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Refinement of genetic signals for psoriasis by combining European-origin and South Asian populations

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A Michigan Medicine study found that combining genetic samples from patients of different ethnic backgrounds created a clearer picture for analyzing genetic variants in psoriasis patients and led to the discovery of new genetic signals.

In this international effort, researchers analyzed blood samples from 2,590 psoriasis cases and 1,720 control subjects of South Asian origin, most seen at dermatology clinics in India and Pakistan. The group of South Asian volunteers was then compared to a much larger existing group of psoriasis cases and controls of European origin.

The goal was to compare the frequency of genetic variants—which exist in everyone—between the cases and the controls to help understand which genes are the most important drivers of psoriasis. They found that inclusion of South Asian subjects allowed them to identify two psoriasis genetic signals that they had not previously discovered. The results are published in *Human Genetics and Genomics Advances*.

"We found that these European-origin and South Asian populations were not greatly different in genetic terms, meaning that we could combine them in genome-wide association studies," said James Elder, M.D., Ph.D., senior author of the paper and Kirk D. Wuepper Professor of Molecular Genetic Dermatology at Michigan Medicine. "This can be very valuable for mapping genetic susceptibility signals not only in

psoriasis, but other conditions as well. Due to the large effects of Human Leukocyte-Associated genes on immune system function, combining these two populations allowed us to pinpoint several genetic variations within HLA genes that are very likely to play a causal role in psoriasis, by either altering the antigen-presenting function of these genes, or the way that they are regulated in cells of our immune system."

A genome-wide association study allows researchers to zero in on particular genetic regions, bringing them closer to identifying what particular genes are experiencing altered structures or regulation due to a disease. Elder says this study is another step towards connecting these genetic signals to the genes they affect in psoriasis.

"In order to be able to develop better treatments, we have to know which gene is really being affected and how it occurs," he said. "This starts with increasing the resolution of our individual genetic profiles, which we believe will get us out of the current logjam of not knowing for sure which genes the 'genetic signals' that we have tracked down actually affect. Once we know the genes, we can start devising treatment that specifically target the proteins that they produce. Hopefully, these differences between each of us will allow us to develop personalized medical treatments, based on the genetic differences between people that we measured in the lab during our research studies, but now can readily be tested for in the clinic."

More information: Philip E. Stuart et al, Transethnic analysis of psoriasis susceptibility in South Asians and Europeans enhances fine mapping in the MHC and genome wide, *Human Genetics and Genomics Advances* (2021). DOI: 10.1016/j.xhgg.2021.100069

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