Gene variation is 'major genetic determinant of psoriasis'

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A specific genetic region that has been increasingly identified as the strongest genetic link to psoriasis has an even more significant role in the chronic skin disease than has been suspected, University of Utah medical researchers show in a new study.

In the Aug. 13 issue of *PLoS Genetics*, researchers in the U School of Medicine's Department of Dermatology confirm that the presence of HLA-Cw*0602, a gene variation or allele on chromosome 6 found to be associated with psoriasis by numerous investigators, is the "major genetic determinant" of psoriasis, but that other nearby genetic variations also play an independent role in contributing to the disease

"The HLA-Cw*0602 gene variation stands alone as a high risk for psoriasis," said Gerald G. Krueger, M.D., professor of dermatology, Benning Presidential Endowed Chair holder, and a co-author on the study. "A major question has been: are there other genetic variations in this region that associate with psoriasis?"

The study reported in PLoS Genetics identifies two other genetic variations on chromosome 6 that also have significant association with psoriasis. People who have all three genetic variations are nearly nine times more at risk for psoriasis.

Psoriasis is a chronic disease that causes red scaly patches on the skin and affects up to 7.5 million people in the United States. About 25 percent of subjects with the disease also develop a painful inflammation

of the joints called psoriatic arthritis.

University researchers, led by first author Bing-Jian Feng, Ph.D., postdoctoral fellow, and senior author David E. Goldgar, Ph.D., research professor of dermatology in the U of U School of Medicine, reached their conclusion after an expanded analysis of data from a study published earlier this year by investigators at Utah in collaboration with colleagues from the University of Michigan and Washington University.

That study (Nature Genetics, Jan. 25) used new technology to scan nearly 500,000 genetic variants (single nucleotide polymorphisms or SNPs) in 1,359 people with psoriasis and 1,400 without to find those with the strongest relationship with psoriasis. After identifying 18 SNPs with the highest associations with psoriasis, the researchers expanded the study to include 5,048 people with psoriasis and 5,051 without the disease. From that, they identified four new genetic "hotspots" for psoriasis and confirmed two others that Krueger and colleagues identified in previous studies.

Using the data from the *Nature Genetics* study, Feng, Goldgar, and colleagues employed two statistical methods, imputation and logistic regression analysis, to determine with a much greater degree of accuracy those genes that have the highest association with psoriasis. Using imputation they were able to reliably predict the *0602 status of all subjects in the recent Nature Genetics study. This did two things; first, it increased the confidence that *0602 is the major genetic variation on this chromosome and, second, it permitted them to determine if there was any other associated genetic variation in this region.

Removing the strong effect of *0602 resulted in the identification of two other loci (fixed position on a chromosome) that are independently associated with psoriasis (MICA/HLA-B and c6orf10). These two loci increased the risk for the disease by 1.23 and 1.6 times, respectively.

However, when all three genetic variations that Feng, Goldgar, and colleagues report are present, the risk for psoriasis is 8.9 times higher than when none of these is present.

To confirm the results, the researchers examined an independent patient population in China, which corroborated their conclusions.

While *0602 and the associated, but independent, genetic variations reported have a major genetic contribution to psoriasis, many other genes undoubtedly play a role, according to Krueger. The number of DNA sites discovered to have strong associations with psoriasis has more than doubled in the past two years.

Source: University of Utah Health Sciences (news : web)