November 2021
Shiseido Company, Limited

Press Release

Shiseido Reveals Part of Mechanism that Photoaging Induces Dull Skin via Cutting-Edge Epigenetics Research

~TIPARP gene, the key to radiant skin, discovered from approximately 30,000 genes~

Shiseido Company, Limited ("Shiseido") has elucidated part of the mechanism by which photoaging*1 and other factors induce acquired genetics (epigenetics) to make skin dull. By analyzing two types of massive dataset; gene expression data independently collected by Shiseido and Methylated DNA*2 data through external big data source, we revealed that the methylation of the TIPARP gene due to photoaging leads to hindered transmission of information that would normally suppress dullness of the skin. We also found that an extract from a microorganism living in the deep sea promotes the expression of the TIPARP gene. This prevents DNA methylation of TIPARP gene and supports the make skin brighter without spots and dullness. Some of these research results were presented at the 45th Annual Meeting of the Japanese Society for Investigative Dermatology held from December 11 to 13, 2020 and the 30th Annual Meeting of the Japanese Society for Pigment Cell Research held on October 23 and 24, 2021.

This research is being conducted in the Individual/Universal approach under the Shiseido's unique R&D philosophy "DYNAMIC HARMONY". By collecting and analyzing a vast amount of human gene expression data and clarifying the relationship with skin concerns, we aim to offer new solutions that will lead consumers to their ideal skin.

*1 Skin aging phenomena such as spots and wrinkles caused by UV rays in sunlight. It is considered to be a major cause of skin aging.

*2 Methylated DNA data: An epigenetic regulation of genes in which genetic information is locked and cannot be read properly.

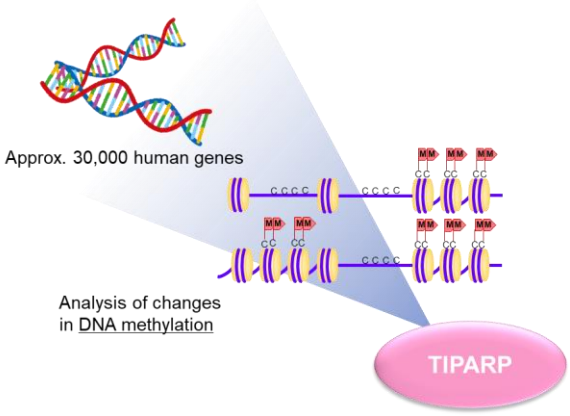

Figure 1: TIPARP, the gene responsible for epigenetic skin dullness.

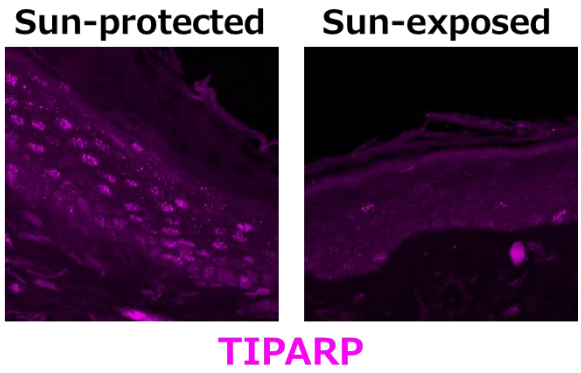

Figure 2: TIPARP expression is reduced at Sun--exposed area

Research Background

Shiseido has conducted research on a wide range of genes to study the differences between normal skin and photoaged skin. In 2006, we independently collected genetic information of approximately 30,000 genes in the skin of sun-protected, sun-exposed, and spots by using a comprehensive analysis method called the "DNA microarray method", which was very innovative in the cosmetics industry back then, and clarified the differences in gene expression by area. After that, we conducted further research assuming that epigenetics, a mechanism in which DNA information is acquired depending on the amount of UV exposure and lifestyles, as examples might be partly responsible for the changes in gene expression. This time, we analyzed a huge amount of data that combines our accumulated research findings and public big data to identify the causes and effects of photoaging on the skin more fundamentally and accurately.

TIPARP, a gene epigenetically regulated by photoaging

TIPARP is a type of antioxidant factor and associates with skin lightness such as by preventing yellowish dullness in the skin and melanin production. In this study, we conducted a bioinformatics analysis*3 on two types of massive genetic information dataset using our proprietary method, and found that the expression control region of the TIPARP gene is methylated due to photoaging caused by UV rays, etc., and TIPARP expression is epigenetically suppressed, resulting in dull skin.

*3 Bioinformatics analysis: Technology to analyze mainly biological data using information science methods such as statistics and programming skills.

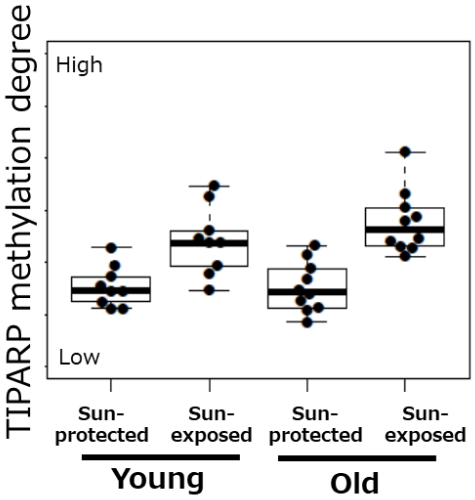

Figure 3: TIPARP epigenetically increases the degree of methylation.

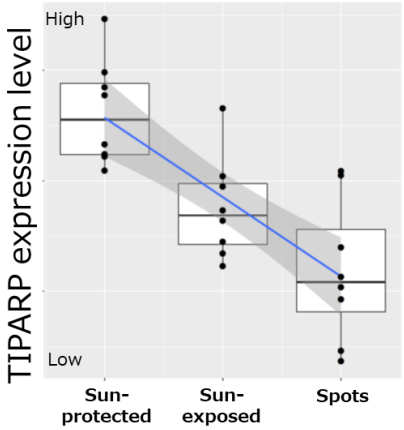

Figure 4: TIPARP expression is epigenetically reduced.

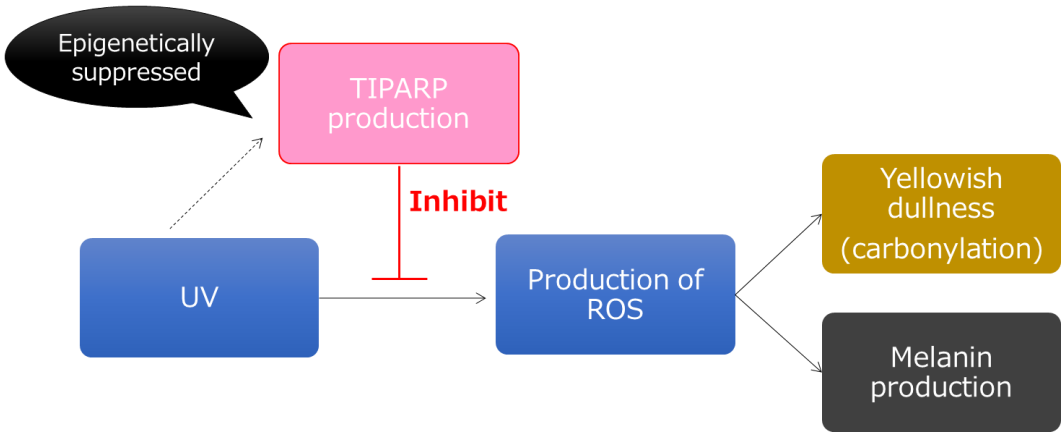

Figure 5: Relation between TIPARP and dull skin.

Search for ingredients that promote TIPARP production

Once a gene is methylated, it cannot be reversed and its information can be no longer read properly. It is also known that even when genes are not methylated, they become more susceptible to methylation if they are being inactive for a long time. Therefore, we thought that we could maintain the skin less prone to dullness by promoting the expression of the TIPARP gene and creating a state of being always active. Meanwhile, we searched for useful ingredients and found that an extract derived from a microorganism living in the deep sea was effective in promoting the expression of the TIPARP gene. In addition, the appearance of yellowish, dulled skin could be reduced by continuous application of a base containing the extract.

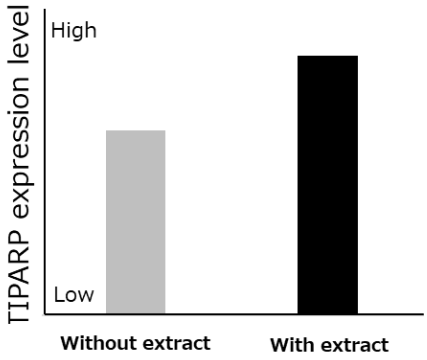

Figure 6: Extract -induced increase in TIPARP expression

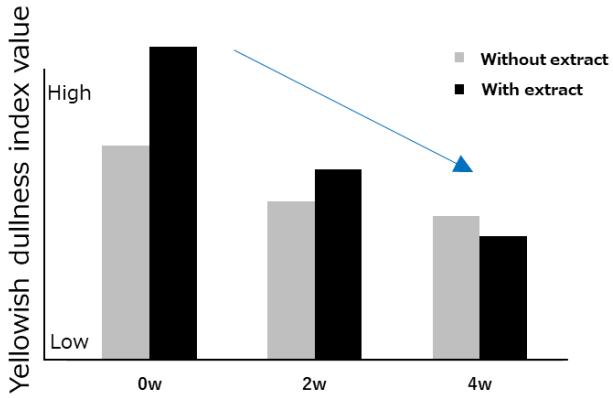

Figure 7: Extract's improvement effect on yellowish dullness in the skin

Future Prospects

Through our most advanced epigenetics research, we have succeeded in finding a new approach to treat skin dullness regardless of the amount of UV exposure. By increasing the TIPARP expression, we may be able to modify the skin's function of improving dullness deteriorated by epigenetic changes, bringing closer to its normal state. In order to realize our corporate mission, "BEAUTY INNOVATIONS FOR A BETTER WORLD", we will continue to promote research focusing on epigenetic changes and skin concerns, and deliver beauty innovations to realize the ideal skin for each individual.

Shiseido's new R&D philosophy "DYNAMIC HARMONY"

Shiseido Formulates its Unique R&D philosophy "DYNAMIC HARMONY" (2021)
https://corp.shiseido.com/en/news/detail.html?n=00000000003252
The DYNAMIC HARMONY special website:
https://corp.shiseido.com/en/rd/dynamicharmony/

<Reference Information>

Researchers' Challenge

■ Challenge to the cutting-edge epigenetics research

This research was carried out working together with a team that analyzed DNA methylation and gene expression, etc., and a team that studied the mechanism by which the factors selected by the team create dull skin and searched for ingredients useful for improving dullness.

This time in particular, we had to fuse two different types of enormous dataset and perform integrated data processing, a highly challenging bioinformatics analysis that required all kinds of knowledge, including programming skills, biology, statistics, etc. Through these efforts, we could reach TIPARP, the gene responsible for epigenetic dullness of the skin.

■ Thoughts on this research

By elucidating some of the fundamental causes of skin dullness, we revealed the possibility that anyone can achieve their innate healthy beautiful skin regardless of their age or lifestyle. Going forward, we will further develop this technology, aiming to develop a variety of products and services that will lead to solutions for consumers suffering from dull skin with an unprecedented approach.