2 XSOME SKIN BOOSTER

1Some Exosome Powder – 100mg / 0.0035oz
2Some Activating Diluent – 6ml / 0.203oz

CPNP


2SOME
EXOSOME ACTIVATING DILUENT
Efficient Absorption Of Active Ingredient
5G
6ml / 0.203oz
1SOME
1SOME EXOSOME REJUVENATING POWDER
Multipotent Cell Exosomes
5G
100mg / 0.0035oz
HA
PCL
PLLA
EXO
PDRN

2XSome:

New Generation Skin Booster

2Xsome is the premium Exosome skin booster, formulated to provide the anti-inflammatory, regenerative and skin barrier boosting benefits of Exosomes naturally found in the human body.

2Xsome consists of 2 agents:

1. 1Some Exosome Rejuvenating Powder

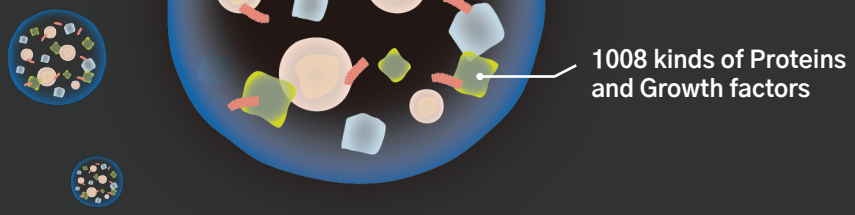
A high concentration stem-cell-derived Exosome lyophilized powder with Sodium Hyaluronate.

2. 2Some Exosome Activating Diluent

An activating fluid with a mixture of Hydrolyzed Collagen, Sodium DNA, Copper Tripeptide-1 and vitamins that works to maximize Exosome absorption.

2Xsome Main Ingredient

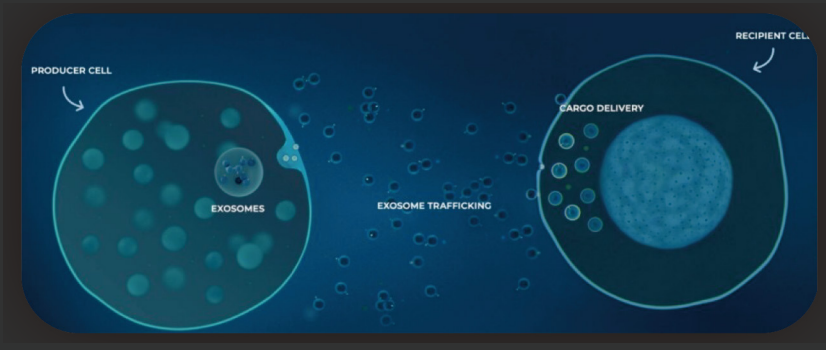
‘Exosomes’



Exosomes are tiny extracellular vesicles about 100 nanometres in size. They are the most important mechanism in cell-to-cell communication in our bodies, acting as messengers delivering lipids, proteins and RNA to activate biological responses in the recipient cells.

Exosomes were shown to intervene in processes such as protein delivery, blood coagulation, cell waste disposal, etc. With their cell-penetrating ability, they are gaining popularity for clinical applications as a next-generation cell regenerative ingredient.

Exosomes Mechanism of Action



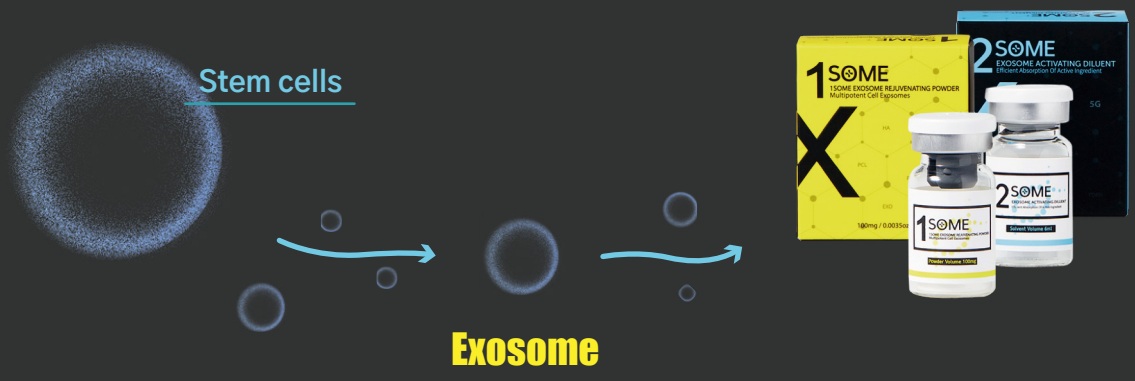
1. Anti-inflammatory Action

Exosomes have a big role in relieving inflammation, transporting the enzymes needed in the generation of extracellular Adenosine, a powerful anti-inflammatory agent which regulates immune activity and prevents skin inflammation, as well as possible post-inflammatory hyperpigmentation.

2. Promotion of Skin Barrier Structural Components

Exosomes promote the synthesis of critical components of the skin barrier – Sphingolipids. These are essential molecules of the epidermis that intervene in the modulation of our skin cells, involved in ceramide production, keratinocyte proliferation and differentiation, maintaining the skin barrier health.

Exosome Purification Process



Exosome

composes only 0.1~0.5% of the stem cell culture fluid

Exosomes are isolated from a Stem Cell Culture Media, which refers to the remaining solution after a cell culture process that contains various growth factors, such as EGF, as well as peptides, amongst other elements from cells during the culture process.

The Culture Media is prone to also contain undesired ingredients.

- Exosomes, the key ingredient, comprise only 0.5% of the solution.
- **2Xsome** has successfully isolated and purified the 0.5% of Exosomes from the culture solution and applied them to its skin booster formula.

Exosome Applications

From cosmetics to cell therapy

Exosomes, as a body-identical ingredient with high stability, are very unlikely to cause adverse reactions. At the same time, with their cell penetrating mechanism, they penetrate into the skin to deliver regeneration signals. It is not an irritant agent, and can be used by patients suffering from skin conditions such as acne and atopic dermatitis.

“Exosomes will eventually replace over 70% of the current Stem Cell Market”

— Chung-Ang University Hospital Prof. Yoo Kwang-Ho

Prof. Yoo, A Dermatology Professor at the Chung-Ang University Hospital, is currently conducting Exosome based research regarding its properties beyond just cell waste disposal, funded by the National Research Foundation of Korea.

Cho et al. Stem Cell Research & Therapy (2018) 9:187
https://doi.org/10.1186/s13287-018-0939-5

Stem Cell Research & Therapy

LETTER Open Access

Exosomes derived from human adipose tissue-derived mesenchymal stem cells alleviate atopic dermatitis

Byong Seung Cho, Jin Ock Kim, Dae Hyun Ha and Yong Weon Yi

Abstract

Exosomes are nano-sized vesicles (30–200 nm) constantly released by almost all cells. The ability of exosomes to travel between cells and deliver their cargo, which includes lipids, proteins, and nucleic acids, makes them an appealing cell-free therapy option to treat multiple diseases. Here, we investigated for the first time whether human adipose tissue-derived mesenchymal stem cell-derived exosomes (ASC-exosomes) can ameliorate atopic dermatitis (AD) in an in vivo mouse model. When injected either intravenously (IV) or subcutaneously (SC) into NC/Nga mice treated with house dust mite antigens, ASC-exosomes were found to reduce pathological symptoms such as clinical score, the levels of serum IgE, the number of eosinophils in blood, and the infiltration of mast cells, CD86+, and CD206+ cells in skin lesions. ASC-exosomes also significantly reduced mRNA expression of various inflammatory cytokines such as interleukin (IL)-4, IL-23, IL-31, and tumor necrosis factor-α (TNF-α) in AD skin lesions of Nc/Nga mice. Taken together, these results suggest that ASC-exosomes can be a novel promising cell-free therapeutic modality for AD treatment.

Keywords: Exosome, Adipose tissue-derived mesenchymal stem cells, Atopic dermatitis, Inflammation

Introduction

Since current treatment options for atopic dermatitis (AD) are limited and have potentially harmful side effects, there are unmet needs to develop novel therapies that are safe and efficacious [1]. Several biologics targeting pro-inflammatory cytokines are currently under development and dupilumab, a dual inhibitor of IL-4 and IL-13, was recently approved by the US FDA for treating adults with moderate to severe AD [1]. Although long-term follow-up study is needed to determine late side effects of dupilumab [1], its efficacy indicates that multiple targeting is a plausible way to treat AD [2].

Several studies have demonstrated that the allergic progress in AD could be suppressed by mesenchymal stem cells (MSCs) derived from human umbilical cord blood (UCB-MSC), bone marrow (BM-MSC), or adipose tissue (ASC) by modulating multiple targets [3]. However, therapeutic use of MSCs has several drawbacks, such as poor engraftment efficiency, potential tumor formation, unwanted immune responses, non-specific differentiation, short half-life, and the difficulty of quality control before administration [4].

Exosomes are nanovesicles (30–200 nm) released by almost all cells and found in all body fluids [4]. Exosomes deliver their cargo (proteins, lipids, and nucleic acids) from originating cells to recipient cells. Growing evidence suggests that exosomes derived from stem cells could be a promising alternative to cell-based therapy because exosomes would avoid most of the problems associated with cell-based therapy while recapitulating the therapeutic efficacy of stem cells [4]. For example, exosomes have no risk of tumor formation as they cannot replicate. They also can be sterilized by filtration and have a longer shelf-life than cells themselves. Being much smaller than stem cells, exosomes easily circulate through the body and reach sites of injury. In addition, long-term repetitive administration of exosomes does not elicit toxicity [5]. Here, we for the first time investigated the therapeutic effect of exosomes derived from human ASC (ASC-exosomes) on AD in a mouse model.

* Correspondence: cbs@exocobio.com
ExoCoBio Exosome Institute (EEI), ExoCoBio Inc., STE 306, 19 Gasan digital 1-ro, Geumcheon-gu, Seoul 08594, Republic of Korea

J. Soc. Cosmet. Sci. Korea
Vol. 42, No. 4, December 2016, 359-366

pISSN 1226-2587
eISSN 2288-9507
http://dx.doi.org/10.15230/SCSK.2016.42.4.359

각질형성세포 유래 엑소좀이 피부각질형성세포의 증식과 이주에 미치는 영향

김도윤·유호진·황대일·장상희*·이환명†

호서대학교 화장품과학과,
*구미대학교 식품영양전공

(2016년 10월 11일 접수, 2016년 11월 21일 수정, 2016년 11월 29일 채택)

Effect of Keratinocyte Derived Exosome on Proliferation and Migration on Human Skin Keratinocyte

Do Yoon Kim, Ho Jin Yu, Dae Il Hwang, Sang Hee Jang*, and Hwan Myung Lee†

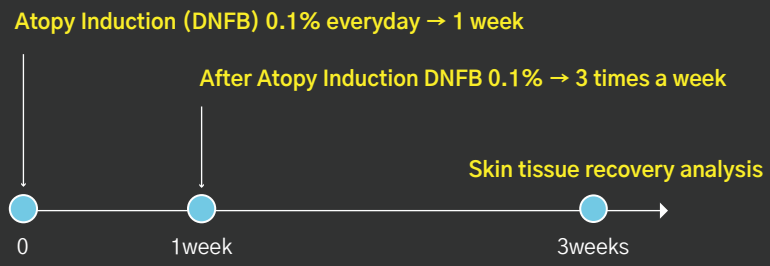
Department of Cosmetic Science, College of Life and Health Science, Hoseo University, 20 Hoseo-ro, Baebang-eup, Asan, Chungcheongnam-do 31499, Korea
*Department of Food and Nutrion, Gumi University, Gumi, Gyeongsangbuk-do 39213, Korea

(Received October 11, 2016; Revised November 21, 2016; Accepted November 29, 2016)

요 약: 엑소좀은 세포에서 분비되는 작은 소낭체로서, 기원세포와 조직에 따라 다양한 기능을 수행하며, 세포생존 및 세포 간 커뮤니케이션에 중요한 역할을 한다. 최근 엑소좀을 활용하여 종양연구, 면역질환 개선, 질병진단 bio-marker 개발 등 다양한 분야에서 연구가 진행되고 있으나, 피부세포에서 분비기전 및 피부 생리적 기능에 대한 연구는 미흡한 실정이다. 따라서 본 연구에서 인체피부 유래 각질형성세포(HaCaT)로부터 분리된 엑소좀이 피부각질형성세포의 증식과 이주에 미치는 영향을 확인하고자 하였다. HaCaT으로부터 ExoQuick-TC를 활용하여 엑소좀을 분리하고, 열처리 엑소좀(boiled exosome)과 무처리 엑소좀(unboiled exosome)으로 구분하였다. HaCaT 유래 엑소좀은 농도 의존적으로(0.1 ~ 20 μg/mL) HaCaT의 증식을 유도하였으며, 20 μg/mL에서 대조군(control)에 비해 각각 186.96 ± 3.87%(열처리) 또는 193.48 ± 10.48%(무처리)의 증식 유도활성을 나타내었다. 또한 HaCaT 유래 무처리 엑소좀은 농도 의존적인(0.1 ~ 20 μg/mL) HaCaT의 이주활성을 나타내었고, 20 μg/mL에서 대조군에 비해 179.39 ± 4.89%의 이주를 유도하였다. 그러나 열처리 엑소좀은 이주 유도활성을 나타내지 않았다. 뿐만 아니라 무처리 HaCaT 유래 엑소좀은 collagen sprout outgrowth를 농도 의존적으로 유도함을 확인하였다. 이러한 결과를 통해서 HaCaT 유래 엑소좀은 지질 및 열에 안정한 물질이 세포의 증식을 유도하고, 단백질 또는 열에 불안정한 물질이 세포의 이동 및 sprout out growth 활성에 관여하는 것으로 확인되었다. 따라서 피부각질형성세포 유래 엑소좀은 피부의 재상피화 및 상처치유 등의 활성을 나타낼 수 있으며, 향후 화장품소재로서 응용 가능성이 확인되었다.

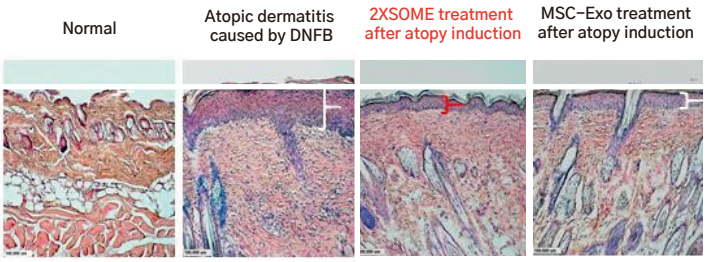
Non-clinical Study Results – Atopy Improvement

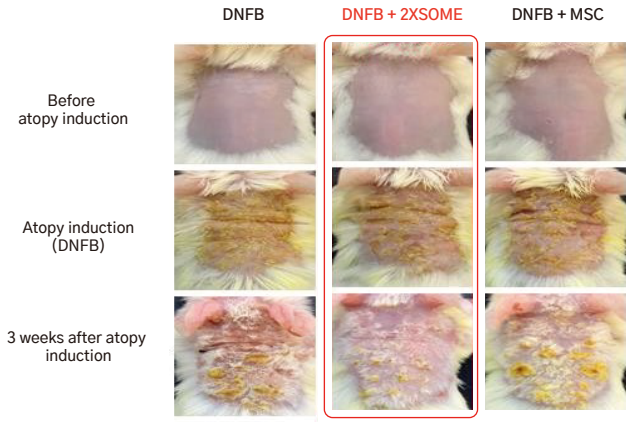
6 weeks old
Mouse (BALB/c Male)



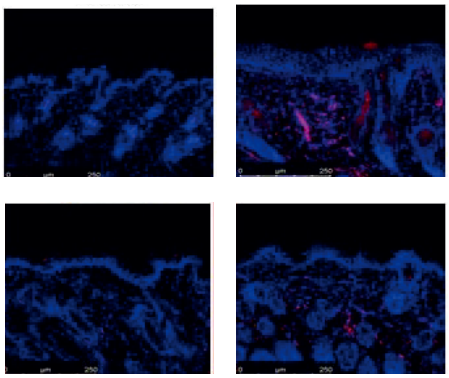
Daily Exosome Application (Spray) Concentration: 1x10particles/ml

Changes in skin thickness after atopy induction

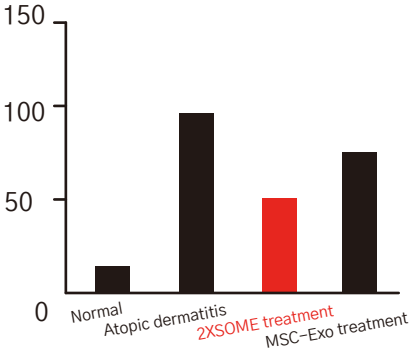




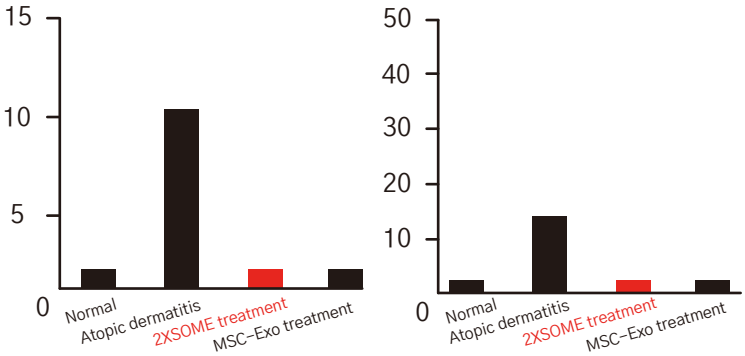
Atopic inflammatory factor change (Cox2)



Changes in skin thickness



Atopic inflammatory factor change



Stability Study Results

Safety inspection conducted by the KFDA through an external agent

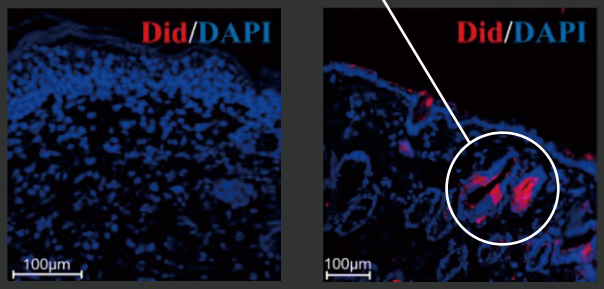
Safety test items	Status	Progression	Company	Remarks
Single dose toxicity test	Completed	100%	Biotox Tech	No adverse reaction
13-week repeated administration toxicity test	Completed	100%	Biotox Tech	No adverse reaction
Skin sensitization test (LLNA – alternative test method)	Completed	100%	Biotox Tech	No adverse reaction
Invitro 3T3 NRU phototoxicity test	Completed	100%	Biotox Tech	No adverse reaction
Photosensitivity writing test	Completed	100%	Biotox Tech	No adverse reaction
Return mutation test	Completed	100%	Biotox Tech	No adverse reaction
Chromosomal abnormality test	Completed	100%	Biotox Tech	No adverse reaction
Micro-nucleus test	Completed	100%	Biotox Tech	No adverse reaction
Skin irritation test (alternative test method)	Completed	100%	Biotox Tech	No adverse reaction
Irritation test (alternative test method)	Completed	100%	Biotox Tech	No adverse reaction
Body patch test	Completed	100%	Korea Institute of Skin Science	No adverse reaction

COA	Status	Progression	Company	Remarks
Mycoplasma test	Completed	100%	Bio PS	No adverse reaction
Aseptic (fungus, germs) test	Completed	100%	Bio PS	No adverse reaction
Virus test (invitro)	Completed	100%	Bio PS	No adverse reaction
Virus test (invitro)	Completed	100%	Notus	No adverse reaction

Exosomes have been confirmed as a safe ingredient through extensive testing by the KFDA

Exosome Skin Tissue Penetration Study Results

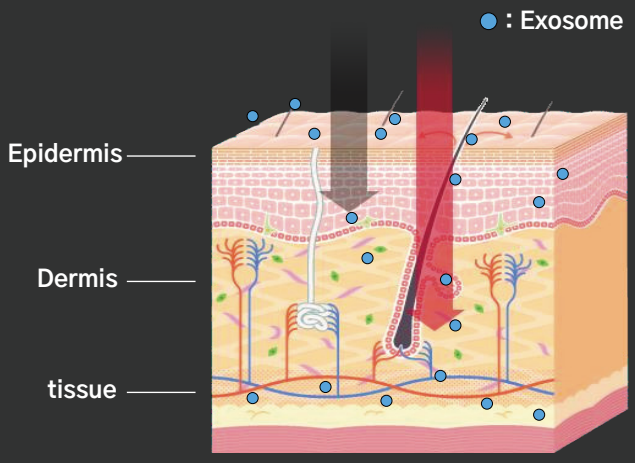
Exosomes are shown
as red beads below



Before

24 hours later

Exosome penetration power
has been confirmed through testing
showing penetration into the dermis



Location tracked through DID dye

Exosome Regeneration Case Study

Scalp rejuvenation & hair growth after Exosome application

Before

4 weeks

8 weeks

Exosomes have shown excellent scalp and hair follicle regeneration effects after only 8 weeks.

2Xsome Skin Booster Benefits

- Inflammation relief
- Skin cell regeneration
- Skin elasticity recovery
- Skin hydration improvement
- Wrinkle appearance improvement
- Compromised skin barrier restoration
- Skin tone & complexion improvement

2Xsome Target Areas

2Xsome Efficacy Case Study

BEFORE

AFTER

2 XSOME SKIN BOOSTER

2XSOME
SKIN BOOSTER

1Some Exosome Powder – 100mg / 0.0035oz
2Some Activating Diluent – 6ml / 0.203oz