

PRESS RELEASE

New findings on hair loss in men

Researchers in Bonn identify rare genetic variants involved in male-pattern hair loss

Bonn, September 22 – A receding hairline, a total loss of hair from the crown, and ultimately, the classical horseshoe-shaped pattern of baldness: Previous research into male pattern hair loss, also termed androgenetic alopecia, has implicated multiple common genetic variants. Human geneticists from the University Hospital of Bonn (UKB) and by the Transdisciplinary Research Unit "Life & Health" of the University of Bonn have now performed a systematic investigation of the extent to which rare genetic variants may also contribute to this disorder. For this purpose, they analyzed the genetic sequences of 72,469 male participants from the UK Biobank project. The analyses identified five significantly associated genes, and further corroborated genes implicated in previous research. The results have now been published in the prestigious scientific journal *Nature Communications*.

Male-pattern hair loss is the most common form of hair loss in men, and is largely attributable to hereditary factors. Current treatment options and risk prediction are suboptimal, thus necessitating research into the genetic underpinnings of the condition. To date, studies worldwide have focused primarily on common genetic variants, and have implicated more than 350 genetic loci, in particular the androgen receptor gene, which is located on the maternally inherited X chromosome. In contrast, the contribution to this common condition of rare genetic variants has traditionally been assumed to be low. However, systematic analyses of rare variants have been lacking. "Such analyses are more challenging as they require large cohorts, and the genetic sequences must be captured base by base, e.g., through genome or exome sequencing of affected individuals," explained first author Sabrina Henne, who is a doctoral student at the Institute of Human Genetics at the UKB and the University of Bonn. The statistical challenge lies in the fact that these rare genetic variants may be carried by very few, or even single, individuals. "That is why we apply gene-based analyses that first collapse variants on the basis of the genes in which they are located," explained corresponding author PD Dr. Stefanie Heilmann-Heimbach, who is a research group leader at the Institute of Human Genetics at the UKB at the University of Bonn. Among other methods, the Bonn researchers used a type of sequence kernel association test (SKAT), which is a popular method for detecting associations with rare variants, as well as GenRisk, which is a method developed at the Institute of Genomic Statistics and Bioinformatics (IGSB) at the UKB and the University of Bonn.

Possible relevance of rare variants in male-pattern hair loss

The research involved the analysis of genetic sequences from 72,469 male UK Biobank participants. Within this extensive data set, Bonn geneticists, together with researchers from the IGSB and the Center for Human Genetics at the University Hospital Marburg, examined

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rare gene variants that occur in less than one percent of the population. Using modern bioinformatic and statistical methods, they found associations between male-pattern hair loss and rare genetic variants in the following five genes: *EDA2R*, *WNT10A*, *HEPH*, *CEPT1*, and *EIF3F*.

Prior to the analyses, *EDA2R* and *WNT10A* were already considered candidate genes, as based on previous analyses of common variants. "Our study provides further evidence that these two genes play a role, and that this occurs through both common and rare variants," explained Dr. Stefanie Heilmann-Heimbach. Similarly, *HEPH* is located in a genetic region that has already been implicated by common variants, namely the *EDA2R*/Androgen receptor, which is a region that has consistently shown the strongest association with male-pattern hair loss in past association studies. "However, *HEPH* itself has never been considered as a candidate gene. Our study suggests that it may also play a role," explained Sabrina Henne. "The genes *CEPT1* and *EIF3F* are located in genetic regions that have not yet been associated with male-pattern hair loss. They are thus entirely new candidate genes, and we hypothesize that rare variants within these genes contribute to the genetic predisposition. *HEPH*, *CEPT1*, and *EIF3F* represent highly plausible new candidate genes, given their previously described role in hair development and growth." Furthermore, the results of the study suggest that genes that are known to cause rare inherited diseases affecting both skin and hair (such as the ectodermal dysplasias) may also play a role in the development of male-pattern hair loss. The researchers hope that the puzzle pieces they have discovered will improve understanding of the causes of hair loss, and thus facilitate reliable risk prediction and improved treatment strategies.

The research was supported by funding from the Medical Faculty of the University of Bonn. Prof. Dr. Markus Nöthen, Director of the Institute of Human Genetics at UKB and co-author of the study, is a member of the Transdisciplinary Research Area (TRA) "Life and Health" at the University of Bonn. The publication costs in open access format were funded by the DEAL project of the University of Bonn.

Publication:

Sabrina Henne et al.: Analysis of 72,469 UK Biobank exomes links rare variants to male-pattern hair loss; Nature Communications; DOI: <https://doi.org/10.1038/s41467-023-41186-w>

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Visuals:



Caption: Researchers at the UKB and University of Bonn uncover rare genetic variants involved in male-pattern hair loss: (from left to right) PD Dr. Stefanie Heilmann-Heimbach (Institute of Human Genetics), second author Rana Aldisi (Institute of Genomic Statistics and Bioinformatics), and Sabrina Henne (Institute of Human Genetics).

Image credit: University Hospital Bonn / Katharina Wislsperger

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About the University Hospital Bonn: The UKB cares for about 500,000 patients per year, employs about 9,000 people and has a balance sheet total of 1.6 billion euros. In addition to the more than 3,300 medical and dental students, a further 585 people are trained in numerous healthcare professions each year. The UKB is ranked number one among university hospitals (UK) in NRW in the Science Ranking as well as in the Focus Clinic List and has the third highest case mix index (case severity index) in Germany. The F.A.Z. Institute has named the UKB Germany's most sought-after employer and training champion among public hospitals in Germany in 2022 and 2023.