Lupus Nephritis Susceptibility Loci in Women with Systemic Lupus Erythematosus.

Lupus nephritis is a manifestation of SLE resulting from glomerular immune complex deposition and inflammation. Lupus nephritis demonstrates familial aggregation and accounts for significant morbidity and mortality. We completed a meta-analysis of three genome-wide association studies of SLE to identify lupus nephritis-predisposing loci. Through genotyping and imputation, >1.6 million markers were assessed in 2000 unrelated women of European descent with SLE (588 patients with lupus nephritis and 1412 patients with lupus without nephritis). Tests of association were computed using logistic regression adjusting for population substructure. The strongest evidence for association was observed outside the MHC and included markers localized to 4q11-q13 (PDGFRA, GSX2; P=4.5×10(-7)), 16p12 (SLC5A11; P=5.1×10(-7)), 6p22 (ID4; P=7.4×10(-7)), and 8q24.12 (HAS2, SNTB1; P=1.1×10(-6)). Both HLA-DR2 and HLA-DR3, two well-established lupus susceptibility loci, showed evidence of association with lupus nephritis (P=0.06 and P=3.7×10(-5), respectively). Within the class I region, rs9263871 (C6orf15-HCG22) had the strongest evidence of association with lupus nephritis independent of HLA-DR2 and HLA-DR3 (P=8.5×10(-6)). Consistent with a functional role in lupus nephritis, intra-renal mRNA levels of PDGFRA and associated pathway members showed significant enrichment in patients with lupus nephritis (n=32) compared with controls (n=15). Results from this large-scale genome-wide investigation of lupus nephritis provide evidence of multiple biologically relevant lupus...
nephritis susceptibility loci.