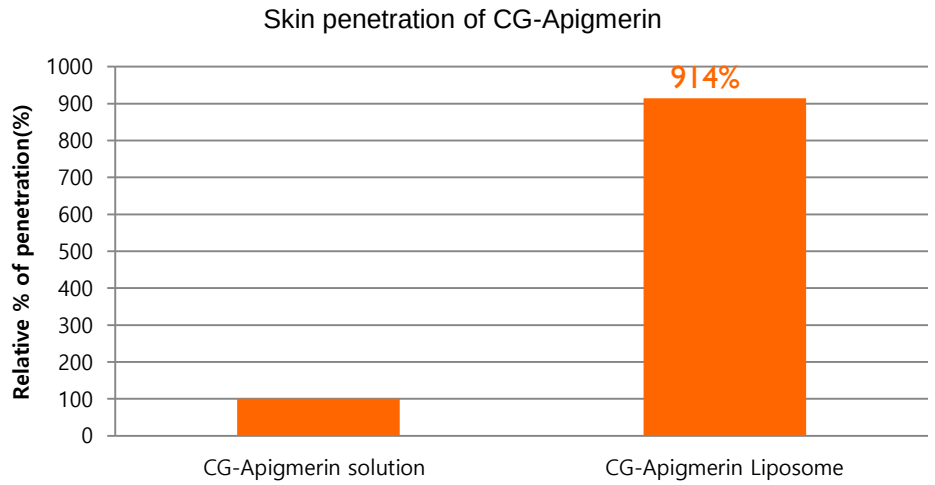


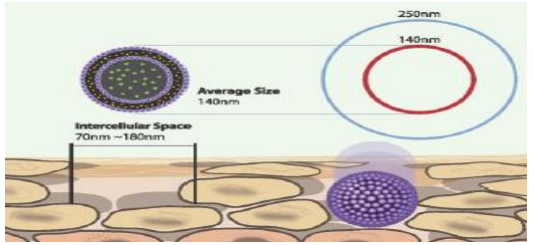
Transdermal Delivery Technology

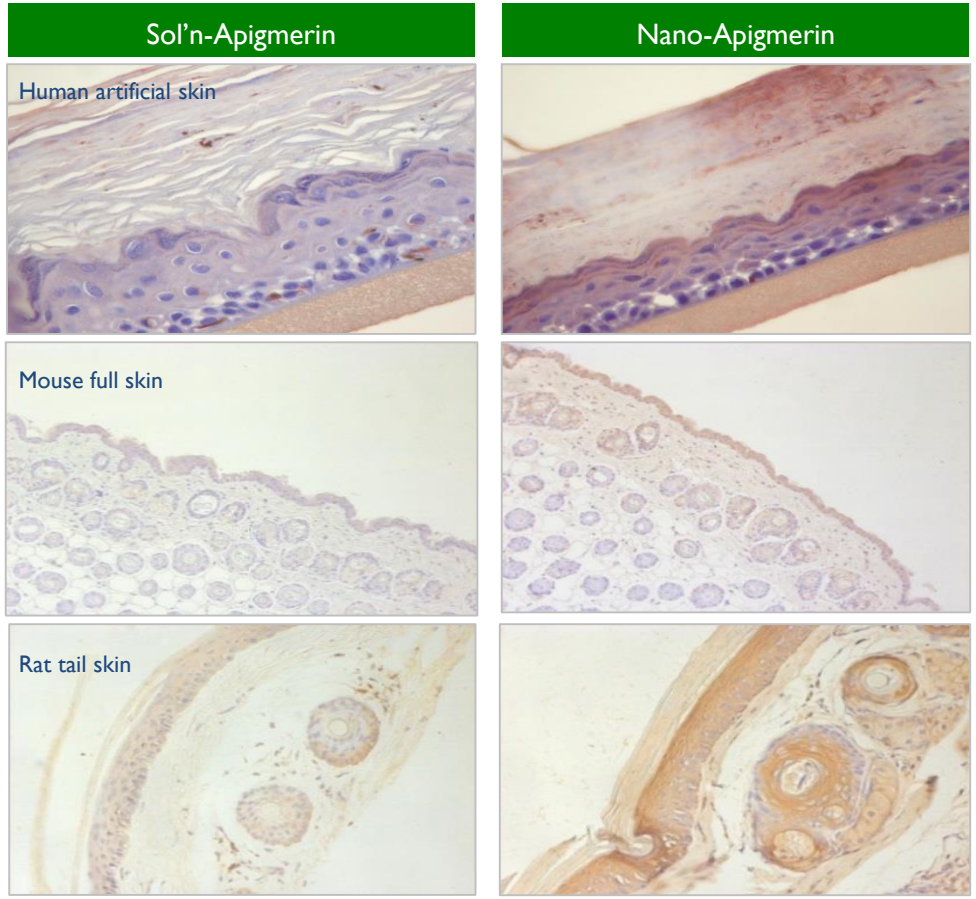
- Franz diffusion cell test : Human Artificial skin, 1hr
- Test Sample : CG- Apigmerin 2500ppm solution, Liposome
- Analysis method : HPLC C18 (250mm*4.6mm,5um,100A), flow rate : 1ml/min, UV:214nm

HPLC chromatogram







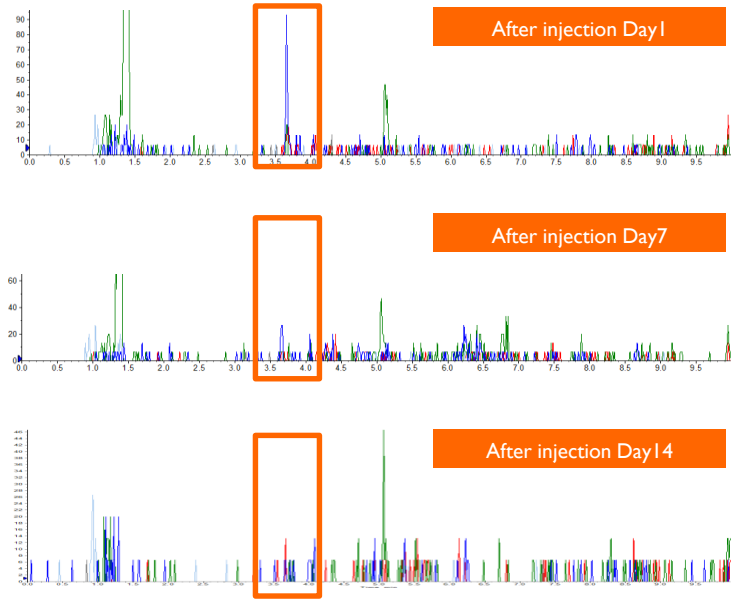


Sustained Release Technology

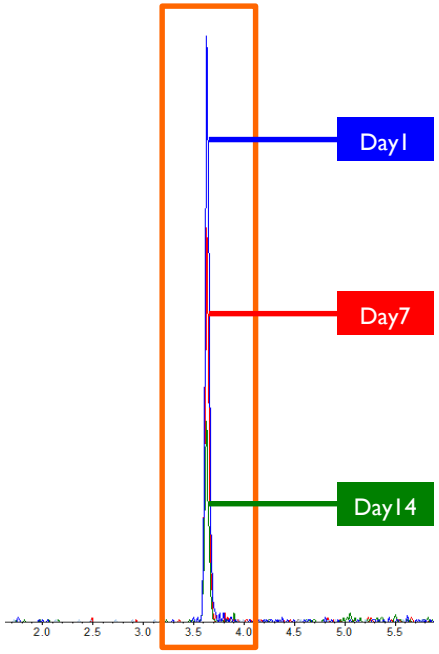
- In vitro and in vivo delivery test
- Test Sample : CG-Keramin2 (Texas red) in DR.CYJ Hair filler
- In vitro release test : Dialysis tube bag, 0.1~14day, HPLC analysis
- In vivo release test : Intradermal injection (SD Rat Dorsal skin)

  Ultra sound detection, Alcian blue staining IHC (Anti- keramin2), Texas red detection

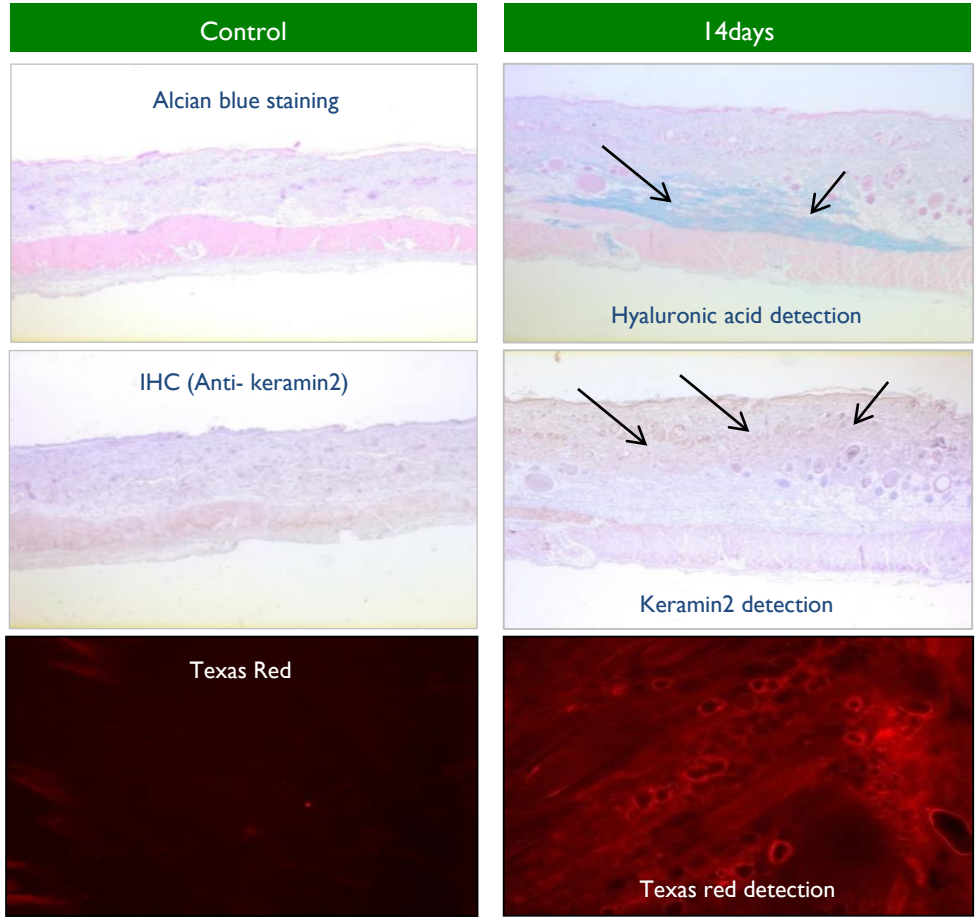
Detection Method: LC-MassMass



Merge



Sustained release of CG-Keramin2



Caregen can provide Total Healthcare Solution based on Peptide technology

Anti-acne

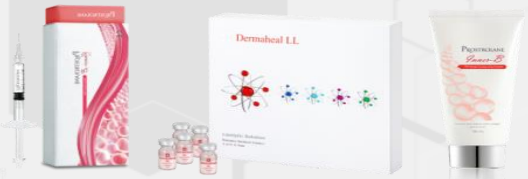
cosmeceutical

Skin Rejuvenation

Injectable / meso-therapy / cosmeceutical

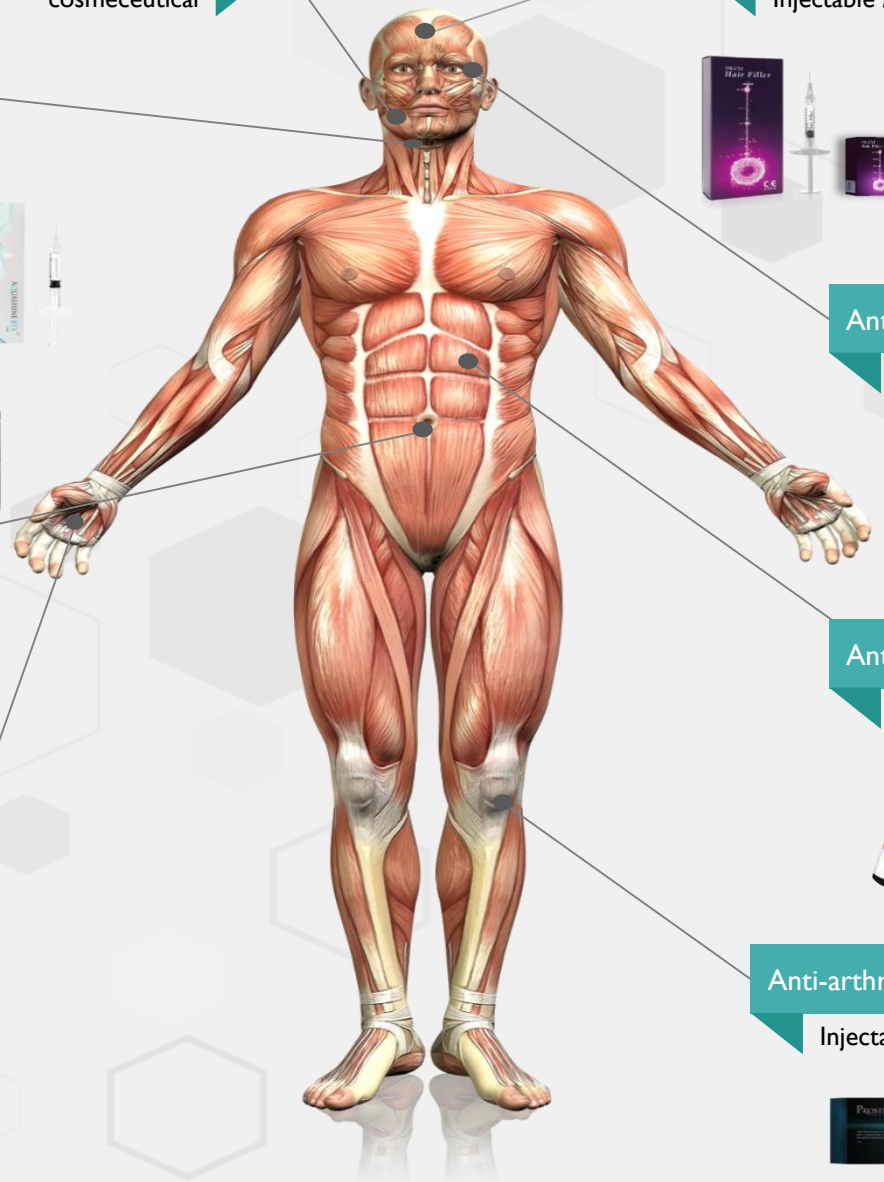
Body Slimming

Injectable/ meso-therapy / cosmeceutical



Anti-dioxin

cosmeceutical

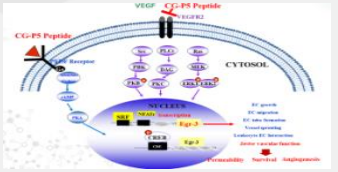


Anti-hair loss & hair regrowth

Injectable / meso-therapy / cosmeceutical

Anti-macular degeneration

Medicine (Eye drop) / Pre-clinical study in progress



Anti-diabetes

Food / Food supplement

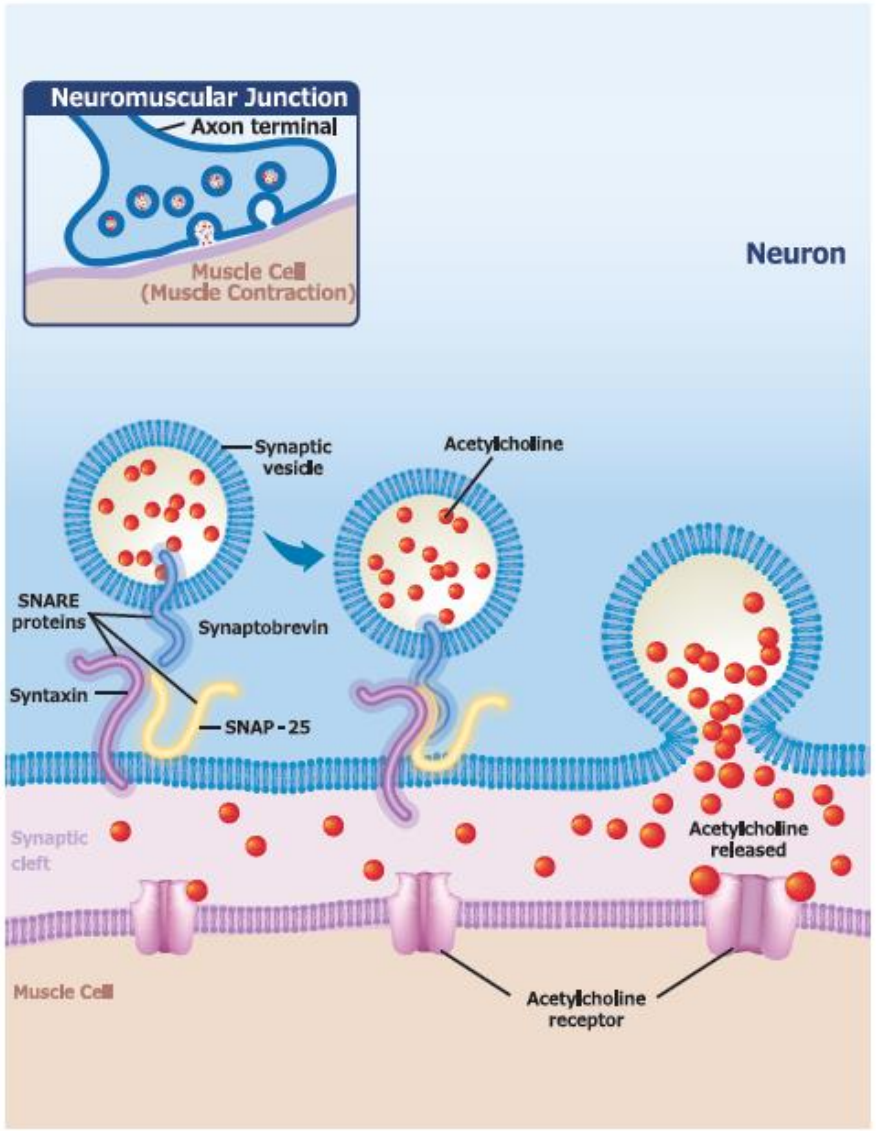
Anti-arthritis

Injectable

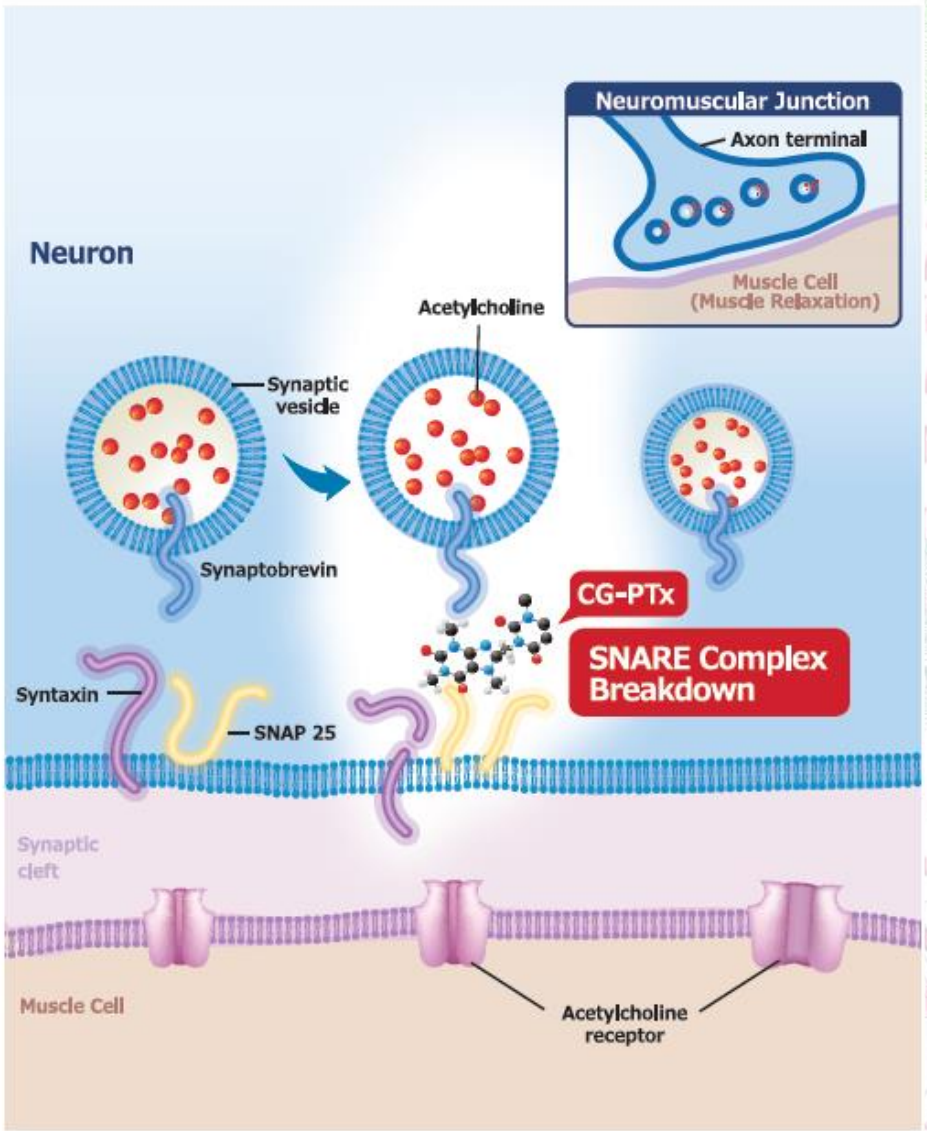

Erase wrinkles
without injection
PTx Serum
Needle free
First Botulinum Toxin type C Peptide

Mechanism of PTx (acting like Botulinum Toxin Type C)

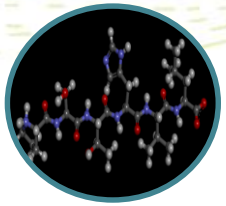
Normal Neuro Transmitter Release



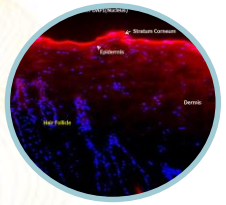
Muscle Relaxation



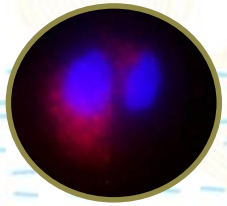
Key Features of PTx



01 Superiority of PTx Peptide
(The First Protease Peptide)

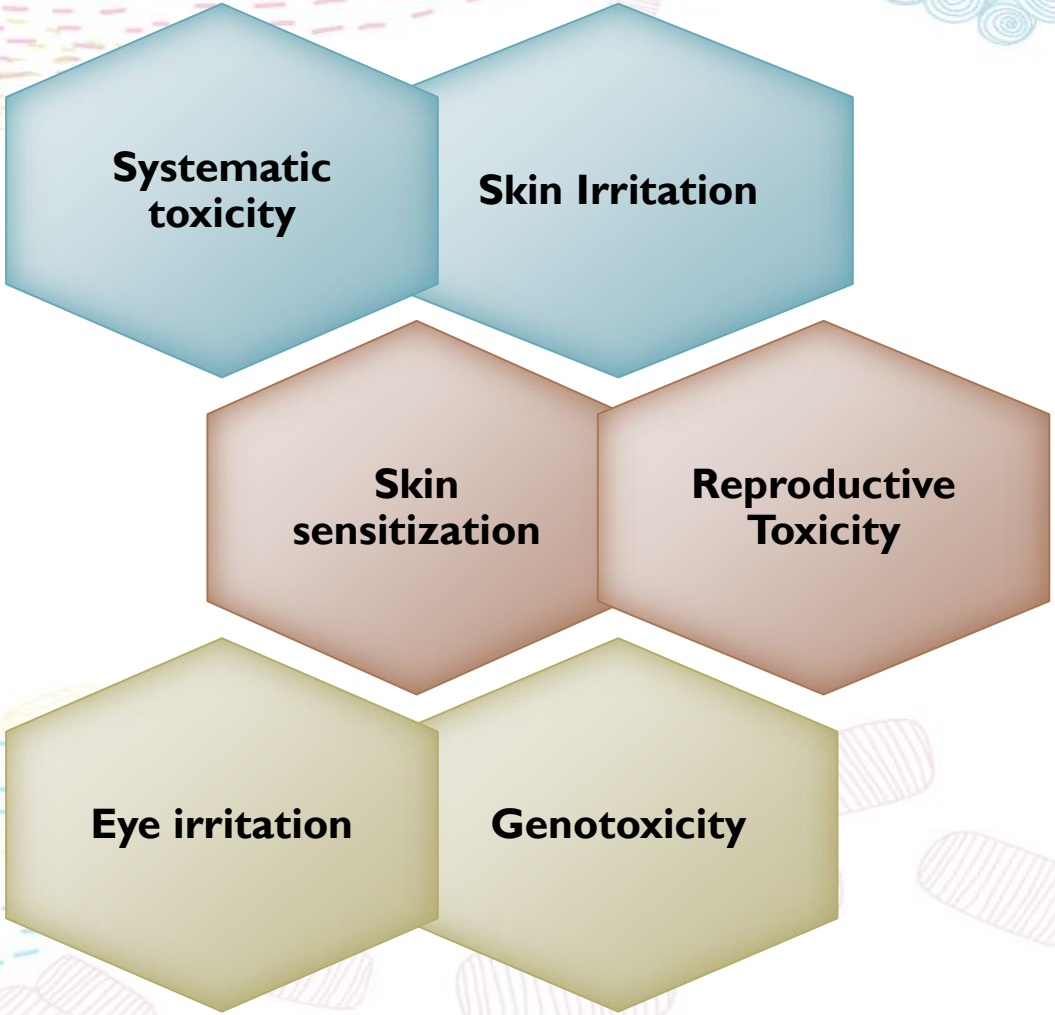


02 Transdermal Delivery System
(Needle Free Application)



03 Nerve Cell Membrane Penetration

Safety of PTx : Toxicology Studies



Preclinical Trial (Pharmaceutical level) is on the way and expect to be done in July, 2020.

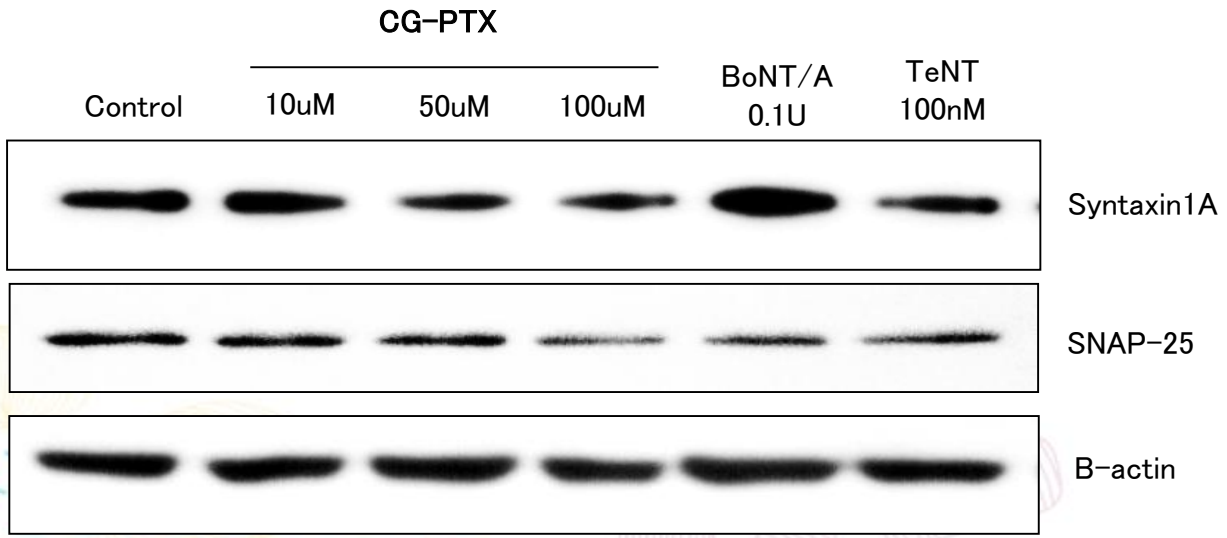
in-vitro Studies

1. Inhibition of Acetylcholine Release
2. SNARE Complex inhibition
3. Nerve Cell membrane Penetration

CG-PTx Cleavage Test on Syntaxin 1a and SNAP-25 in isolated Nerve Cell Total Protein

The First Report of Protein Cleavage Peptide in Scientific History

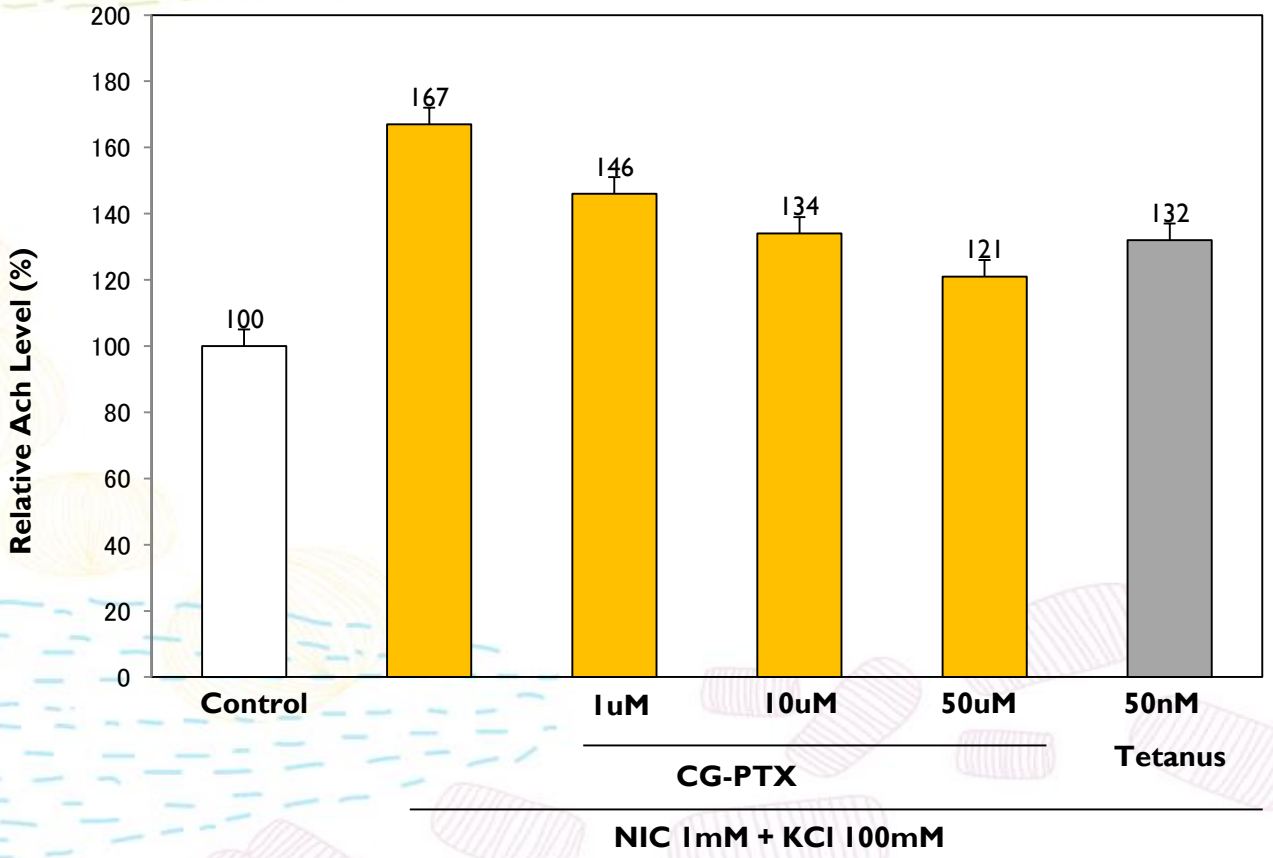
Cell: Human Bone Marrow Neuroblastoma(SH-sy5y)
Sample: Cell Harvest → protein isolation
Reaction Time: 4hours
Analysis: Western blot analysis



CG-PTX enzymatically cleaved syntaxin-1a and SNAP-25 in nerve cells

Inhibition of Acetylcholine Release of CG-PTX

Cell: Human Bone Marrow Neuroblastoma(SH-sy5y) passage11
Culture condition: Serum free DMEM for 48hrs
Induction: NIC(Nicotine)+KCl(Potassium chloride) /30min
Analysis: Choline/Acetylcholine assay Kit(Fluorescence:Ex/Em)

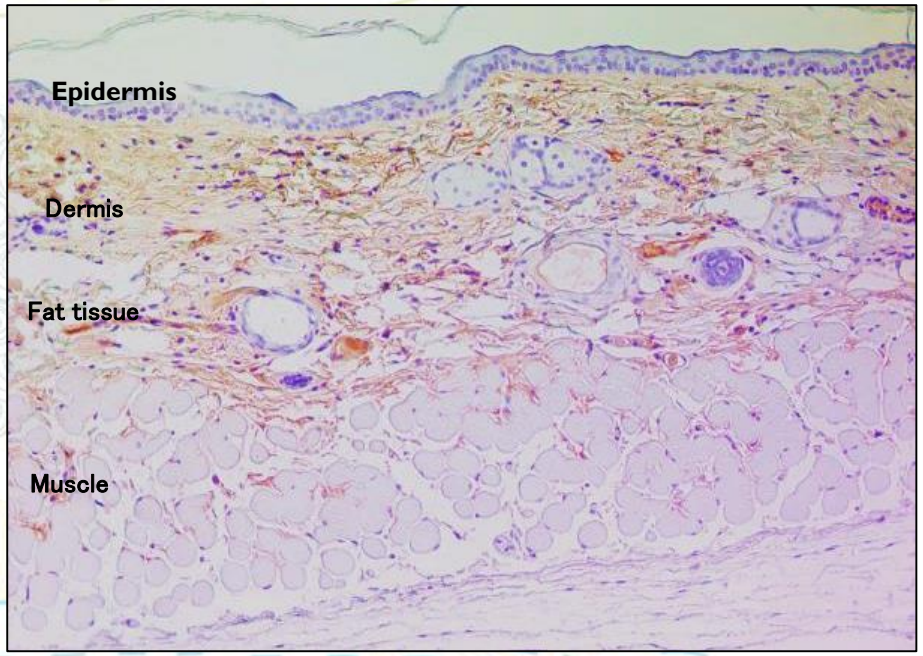


The release of Acetylcholine, a neurotransmitter, was reduced by CG-PTX

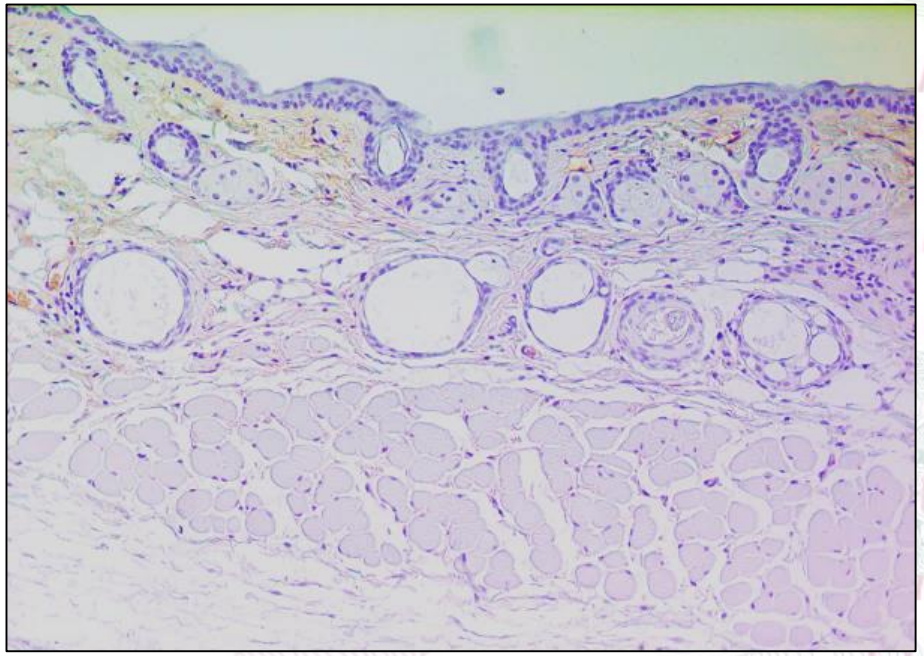
In vivo study of Syntaxin Expression by PTx

Method: immuno histochemitry (Anti-Syntaxin1a)

PBS Topical application



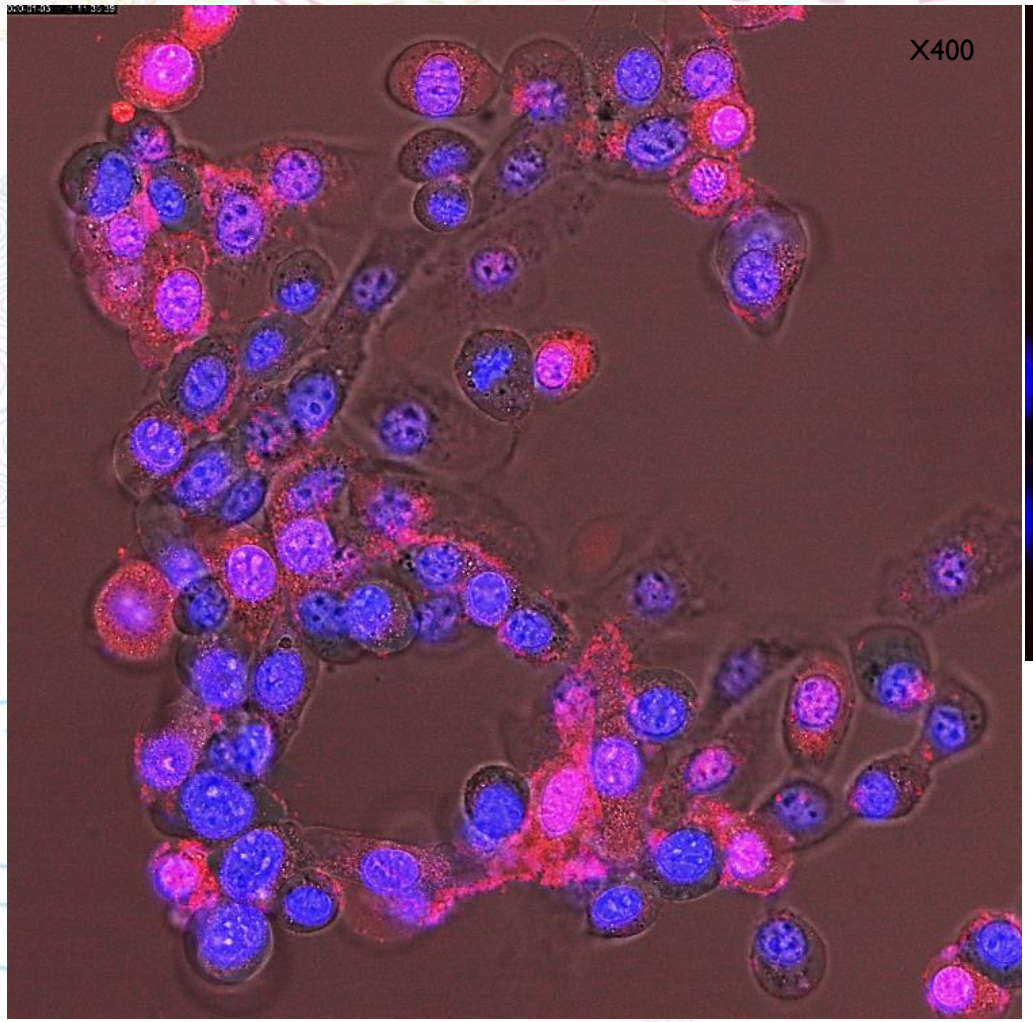
CG-PTx Topical application



Brown: Syntaxin 1a

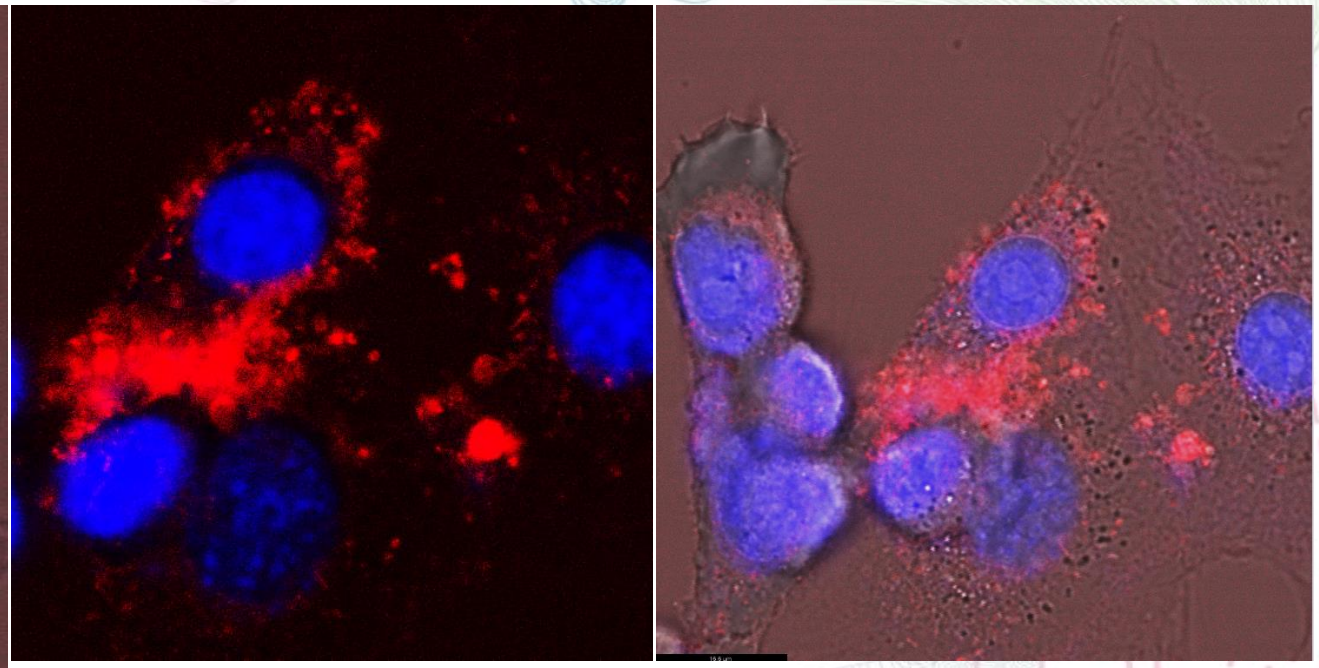
Nerve Cell Membrane Penetration Assay

Cell: Human Bone Marrow Neuroblastoma (SH-sy5y)
Treatment condition: Treat 1hr in serum free DMEM
Concentration: CG-PTX 50uM / BoNT A 0.5U / Tetanus 50nM
Analysis: Confocal Fluorescent microscope



CG-PTX Penetrated into the cytosol of Neuronal Cells

X1400



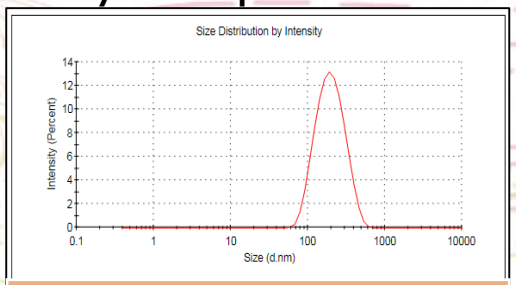
Blue: DAPI; Nucleus
Red: Rhodamine_CG-PTX
Pink: Merge (Blue/Red)

in-vivo Studies

1. Transdermal Delivery
2. Pharmacodynamics
3. Topical Applications

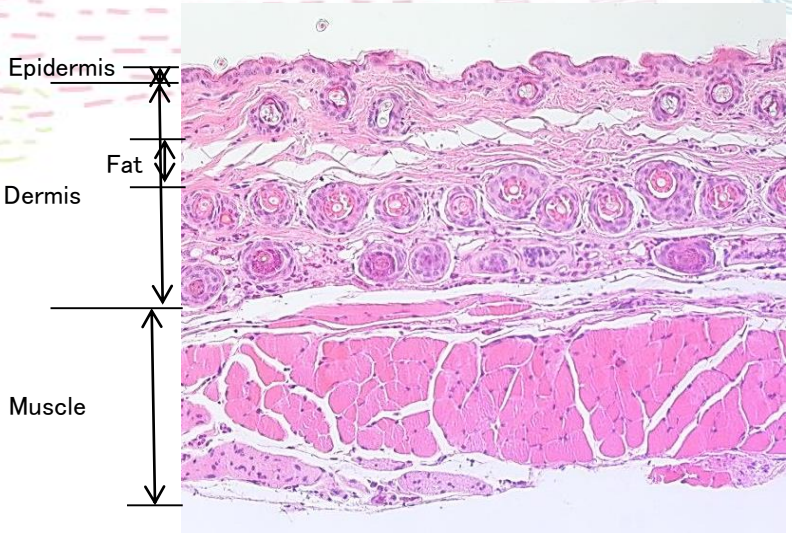
Transdermal Delivery of CG-PTx into Muscle layer

Analysis of Capsulated CG-PTx

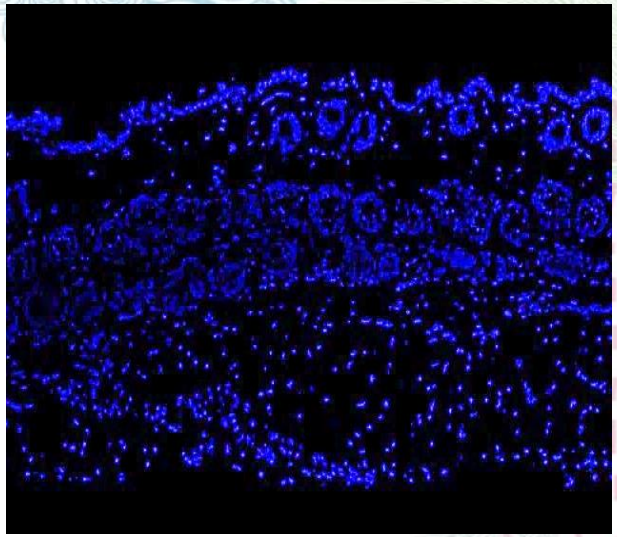


Particle Size (nm)
154.7
Zeta potential(mV)
-64.9
Capsulation ratio (%)
85

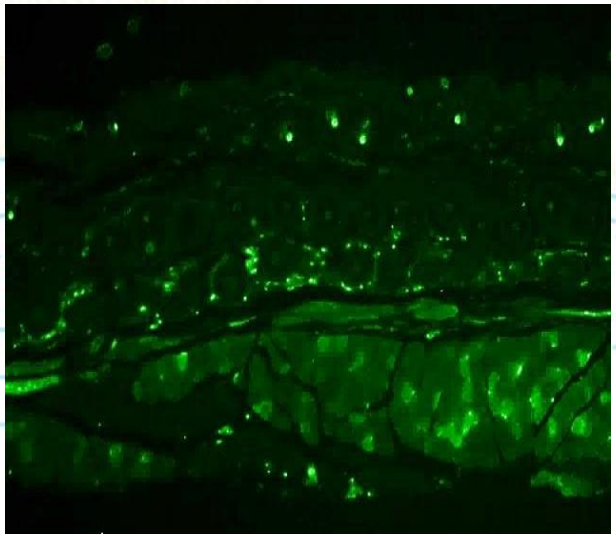
H&E staining



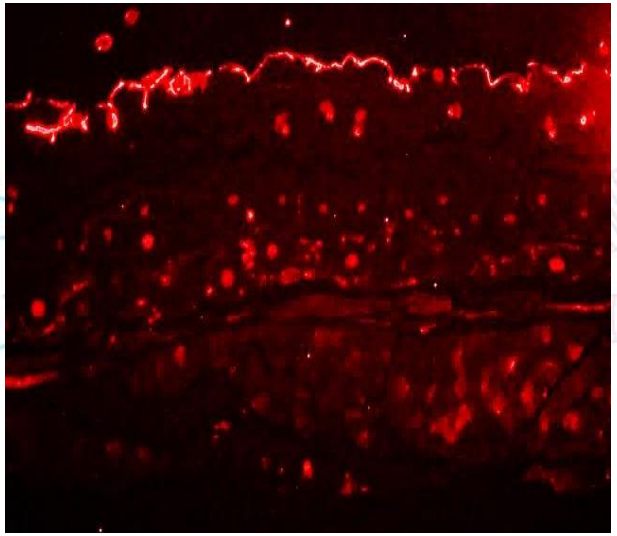
Blue: DAPI-Nucleus



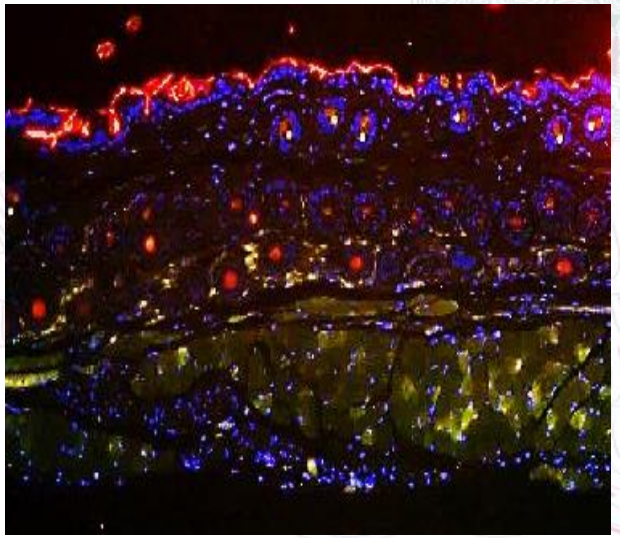
Green: TrkB -Nerve cell



Red: Rhodamine-PTX -PTX Peptide



Merge-yellow, yellowish green



Summary of Clinical Study

Measurement	2weeks (%change)		4weeks (%change)
Sebum	-44.98	↓	-62.25
Pore	-20.83	↓	-37.37
Hydration	15.94	↑	25.02
Skin Surface Elasticity	8.38	↑	17.15
Skin Density	5.24	↑	11.19
Crow's feet	-4.84	↓	-9.30
Skin Redness	-4.78	↓	-7.43
Face Lifting	-1.83	↓	-3.61
Skin Lightening	1.28	↑	2.20

Summary of Clinical Study

Measurement	2weeks (%change)		4weeks (%change)
Open Comedones	-28.29	↓	-58.55
Closed Comedones	-36.84	↓	-61.40
Sebum Contents	-12.47	↓	-30.74
Oil Contents	-22.53	↓	-28.09

Global Assessment of Efficacy	Improvement effect on acne – 95%
	Skin oil contents Improvement effect – 95%
	Skin Sebum Improvement effect – 95%

Summary of Clinical Study

Measurement	2weeks (%change)		4weeks (%change)
VAS (Itching)	-36.638	↓	-68.190
Skin Moisture Content	51.329	↑	65.487
Transepidermal Water Loss (TEWL)	-8.457	↓	-14.418

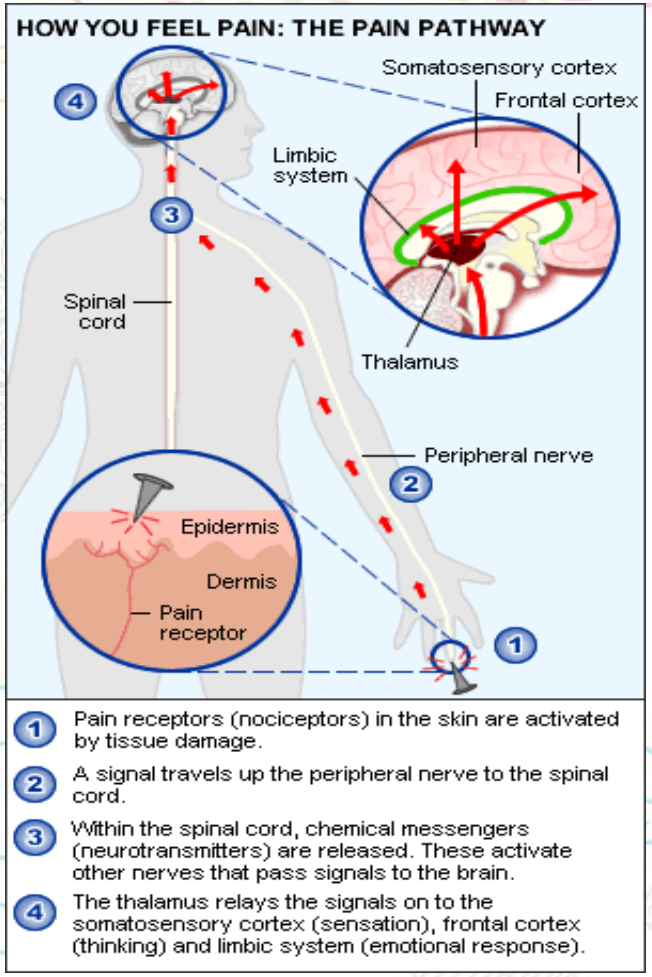
Global Assessment of Efficacy	**effect on atopic dermatitis – 90.5%**

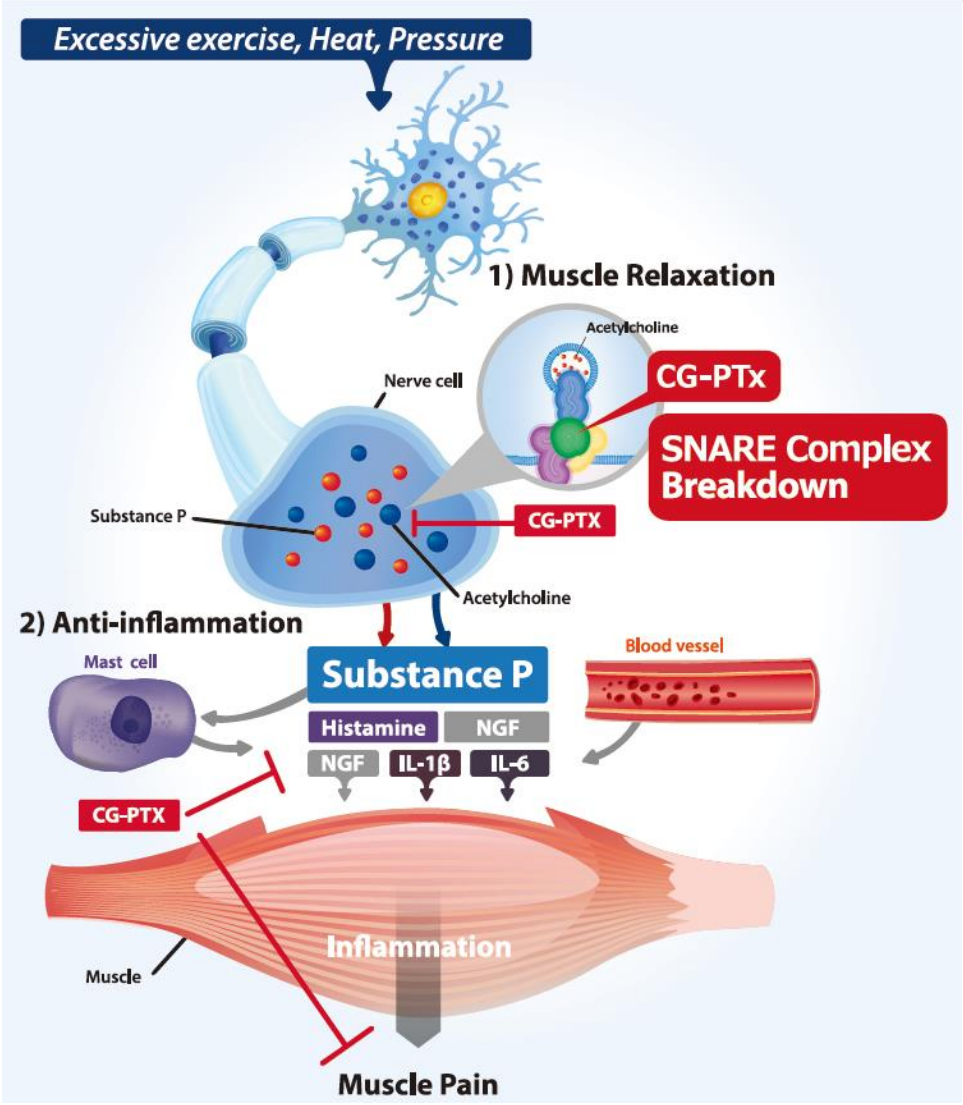
PTx Solution **Control**

PTx Sports-Applications- Stop pains in 5 min!

Pain mechanisms

Muscle pain is produced by the activation of specific receptors (so-called nociceptors): these receptors are specialized for the detection of stimuli that are objectively capable of damaging tissue and that are subjectively perceived as painful.

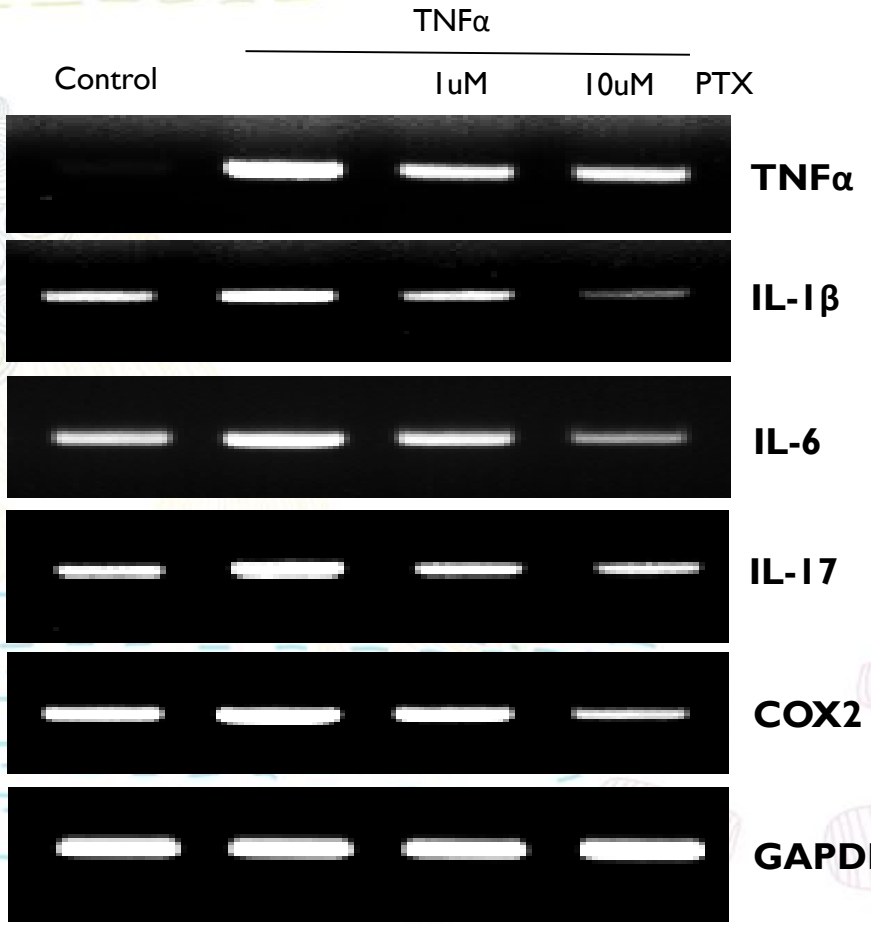




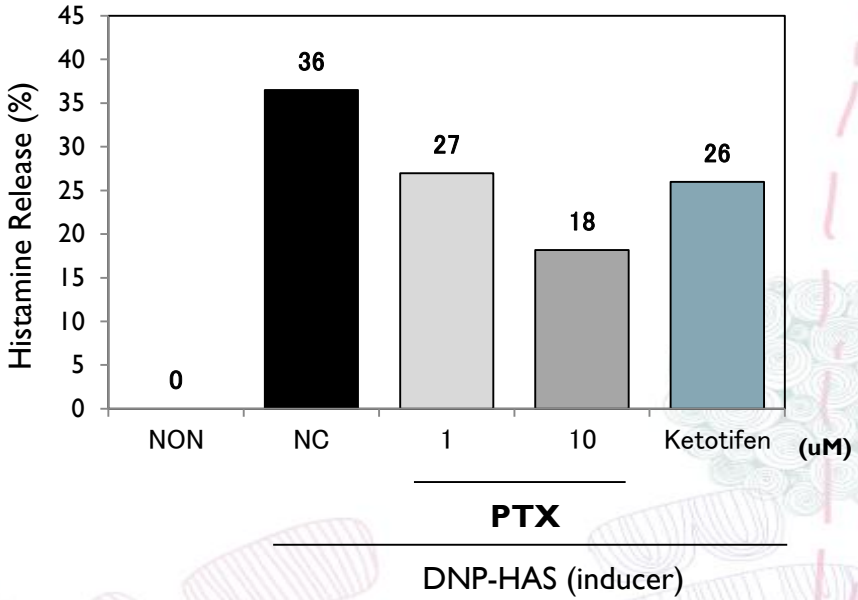
Anti-inflammation (immune cells)

Cells: human Splenocyte
Stimulator: TNFα 20nM for 30min
Method: RT-PCR analysis / ELSIA analysis

Pro-inflammatory cytokine



Histamine Release



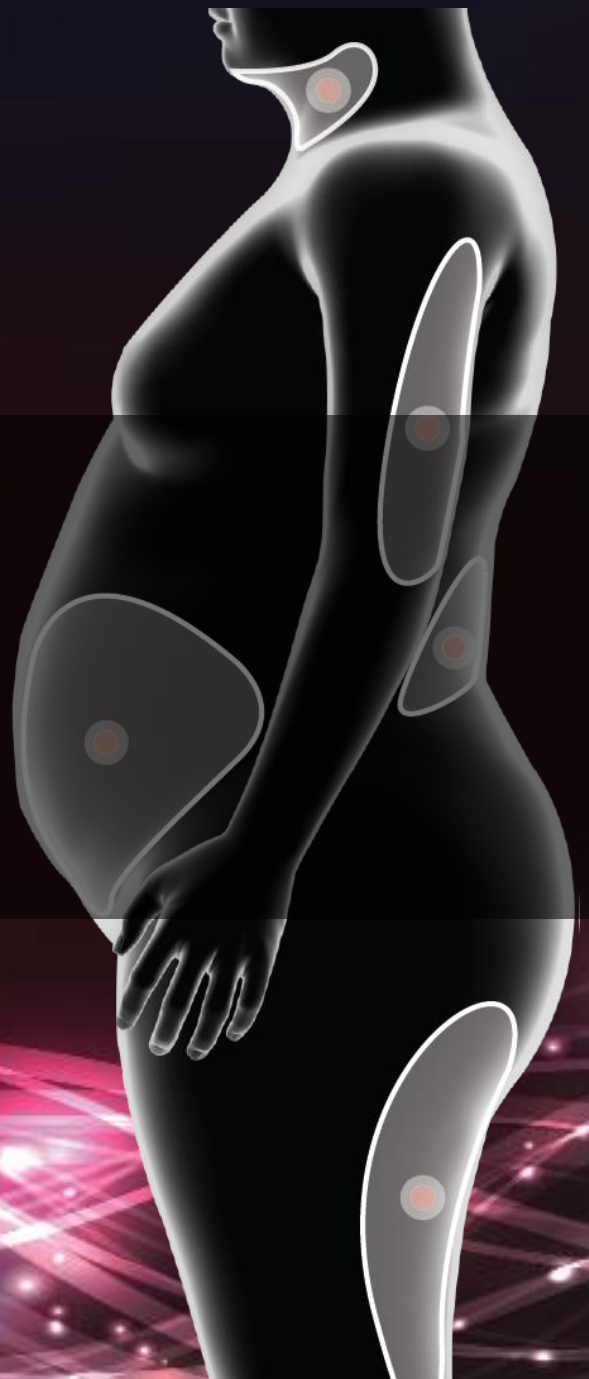
2020
New Products

CG STYLER600

PTx Filler

2. Anti-Obesity

PTx Lipo Serum
(Localized Fat Reduction with Topical Serum)



Summary of Clinical Study

Measurement	2 Weeks (%change)		4 Weeks (%change)
Double Chin	-6.0	↓	-11.0
Calf Swelling	-8.6	↓	-8.7
Skin Surface roughness (Cellulite)	-6.3	↓	-8.5
Femoral Subcutaneous Fatty Layer Interface Length	-4.6	↓	-8.0

SARS-CoV-2 억제 기능의 CG-PEPTIDE

Patent number: 10-2020-0088076 (Peptides able to neutralize servers acute respiratory syndrome coronavirus 2(SARS-CoV-2))

1) Identification

- **Name**: CG-SpikeDown
- **Type(biologic classification):** Synthetic Peptide (chemical synthesis)
- **Molecular weight**: 1663.9Da (12A.A)
- **Solubility**: water soluble

2) Pharmacology

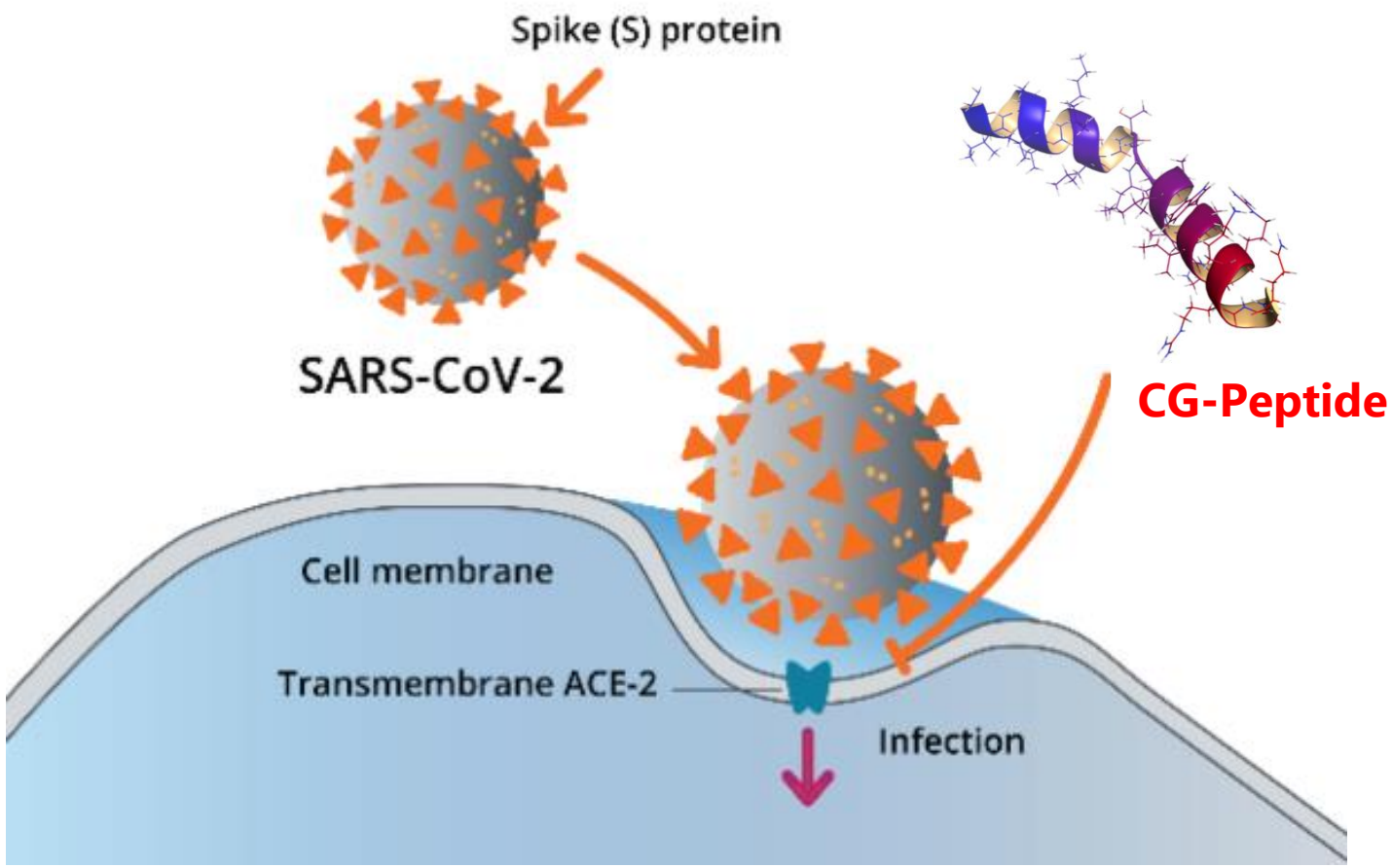
- **Indication**: COVID-19 (코로나 바이러스 감염증 19)
- **Pharmacodynamics**: SARS-CoV-2 Spike protein binding peptide
- **Mechanism of Action**: SARS-CoV-2 (신종코로나 바이러스) 의 Spike protein 에 결합하여, SARS-CoV-2 가 Host Cell 에 침입하는 것을 막는다

3) Pharmacoeconomics

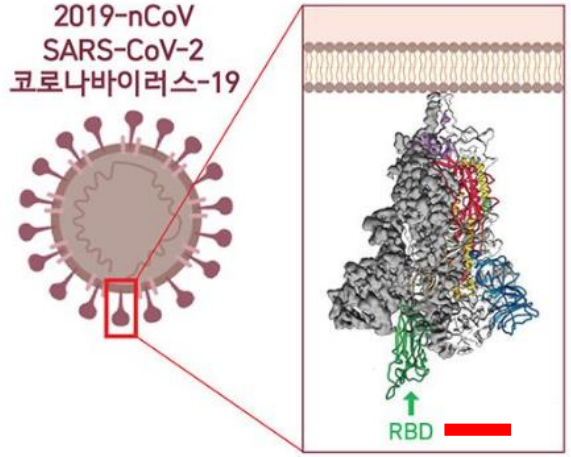
- **Manufacturers**: ㈜케어젠
- **Packagers**: ㈜케어젠

Mode of Action (MOA)

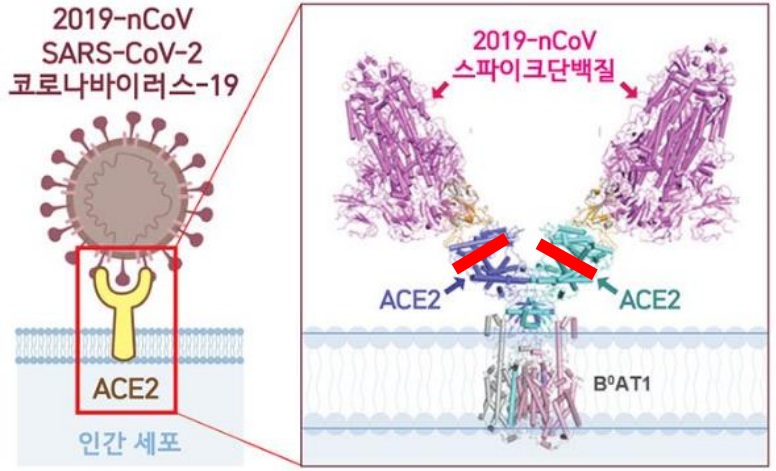
CG-Peptide (Oligopeptide-139;INCI Name)는 SARS-CoV-2 (신종코로나 바이러스) 의 Spike protein 에 결합하여, SARS-CoV-2 가 Host Cell 에 침입하는 것을 막는다.



CG-Peptide



Spike protein RBD binding peptide



Development of Noble Topical Peptide, Spike Down, for COVID-19