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Introduction The heritability of irritable bowel syndrome (IBS) has been estimated at approximately 50–60%. An important subgroup (18%) of all IBS patients develop symptoms after gastrointestinal infection (postinfective IBS, PI-IBS). PI-IBS develops in 10% of *Campylobacter jejuni* infection, 2/3 of which are of the IBS with diarrhoea subtype (IBS-D).

Aims To use changes in rectal mucosal gene expression following *C jejuni* infection which were also seen in irritable bowel syndrome as a guide to identify and test candidate genes in IBS.

Methods Study 1: 31 patients with documented C. jejuni infection, 37 IBS with diarrhoea and 25 healthy volunteers provided blood and rectal biopsies for mRNA assessment using an Affymetrix array. Genes showing >1.5-fold change in both Group 1 and 2 compared with HV were validated by qPCR. Polymorphisms of these candidate gene were assessed in 168 IBS-D, 132 IBS with constipation (IBS-C) and 153 healthy volunteers (HV).

Results As previously reported[1] the following proinflammatory genes were increased in rectal biopsies following *C jejuni* infections and in IBS-D: *CCL11, CCL13, TNFSF15, Calpain* and *GABRE* while *NR1D1* and *GPR161* were depressed. We found no difference in the distribution of genetic polymorphisms of the *CCL11, CCL13,* genes between HV and IBS. We found an increased frequency of the T allele in the TNFSF15 SNP rs6478108 in IBS-D (72% versus 62% in HV, p=0.007) but not IBS-C, in keeping with the T allele being associated with an increased risk of Crohn's disease. Similarly we found increased frequency of the proinflammatory C allele from the TNFSF15 SNP rs7848647 and the G allele from TNFSF15 SNP rs6478109 in D-IBS (p=0.007 and p=0.015 respectively). Although owing to small numbers we found a non-significant difference in TNFSF15 gene expression associated with the risk alleles (p=0.1) there was a linear test for trend for the CC genotype of rs6478108 to have a lower TNFSF15 expression.

Conclusion We have identified a proinflammatory genetic tendency for increased TNFSF15 expression which may predispose to the development of IBS with diarrhoea.

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IDENTIFYING AND TESTING CANDIDATE GENES UNDERLYING THE INFLAMMATORY BASIS OF IRRITABLE BOWEL SYNDROME

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