

Four new psoriasis 'hotspots' identified

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Dr. Elder uses a robot to help pipette DNA samples in his lab. Credit: U-M Photo Services

Scientists at the University of Michigan Heath System and their collaborators have found four new DNA "hotspots" that may one day help guide new treatments for psoriasis, one of the most common autoimmune diseases in the country.

Using cutting-edge methods to peer into the hidden genetic underpinnings of the disabling and disfiguring disease, the research, published in <u>Nature Genetics</u>, further maps the as-yet unknown territories of psoriasis and psoriatic arthritis.

The findings could lead to new drug targets and tailored treatments for the <u>skin disease</u>, says James T. Elder, M.D., Ph.D., the Kirk D. Wuepper Professor of Molecular Genetic Dermatology and lead investigator on



the study, which included researchers from the Department of Dermatology and School of Public Health.

"This is a hot topic in genetics these days," Elder says. "Even when you add up all the genes that have been found around the world so far, they only account for about 40 percent of the genetic liability to psoriasis. The question among geneticists continues to be, 'Where is the dark matter?' "

The new research builds on past work by the U-M team, whose discoveries have helped to unveil the hereditary factors of the disease and provide scientists with a better understanding of psoriasis' relationship to other <u>autoimmune diseases</u>, such as Crohn's disease, <u>rheumatoid arthritis</u> and lupus.

So far, research worldwide has linked 25 genes to psoriasis, which has a strong hereditary component. Including the new discoveries, Elder's team was involved in finding more than half of them.

Two of the four new susceptibility loci – or "hotspots" – were strongly linked to psoriatic arthritis, a painful and destructive form of arthritis that affects about 1 in 4 psoriasis patients, Elder says.

The roughly 7.5 million Americans with psoriasis also have a higher risk of dying from related cardiovascular problems.

Once a full catalog of psoriasis genes has been identified, scientists hope to generate a "psoriasis gene profile" that can predict one's risk of developing the disease and pave the way for innovative treatments. Current treatments, including different types of immunosuppressive agents, aren't always effective and can cause serious side effects – though a new drug called Stelara (ustekinumab), which targets one of the genes they discovered, has been giving patients months-long relief, Elder



says.

U-M Professor of Biostatistics Goncalo R. Abecasis, D. Phil, was instrumental in designing software and statistical methods to analyze more than 6 million genetic variants from more than 4,000 people.

"It was a pretty daunting task," Abecasis says. "We looked in greater detail at genetic variation than is typical so that we can understand the biology behind <u>psoriasis</u> and build better drugs."

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