# PRESS RELEASE



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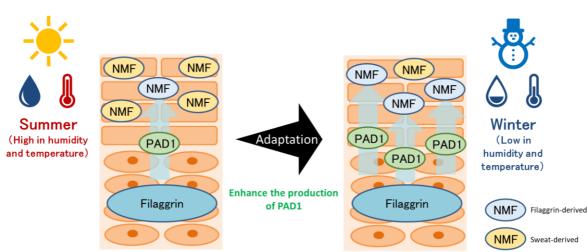
# Shiseido Elucidates Skin's Adaptation Mechanism to Dry Environment

~Its second technology to create beauty in harmonious coexistence with environment and based on the wealth it provides~

Shiseido Company, Limited ("Shiseido") has revealed that in a dry environment, the skin promotes the production of Peptidyl Arginine Deiminase 1 (PAD1), an enzyme that produces Natural Moisturizing Factor (NMF). This suggests that the skin has the ability to retain moisture, coexisting with the environment. In addition, we have found a new ingredient that enhances PAD1 expression and supports the skin's moisture retention ability. These findings are expected to be applied to the development of cosmetics that boost the skin's abilities to adapt and resist to a dry environment. Some of these results were presented at the 46th Annual Meeting of the Japanese Society for Investigative Dermatology held from December 3 to 5, 2021.

We, at Shiseido, are aiming to realize beauty in positive coexistence with the environment through the Premium/Sustainability approach of our unique R&D philosophy, "DYNAMIC HARMONY". While focusing on the skin's response mechanism to environmental changes, we will be engaged in the development of the technologies that convert natural environmental factors such as humidity and temperature into the power of beauty, following the announcement of UV conversion technology\* in November, 2021.

\*Shiseido develops innovative technology to convert ultraviolet light into light that brings about beneficial effects on the skin (2021)



https://corp.shiseido.com/en/news/detail.html?n=0000000003256

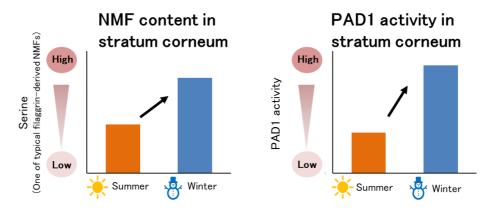
Figure 1. Environment-adaptive moisture retention ability (image)

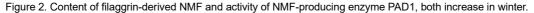
# Research background

Our skin has acquired adaptability to the external environment, such as sweating at high temperatures and production of melanin during UV exposure, etc., in the evolution of mankind. However, skin's adaptive capability to a dry environment caused by low humidity and low temperature has not been fully clarified. Thus, by applying our knowledge and findings on the production pathway of skin's natural moisturizing factor NMF gathered through more than 40 years of research, we have conducted research to elucidate the skin's innate adaptation mechanism to a dry environment.

### Discovering the skin's ability to create "moisture" to adapt to a dry environment

NMF is supplied mainly through the pathways of "filaggrin", a protein that makes up the skin, and "sweat" and serves as an essential component of moisture retention in the stratum corneum. In this study, we compared the NMF contents between summer and winter in the same individuals and found that filaggrinderived NMF was more abundant in winter than in summer (Figure 2 left). Then, we further analyzed NMFproducing enzymes in the same individuals in summer and winter in order to clarify the mechanism of seasonal variation of filaggrin-derived NMF and found that the activity of PAD1, which promotes NMF production, was also increased in winter. In addition, through our culture experiments on a 3D skin model under controlled temperature and humidity conditions, we confirmed that PAD1 was upregulated in a lowhumidity and low-temperature environment. With these results, it was revealed that skin enhances its moisture retention ability by boosting the production of NMF-producing enzyme PAD1 in order to adapt to a dry environment caused by low humidity and low temperature.





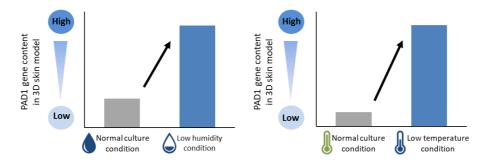
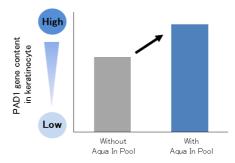


Figure 3. PAD1 gene content increased in low-humidity and low-temperature environment.

#### Discovery of an ingredient promoting PAD1 expression

After searching for ingredients that promote the expression of PAD1, a key enzyme for environmentadaptive moisture retention, we discovered that "Aqua In Pool", an ingredient uniquely developed by Shiseido, has the effect of inducing PAD1 production. In addition, we also identified several plant extracts with similar effects. These ingredients are expected to help further enhance the skin's adaptive ability to a dry environment.



# Future prospects

While changes in the natural environment become increasingly noticeable worldwide, we will further advance our technologies based on the new idea of "accepting the environment and living in harmony". Following the first phase of our technology for coexistence with ultraviolet light and then the environmental factors such as low humidity and low temperature that we revealed in this research, we will continue to take on new challenges to develop technologies that make positive, beneficial use of various environmental factors and deliver beauty innovations to people around the world with the aim of realizing our corporate mission, "BEAUTY INNOVATIONS FOR A BETTER WORLD".

### <Reference>

## Researchers' challenge

Research started with our belief in the power of skin

Changes of the four seasons add color to our hearts. That said, environmental factors such as UV rays, dryness, and pollen also pose a threat to healthy skin. Winter is a particularly difficult season for those who suffer from dry skin as the skin can be easily damaged. With the wish to solve such skin problems, we focused on the skin's innate ability to adapt to the external environment. Our skin has been evolving over a very long period of time, and its ability to adapt to heat and UV rays is well known. Inspired by these findings, we started the research with our belief in the power of the skin thinking that our skin shouldn't be totally vulnerable to a dry environment.



Researcher, Daichi Murata

## Discoveries based on "more than 40 years of research"

The NMF production mechanism, including PAD1, is an area that Shiseido has been studying for more than 40 years. By comprehensively analyzing 860 types of stratum corneum proteins through combining the findings of our long-established research with cutting-edge research methods and techniques, we have elucidated new functions of a key enzyme PAD1. Going forward, we will pursue research on the relationship between the skin and the external environment and apply the findings to beauty care solutions that maximize the skin's innate ability, while aiming to create a world in which people around the world can live positively in harmony with the beautiful environment.