[BIOINFO 2023]

Identification of genetic loci associated with skin aging traits in a large Korean population

Joong-Gon Shin[1], Jung Yeon Seo[1], Seo-Gyeong Lee[1], Beomsu Kim[2], Yunkwan Kim[1], Sangseob Leem[1], Seung Won You[1], Sun Gyoo Park[1], Hong-Hee Won[2]* and Nae Gyu Kang[1]*

[1] *Research and Innovation Center, CTO, LG Household & Healthcare*
[2] *Samsung Advanced Institute for Health Sciences and Technology (SAIHST), Sungkyunkwan University, Samsung Medical Center*
**Corresponding author: wonhh@skku.edu, ngkang@lghnh.com*

Aging is a consequence of the long-term accumulation of intrinsic and extrinsic influences, and visible signs of aging, such as wrinkle formation, changes in skin tone, and pigmentation, mainly appear on the face. Intrinsic aging is a series of physiological changes mostly caused by genetic factors, and the discovery of genetic variants and their molecular functions is essential to understand the biology of skin aging. Recent genome-wide association studies (GWASs) have shown efforts to identify the genetic factors for several skin traits, including skin color and pigmentation. However, these GWAS primarily focused on European populations, and only a few studies have been conducted on Asian populations, limiting our understanding of the genetic basis of skin traits in Asians.

To discover the genetic factors related to skin aging, we conducted a large-scale GWAS on skin traits of 17,019 Korean women, including two types of periorbital wrinkles (under-eye wrinkles and crow's feet), three skin color indexes (CIE L^*, a^*, and b^*), and facial pigmented spots.

We identified 13, 10, and 7 significant genetic loci associated with periorbital wrinkles, skin color, and facial pigmented spots, respectively (P-value $< 5.0 \times 10^{-8}$). Interestingly, we observed common genetic loci affect different skin traits (*OCA2* for periorbital wrinkles and skin color, *BNC2* for periorbital wrinkles and facial pigmented spots), and observed potential causal relationship between progressions of facial pigmented spots and facial wrinkles from Mendelian randomization analysis. Additional genetic correlation analysis between skin traits demonstrated the genetic similarities or differences between subtypes (genetic correlation = 0.56 (under-eye wrinkles and crow's feet), -0.99 (L^* and a^*), -0.70 (L^* and b^*), and 0.56 (a^* and b^*)). These results implied that there may exist a

possibility of the shared or distinctive biological pathways between skin traits and/or within subtypes. Our results revealed the genetic determinants of skin aging in Koreans. Further functional evaluation of the identified genes will help to further understand the genetic aspects of each skin trait and the overall skin aging process. Interestingly, we observed shared or distinctive genetic factors between skin aging traits in Korean women.