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Commentary

The genetic and environmental architecture of human hair traits: a shift toward precision medicine in hair disorders

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Human hair exhibits remarkable diversity at the macroscopic level, with visible and quantifiable variations in shape, density, geometry, colour, shine, surface friction, mechanical properties and sensory qualities.[1] These phenotypic differences are largely genetically driven and are mediated through microscopic features and structural and biophysical properties of the hair fibre, which vary across populations with different geo-racial origins.[1] Despite this variability, all hair fibres share a common fundamental structure along with largely consistent chemical composition.[2]

Over recent decades, the genetic basis of hair traits has been extensively studied, particularly through genome-wide association studies (GWAS). For instance, hair colour has been linked to 123 autosomal loci and 1 locus on the X chromosome,[3] while hair greying has been associated with a genetic variant in *IRF4*.[4] Scalp hair shape has been linked with 12 genetic loci[5] and the genetic influences on other traits, including eyebrow thickness, monobrow, beard thickness and balding have been described.[4] Additionally, studies of monogenic Mendelian hair disorders reveal that rare pathogenic variants in single genes can lead to both syndromic and nonsyndromic hair-related conditions, providing new insights into hair follicle (HF) biology and associated pathologies.[6]

Adding to this evidence, Qian *et al*. conducted a GWAS in 5735 individuals of Han Chinese ancestry and identified genetic variants associated with hair traits, including rs11940736 (near *SPRY1*) and rs10908366 (*RSPO1*) with number of hairs per follicular unit, and rs3771033 (*NRP2*) with follicular unit density (FUD).[7] Notably, these genes were found to be expressed in the dermal papillae of both mice and humans, indicating their potential role in HF biology by modulating gene expression within this pivotal structure.[7]

Beyond genetics, environmental factors, including hormones, have been observed to affect hair traits.[2] Qian *et al*. showed the correlation between hair density measurements and factors including age, sex, body mass index, menopausal status, early menarche and age at first pregnancy.[7] These findings are supportive of the contribution of hormonal fluctuations across the reproductive lifespan in HF dynamics. Indeed, hair morphogenesis involves complex interplay between genetic and environmental elements.[2] A recent gene–environment interaction study has successfully identified the evidence of such an interaction in frontal fibrosing alopecia, an increasingly common scarring alopecia.[8] In their analysis, Qian *et al*. reported statistical interactions between rs3771033 with age at first pregnancy and menopause on FUD,[7] although functional validation of these interactions is warranted. Developments in multiomic technologies, including transcriptomics, proteomics and metabolomics, now provide robust tools to dissect underlining mechanisms.[9] Furthermore, gene–gene interactions (epistasis) are known to affect hair traits, such as hair colour,[10] and merit further exploration.

Using the UK Biobank dataset, Qian *et al*. demonstrated that rs3771033 confers a genotype-specific response to finasteride, a 5α-reductase inhibitor commonly used for treatment of male pattern baldness.[7] This underscores the potential of genetic testing to guide treatment decisions and supports the move towards precision medicine in hair disorders. This finding motivates further investigations across diverse ancestral groups to identify genetic markers predictive of therapeutic response, ultimately enabling risk and prognostic stratification and personalized treatment for various alopecia phenotypes.

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