conserved and non-conserved amino acid residues involved in FGN recognition. These results provide new insight into the molecular function and regulation of NOD2 and related NOD family proteins.

**M1562**

Evaluating of SNPs in TNF (C-857T) and MDR1 (C3435T) As Susceptibility Factors for IBD

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Background. Recently, association of the TNF C-857T and MDR1 C3435T polymorphism with inflammatory bowel disease (IBD) has been reported. Strong association of TNF C-857T with ulcerative colitis (UC) was seen, but with Crohn disease (CD) only after removal of individuals carrying the disease predisposing CARD15 mutations. Objective: To replicate and extend the natural case-control associations a German (429 CD patients, 320 UC patients) and UK cohorts (164 CD, 87 UC). Methods: The association of TNF C-857T and MDR1 (C3435T) with IBD, CD and UC was tested in samples using family-based and case-control association tests. Univariate TDT analyses examined association with clinical sub-units. Results: In case-control analyses, the TNF C-857T CC genotype was over-represented relative to controls in German trimers and British families for CD (P = 0.001). No association with UC was observed (P = 0.470). TDT analyses indicated that the C allele was over-transmitted in both CD and UC. German families and trios P = 0.0055. Over-transmission in a British family sample was not significant when this sample was considered independently. No evidence of association was detected between the C3435T MDR1 polymorphism and the CD, UC and UC phenotypes in any analysis. Conclusions: The TNF C-857T polymorphism exhibits a greater role in UC compared with CD. The T allele may be linked against complications of IBD including stenosis, fistulae and arthritis, but may also be due to linkage disequilibrium with other loci within the MHC region.

**M1563**

TNF-Alpha and IL-10 Gene Polymorphisms in Patients with Crohn's Disease

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Introduction: TNF-alpha and IL-10 are cytokines that have both been implicated in the pathogenesis of Crohn’s disease (CD). There are limited data on the effects of both cytokines on disease phenotype in the same population. Certain single nucleotide polymorphisms (SNPs) within the promoter region of the IL-10 (-1082A>G) and TNF-alpha (-308A>G) alleles are associated with significantly higher levels of circulating IL-10 and TNF-alpha, respectively. Aim: to investigate 4 SNPs in the promoter region of both genes in a well-characterized CD cohort by case-control analysis. To examine whether there are significant associations with disease phenotype. Methods: 275 consecutive CD cases from the IBD database and 217 healthy controls were genotyped for 2 TNF-alpha (-308G/A and -857G/A) and 2 IL-10 (-1082A/G and -592A/G) SNPs by PCR-ELFPL. All clinical data were obtained from the database. Genotype-phenotype analysis was only performed for SNPs that attained P<0.2 in case-control analysis. Results: genotype analysis showed a significant difference between controls and CD for IL-10 -1082P=A (P=0.033) and a trend for TNF(-857G=A) (P = 0.16), but not for the other 2 SNPs. Both IL-10 (-1082G) and TNF-alpha (-857T) were associated with disease behaviour (P = 0.02 and P = 0.04 respectively), with patients carrying the IL-10 G allele having a greater risk of stricture disease, and those carrying the TNF C allele having a greater risk of non-stricturing disease. As IL-10 SNP was carried by both SNPs we were able to group all of the patients together, carrying both alleles showed an even stronger association with stricture behaviour which persisted after multivariate analysis (P = 0.008). There was also a weaker association with familial CD (P = 0.03). These findings were unchanged after stratifying for NOD2 genotype (SNPs 813 and 13). Conclusion: specific SNPs in the TNF-alpha and IL-10 genes may help to predict CD behaviour. This may be clinically useful in shaping treatment of the disease at an earlier stage. The above results will need to be verified in an independent ethnically similar cohort using the same methods of assessment of disease-related variables as in this study.

**M1564**

TLR4 Asp299Gly, Inflammation and Response to Infliximab in CD

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INTRODUCTION: Crohn’s disease (CD) is a chronic inflammatory disorder. An excessive immune response to the intestinal bacterial flora, plays a role in the pathogenesis of the disease. This is underscored by the association between CARD15 and Toll-like receptor (TLR) polymorphisms and the Crohn disease risk. TLR4 polymorphisms and TLR9 expression, in the gut mucosa, are associated with post-infectious IBD. TLR4 expression was found to increase in the inflamed mucosa in IBD patients. TLR4 expression was correlated with the severity of inflammation and with the clinical response to Infliximab treatment. In this study we evaluated the effect of the TLR4 polymorphisms on the response to Infliximab in Crohn’s disease. Patients received infliximab in an 1 on 1 ratio. CRP and CDAI was measured before and after each infusion at week 4, 10, 60 and 120. Treatment response was defined as decrease of CDAI of 100 points and a drop below 150 points. Biological response and remission was defined as a 50% decrease of CRP levels and drop below 3 mg/l respectively. Genotyping was done by PCR-FLP. Groups were compared using Chi-square test and t-test. RESULTS: There was no difference in CRP levels at baseline between patients with and without TLR4 mutations.

**M1565**

A Polymorphism in Insulin-Like Growth Factor Receptors May Be Associated with Early Fatalising Behaviour in Colon Cancer Patients

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Crohn’s disease (CD) is a chronic inflammatory bowel disease (IBD) presenting with multifactorial polygenetic disease. Genetic background may influence inflammatory gene expression, TNF-Alpha, LPS inducibility of IGF1R, IGF2R, and IGF2 expression. CD is a complex disease with various CD behaviours except for a functionally significant polymorphism, characterized by a variable number of a simple sequence repeat in the promoter of IGF1R. Homozygosity for the most common allele (4/4) was significantly less frequent in penetrating (38%) than in sticking (89%) disease (P=0.002). This genetic variation was significantly associated with risk of disease severity as defined by disease location, the lower frequency of 4/4 genotype in IBS patients was not found in pure ileal disease, but essentially in colorectal and ileocolonic disease (18.3% of 4/4 in IBS vs 64.2% in IBS and IBD), population study (2000), RR = 2.4, 1.5-4.7. Conclusion: IGF1R polymorphism seems to exist between this functional significant polymorphism in the promoter of IGF1R gene and the inclination to develop early fatalising behavior, particularly in ileocolic CD.

**M1566**

Increased Frequency of a Single Nucleotide Polymorphism in Hypothetical Gene FJ121425 in Patients with Crohn's Disease in a Louisiana Population

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The purpose of this study was to test the hypothesis that polymorphisms in FJ121425, a DNA encoding a hypothetical protein that we have found to be underexpressed in the mucosa of patients with newly diagnosed, active Crohn’s disease, are associated with susceptibility to Crohn’s disease. To test this hypothesis, we sequenced genomic DNA in the LSU Core Genome Sequencing Laboratory from 60 patients with Crohn’s disease and 100 unrelated controls from a genetically similar population using DNA amplified with gene-specific primers designed from a 2700 base pair Incyte cDNA sequence. At base pair 2473, we detected a single nucleotide polymorphism (SNP) resulting in a cysteine to thymine substitution (C2473T) that was present in 84% of patients (n = 27) and 0% of controls (n = 0) (X2 = 5.43, p = 0.02). When unrelated patients were included in the analysis, 42% (n = 20) of patients and 27% (n = 27) controls had the SNP (X2 = 3.08, p = 0.10). These data suggest that a SNP in the 3rd of FJ121425 may be associated with increased risk of Crohn’s disease. DNA from more patients is being analyzed to determine if FJ121425 is a disease-associated gene or is in linkage disequilibrium with a disease-associated gene.

**M1567**

Genetic Crohn's Disease. A Different Entity Than Sporadic. A Study in Monogenic Twins

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Background and Aims: Crohn’s disease (CD) may be divided into a familial form in contrast to sporadic CD, the former being mainly genetically determined while the latter should mainly be caused by environmental factors. Using the Vienna classification the familial form consists of ileal disease, often of ileal localisation and both the biological and clinical response to infliximab. 300 CD patients were collected in a prospective trial to evaluate response to Infliximab. Patients received Infliximab in an on demand schedule. CRP and CDAI were measured before and after each infusion at week 4, 10, 60 and 120. Treatment response was defined as decrease of CDAI of 100 points and a drop below 150 points. Biological response and remission was defined as a 50% decrease of CRP levels and drop below 3 mg/l respectively. Genotyping was done by PCR-FLP. Groups were compared using Chi-square test and t-test. RESULTS: There was no difference in CRP levels at baseline between patients with and without TLIM4 mutations. Medium decrease in CDAI and CRP was 97 points (IQR 35.5-206) and 7.4 mg/l (IQR 0-23.6). A clinical response was seen in 65% of the patients and 49% of these entered clinical remission. Biological response and remission were seen in 69% and 57% of the patients respectively. We did not find a significant difference in response to infliximab treatment between patients with (16%) and without the TLIM2 variant allele (44%). CONCLUSION: Although the functional TLIM4 variant polymorphism results in less translocation of NF-κB upon stimulation with LPS, we did not find a association between this SNP and both clinical and biological response to Infliximab in CD. Similar results have been obtained for CARD15 and suggest that innate immunity genes do not seem to influence response to Infliximab.