Dense genotyping of immune-related disease regions identifies nine new risk loci for primary sclerosing cholangitis.

Primary sclerosing cholangitis (PSC) is a severe liver disease of unknown etiology leading to fibrotic destruction of the bile ducts and ultimately to the need for liver transplantation. We compared 3,789 PSC cases of European ancestry to 25,079 population controls across 130,422
SNPs genotyped using the Immunochip. We identified 12 genome-wide significant associations outside the human leukocyte antigen (HLA) complex, 9 of which were new, increasing the number of known PSC risk loci to 16. Despite comorbidity with inflammatory bowel disease (IBD) in 72% of the cases, 6 of the 12 loci showed significantly stronger association with PSC than with IBD, suggesting overlapping yet distinct genetic architectures for these two diseases. We incorporated association statistics from 7 diseases clinically occurring with PSC in the analysis and found suggestive evidence for 33 additional pleiotropic PSC risk loci. Together with network analyses, these findings add to the genetic risk map of PSC and expand on the relationship between PSC and other immune-mediated diseases.