



MEDIPOST

Alopecia project using MSC conditioned media

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M E D I P O S T

Background

Mesenchymal stem cell (MSC) belongs to an adult stem cells and is often found in some tissues in human body including umbilical cord blood and bone marrow. MSC is the most popular modality in development of stem cell therapeutics at the moment. All six stem cell drugs approved in the world are based on the MSC. As opposed to other modality in stem cell therapeutics, it is free from ethical issues and has some unique properties useful in the therapeutic application including immune neutrality and homing effect to the injury site.

Paracrine effect is known to play a key role in therapeutic efficacy in MSC. Upon being administered in the body, MSC adapts itself to the new environment in the diseased areas and starts to secrete various trophic factors including cytokines and growth factors involving in anti-inflammation, anti-apoptosis, mitogenesis and activation of endogenous stem cells. The therapeutic effects of the trophic factors secreted by the MSC are collectively referred as paracrine effect or paracrine action of MSC. MSC conditioned media (MSC CM) is a collection of such therapeutic trophic factors secreted by the cells.

Alopecia project at MEDIPOST is based on the MSC CM to take advantage of the paracrine effect of MSC for the treatment of one of the most widespread disease in men and women, hair loss.

Priming of MSC for efficacy optimization

MSC is a living organism and can adapt itself upon exposure to a disease environment by changing its trophic factor secretion pattern. MSC CM is a collection of such trophic factors. MSC should be pretreated before collection of CM for use in a specific efficacy of desire to optimize trophic factor composition of the CM, for example, for hair growth potency. For pretreatment, we first exposed MSC in vitro to the artificially designed environment mimicking alopecia state in hair follicles ("Priming"). We selected molecules previously reported in the literature known to involve (or abundant) in hair loss (and in hair loss lesion), which resulted in vast number of combinations of the molecules by statistical experiment design. Screening was done by measuring proliferation of hDP (human derma papillar) cells in vitro. One of the combination was finally chosen as an optimized priming factors for pretreatment of MSC for alopecia, and the MSC CM obtained after optimized treatment was named CM-3¹.

¹ The trade name was registered to ICID as NGF-574H



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Ex vivo testing on human hair growth

Human hair follicles were isolated and tested for hair growth in length in the absence or presence of primed MSC CM. After 6 day treatment, the CM-3 showed superiority in hair growth in length compared with control².

Clinical trial for proof of concept³

Alopecia is known that the efficacy correlation between animal model and human subject is not well established. Active ingredients showing remarkable efficacy in the lab often loses its efficacy in human in large part because disease mechanism and progression for alopecia is complex in human. In order to confirm efficacy in human subjects, an IRB approved double blind placebo-controlled clinical study has been designed and conducted with total 30 subjects after fulfilling safety requirement mandated by MFDS, a regulatory authority in Korea, as an ingredient for cosmetics product. The subjects are diagnosed androgenic alopecia before enrollment and randomly assigned to either test or control group. The cosmetic hair essence formulation containing CM-3 at concentration of 5% or without CM-3, respectively, was applied to subjects in each group for total 16 weeks once daily by topical administration. The subjects were asked to visit the sites for assessment in terms of (a) hair density, (b) hair diameter, and (c) hair growth rate at each 4, 8 and 16 week by phototrichogram. The superiority in all assessment was proved in each assessment in treatment group compared with placebo control group with statistical significance ($p < 0.001$).

Efficacy comparison (literature survey)

Hair density improvement of the CM-3 containing formulation obtained in the above POC clinical trial is compared with those reported in the literature⁴ for Minoxidil (ROGAINE[®]) which is available in the market for treatment or prevention of alopecia as an OTC drug. Despite shorter length of treatment period for CM-3 (16 weeks for CM-3 vs. 48 weeks for Minoxidil, respectively), the improvement in hair density by CM-3 was superior to those by alopecia drug in the market.

² The vehicle media with MSC CM without priming and vehicle media alone, respectively, was employed as a control.

³ The clinical study is not registered to clinicaltrials.gov

⁴ Please refer the literature at [https://www.jaad.org/article/S0190-9622\(03\)04317-2/abstract](https://www.jaad.org/article/S0190-9622(03)04317-2/abstract)



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Mechanism of Action

The study on the mechanism of action (MOA) of CM-3 for hair growth is ongoing. We identified some cytokines in CM-3 that play a key role in the hair growth potency. It is believed that up-regulation of angiogenesis may be involved in the MOA and also CM-3 increases expression of some genes involved in the hair stem cell proliferation.

Commercial Development

CM-3 containing product will be launched in Korea as a functional cosmetics with a claim for improvement of hair loss. The cosmetics law in Korea allow efficacy claims for hair loss in special category of cosmetics product of the functional cosmetics starting May 2017. Currently the CM-3 containing product is in the process of registration to MFDS as a functional cosmetics for hair loss improvement. The market launch in Korea is expected in 4Q 2018 or in 1Q 2019.

About MEDIPOST

MEDIPOST is the largest private cord blood bank in Korea with more than 220,000 cord blood units under storage. The company has dedicated to R&D and commercialization of stem cell therapeutics since its foundation in 2000. With one product already in the market for treatment of osteoarthritis and two other products in the clinical pipeline for broncho pulmonary dysplasia (BPD) and Alzheimer disease (AD), respectively, MEDIPOST is one of the leading stem cell therapeutic companies in the world. The company is listed to KOSDAQ (KQ:078160) in Korea since 2005. For more about the company, please visit our website at www.medi-post.com.