Discoid Cutaneous Lupus Erythematosus Without Signs of Systemic Disease Associates with *ITGAM* Gene Variants

Lupus erythematosus manifests in different forms, ranging from skin-restricted symptoms to a progressive multisystem disease (systemic lupus erythematosus). Genome-wide association studies have identified integrin alpha M (*ITGAM*) as a strong susceptibility gene for systemic lupus erythematosus, while the genetic predisposition to cutaneous discoid lupus erythematosus is less clear. The authors of this article found the risk of discoid lupus erythematosus without signs of systemic disease to be increased with *ITGAM* gene variants.

Below is a summary of a recently published paper by Järvinen et al. The reference for the whole article is the following: *Järvinen TM, Hellquist A, Koskenmies S, Einarsdottir E, Panelius J, Hasan T, Julkunen H, Padyukov L, Kvarnström M, Wahren-Herlenius M, Nyberg F, D'Amato M, Kere J, Saarialho-Kere U. Polymorphisms of the* ITGAM *gene confer high risk of discoid cutaneous than of systemic lupus erythematosus. PLoS ONE 2010 Dec 2. doi: 10.1371/journal.pone.0014212.*

Integrin alpha M (*ITGAM*) encodes the α-chain of αMβ2-integrin, a receptor involved in leukocyte adhesion, phagocytosis and regulation of apoptosis, and has been replicated as an systemic lupus erythematosus (SLE) susceptibility gene in several studies across populations. As abnormal removal of apoptotic cells happens in evolving discoid lesions, *ITGAM* is also a plausible candidate gene for discoid lupus erythematosus (DLE).

The research group, with members from the Universities of Helsinki and Tampere, Helsinki University Central Hospital, Finland, and Karolinska Institutet, Stockholm and University of Uppsala, Sweden, performed a case-control study to investigate the role of integrin alpha M *(ITGAM)* in a cohort of DLE patients and SLE patients. In total, 177 patients with DLE (76% women) and 85 patients with SLE (93% women) with LE-specific skin manifestations and 356 controls (49% women) were recruited from Finland. Furthermore, 164 Swedish patients with a diagnosis of a connective tissue disease from two distinct cohorts and 295 controls (90.5% women) were included in the study.

The association was strongest between *ITGAM* and cutaneous DLE (p-value 3.7×10^{-11}), followed by SLE patients with discoid rash (p-value 3.9×10^{-9}) and all SLE patients together (p-value 8.2×10^{-6}). The effect size (odds ratio; OR) of a risk variant was highest in SLE patients with discoid rash (OR 2.46–3.96) and in DLE patients (OR 1.65–3.20), followed by unstratified SLE patients (OR 1.52–2.14), SLE patients with renal involvement (OR 1.82–2.53) and Ro/SSA-positive patients (OR 1.37–2.03).

These results strengthen the hypothesis that different forms of LE are not genetically distinct entities, even though their clinical course varies. *ITGAM* may predispose to DLE through impaired phagocytosis, leukocyte trafficking or immune suppression in ultraviolet-exposed skin, but the exact mechanism needs further research.

The first author, Tiina M. Järvinen, defended her thesis on the genetics of cutaneous lupus erythematosus at Helsinki University in May 2010, this study being part of her thesis. She now works as Post doctoral fellow at Comprehensive Cancer Center, The Ohio State University, Columbus, Ohio, USA.

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