

Update in Dermatology

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Psoriasis is a chronic, usually recurrent inflammatory skin disease, being considered one of the most prevalent autoimmune diseases, with a world prevalence of 2-3%. Up to 30 percent of patients with psoriasis develop psoriatic arthritis, a related disabling joint disease.

Psoriasis has a large hereditary implication - global research has linked 25 genes to this disease until now, but it is not clear how these genes work together. Most of them involve the immune system, being connected to pathways that lead to inflammation - particularly the major histocompatibility complex (MHC) and T cells.

An array of treatment options exist for patients with psoriasis, but like many other skin diseases, there is no cure yet discovered. The main value of genetic studies is that they identify molecular mechanisms for further study and potential drug targets.

Recently, researchers affiliated to the University of Michigan Health System have discovered four new susceptibility loci (genes) involved in psoriasis that could be the starting point in developing new treatments for this disease.

The newly identified loci include one at NOS2, one at FBXL19, one near PSMA6-NFKBIA, and one near TRAF3IP2, and are also involved in the pathogenesis of psoriatic arthritis. These findings are based on a multi-center, international study involving more than 8,700 patients.

By identifying more genes linked to psoriasis, there is a chance to develop a genetic pro-

file that could predict the risk of developing the disease and may lead to the discovery of innovative treatment options such as the recently approved by the European Commission and FDA for moderate to severe plaque psoriasis - ustekinumab. This is a monoclonal antibody which specifically targets the product of two psoriasis associated genes (IL23R - 5q and IL12B -1p) - namely interleukin (IL) -12 and IL-23, strongly involved in the development and maintenance of psoriasis lesions. It is administered by subcutaneous route in four injections a year (every twelve weeks) following two starter doses at weeks 0 and 4.

So far, ustekinumab has been tested in psoriasis patients, in three phase 3 trials which have been recently reviewed and evaluated as significant. Two of these trials involving nearly 2,000 patients, demonstrated ustekinumab to have superior efficacy compared to placebo. In the third trial, ustekinumab (45 mg and 90 mg for 12 weeks) demonstrated significantly higher rates in achieving 75% improvement in the psoriasis area and severity index (67.5% and 73.8%) compared with etanercept (56.8%). This is the first phase 3 comparative trial between biologic agents in psoriasis. The safety profile for ustekinumab has been evaluated for up to 2 years of continuous administration, with warnings regarding infection and malignancy.

Finding a "cure" for psoriasis continues to be a great challenge and any valuable new information brings hope that someday this quest will come to an end.

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REFERENCES

1. **Ellinghaus E, Ellinghaus D, Stuart PE, et al.** – Genome-wide association study identifies a psoriasis susceptibility locus at TRAF3IP2. *Nature Genetics*, 2010; DOI: 10.1038/ng.689
2. **Stuart PE, Nair RP, Ellinghaus E, et al.** – Genome-wide association analysis identifies three psoriasis susceptibility loci. *Nature Genetics*, 2010; DOI:10.1038/ng.693
3. University of Michigan Health System (2010, October 19). Four new psoriasis 'hotspots' identified: Discovery may aid in developing new therapies. *Science Daily*. Retrieved February 6, 2011, from <http://www.sciencedaily.com>
4. **Schafer JA, Kjesbo NK, Gleason PP** – Formulary review of 2 new biologic agents: tocilizumab for rheumatoid arthritis and ustekinumab for plaque psoriasis. *J Manag Care Pharm.*, 2010; 16:402-16

