a genewide 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 genomewide 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 (ParenTDT) 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

Inducible t cell costimulator ligand (ICOSLG) influences crohn's disease susceptibility in the scottish paediatric ibd population

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Notes