

a genome-wide haplotype-tagging approach and to delineate the region of strongest association.

Methods 416 patients diagnosed with inflammatory bowel disease (IBD) <17 years within Scotland (278 CD, 101 UC and 37 IBD-U) and 735 parents (276 complete trios) were genotyped for 4 single nucleotide polymorphisms (SNPs) tagging the two haplotype blocks encoding *ICOSLG* as well as the region extending to rs762421 which achieved recent genome-wide significance. Detailed phenotypic characteristics of this cohort were previously described. SNPs were selected using HapMap data (based on solid spine of LD, MAF > 0.1). Detailed single marker and haplotype analysis by transmission disequilibrium testing (ParentTDT) was carried out using Haploview (permutation analysis, n=100 000).

Results The two-marker haplotypes rs762421A/G – rs8126734A/G and rs283529G/C – rs4818890C/A (both located within the 3' UTR of *ICOSLG*) showed weak associations with overall IBD susceptibility ($p < 0.05$) which did not retain significance after permutation analysis. However after stringent permutation analysis the rs8126734 A allele showed significant overtransmission to affected CD patients ($p = 0.02$, D' and r^2 with rs762421 was 0.78 and 0.21, respectively). The two-marker haplotype consisting of rs762421A and rs8126734G also showed significant distortion of transmission ($p = 0.03$). Using a sliding-2 marker haplotype analysis to assess the extent of the CD-association signal from the 3'UTR to the 5' end of the *ICOSLG* coding sequence we found that association signals did not extend upstream from rs8126734, thus implicating the 3' interval between rs762421 and rs8126734 as a target region for deep sequencing.

Conclusion We have applied the first family-based association analysis of *ICOSLG* in childhood onset CD (thus minimising the effect of population stratification) to demonstrate that the signal at the 21q22 locus is due to germline variation at the 3' end of *ICOSLG*. Our analysis makes it less likely for non-synonymous *ICOSLG* SNPs or for other genes in the region to contribute significantly to inherited CD susceptibility. Deep sequencing of the 3' UTR of the *ICOSLG* gene is now warranted to identify causative variants, potentially affecting mRNA stability.

Competing interests None.

Keywords genetics, Inflammatory Bowel Disease, Paediatrics.

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INDUCIBLE T CELL COSTIMULATOR LIGAND (ICOSLG) INFLUENCES CROHN'S DISEASE SUSCEPTIBILITY IN THE SCOTTISH PAEDIATRIC IBD POPULATION

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Introduction Inducible T cell costimulator ligand (ICOSLG) is intimately involved in the proliferation and differentiation of T lymphocytes. A locus on Chr. 21q22 harbouring the *ICOSLG* gene has been shown to influence susceptibility to adult and paediatric Crohn's disease (CD) and ulcerative colitis (UC). Our aim was to perform a detailed analysis of *ICOSLG* using