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Titel des Beitrags: Genome-wide Association Analysis of Psoriatic Arthritis and Cutaneous Psoriasis Reveals Differences in Their Genetic Architecture.

Abstract: Psoriasis vulgaris (PsV) is a common inflammatory and hyperproliferative skin disease. Up to 30% of people with PsV eventually develop psoriatic arthritis (PsA), an inflammatory musculoskeletal condition. To discern differences in genetic risk factors for PsA and cutaneous-only psoriasis (PsC), we carried out a genome-wide association study (GWAS) of 1,430 PsA case subjects and 1,417 unaffected control subjects. Meta-analysis of this study with three other GWASs and two targeted genotyping studies, encompassing a total of 9,293 PsV case subjects, 3,061 PsA case subjects, 3,110 PsC case subjects, and 13,670 unaffected control subjects of European descent, detected 10 regions associated with PsA and 11 with PsC at genome-wide (GW) significance. Several of these
association signals (IFNLR1, IFIH1, NFKBIA for PsA; TNFRSF9, LCE3C/B, TRAF3IP2, IL23A, NFKBIA for PsC) have not previously achieved GW significance. After replication, we also identified a PsV-associated SNP near CDKAL1 (rs4712528, odds ratio [OR] = 1.16, p = 8.4 × 10(-11)). Among identified psoriasis risk variants, three were more strongly associated with PsC than PsA (rs12189871 near HLA-C, p = 5.0 × 10(-19); rs4908742 near TNFRSF9, p = 0.00020; rs10888503 near LCE3A, p = 0.0014), and two were more strongly associated with PsA than PsC (rs12044149 near IL23R, p = 0.00018; rs9321623 near TNFAIP3, p = 0.00022). The PsA-specific variants were independent of previously identified psoriasis variants near IL23R and TNFAIP3. We also found multiple independent susceptibility variants in the IL12B, NOS2, and IFIH1 regions. These results provide insights into the pathogenetic similarities and differences between PsC and PsA.