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**Candidate genes for azathioprine treatment response in inflammatory bowel disease patients using an exome-wide genotyping analysis**

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**Background:** Objective: In an effort to detect genetic variants underlying the individual differences in efficacy to AZA treatment, DNA samples of the EIGA and ENEIDA studies, case–control studies including IBD cases of documented good and bad responders, were genotyped to target non-synonymous single nucleotide polymorphisms (SNPs) in 20,000 genes.

**Methods:** DNA samples of IBD patients of the EIGA study (n = 167, 34 cases or bad responders and 133 controls or good responders) were genotyped using the Affymetrix human 20K cSNP panel. Selected SNPs were further replicated in ENEIDA (n = 90, 30 cases or bad responders and 60 controls or good responders) by the Sequenom iPLEX Gold assay and combined meta-analysis was used for statistical analysis.

**Results:** Genetic analyses revealed an association of 3 non-synonymous polymorphisms in 3 genes: PION, OR 4.55 (95% CI: 2.28–9.10, p-value 4.26 × 10^-10), and two zinc finger protein genes, ZNF673, OR 2.58 (95% CI: 1.56–4.27, p-value 1.806 × 10^-4), and ZNF19, OR 2.56 (95% CI: 1.61–4.06, p-value 5.10 × 10^-5).

**Conclusions:** Three SNPs have been identified as top ranked using a 20K non synonymous cSNP panel, and consequently three new gene associations for response to azathioprine treatment in patients with IBD disease. Validation studies in independent cohorts and functional studies are required to confirm these associations.

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**Interleukin 19 gene polymorphisms in patients with ulcerative colitis**

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**Background:** A differential gene expression profile is described in inflammatory bowel disease. Resectional surgery is a cornerstone in the management of Crohn's disease (CD). This subgroup of patients is not characterized with a functional genetic approach. Therefore, our aim is to describe the functional genetic characteristics of the intestinal tissue of CD patients who had undergone resectional surgery.

**Methods:** Ileal inflamed tissue of 20 CD patients was collected from ileo-cecal intestinal resection. Controls were patients with normal ileal tissue, without CD requiring ileo-cecal resection. Human whole genome microarray (Codelink) was performed. Profile comparison and functional analysis of human mRNA was done with LIMa-R Package, GeneCodis, gene set enrichment analysis (GSEA) and informatics database consultation.

**Results:** GSEA analysis showed that CD patients had enrichment of extracellular matrix, collagen and negative regulation of cell differentiation. With FDR restriction to values of <0.0001, CD patients presented 536 down-regulated and 248 up-regulated genes. Down-regulated genes were involved in drug metabolism (cytochrome P450), steroid hormone biosynthesis, and tight junction. By the other hand, up-regulated genes were those involved in chemokine, leukocyte transendothelial migration, adipocytokine and TGF-beta signaling pathways.

**Conclusions:** These preliminary results suggest new deficient pathways in CD pathophysiology as those involved in drug metabolism and steroid hormone biosynthesis.

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**Outcome:**

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**Results:** A total of 200 UC patients were studied, 108 (54%) were female and 92 (46%) male, with ages ranging from 20 to 78 (mean 31.5 years). Evolution of the disease was 12.3 - 9.1 years. Pancolitis was present in 135 patients (67.7%) and distal colitis in 65 (32.3%). Sixty five patients presented extraintestinal manifestations (32.3%) that included arthropathy (18%), primary sclerosing cholangitis (8%), erythema nodosum (2%), sacroilitis (1.5%) and ankylosing spondylitis (1.5%). In regard to surgical treatment, thirty patients (15.2%) underwent radical colectomy due to refractory medical therapy.

We found significant decreased frequencies of the three IL-19 genotypes: AA (rs2243188) [12.1% vs. 20.4%, P = 0.008, OR = 0.53 (95% CI: 0.32–0.88)], TT (rs2243191) [8.4% vs. 19.3%, P = 3.10^-4], and 0.38, 95% CI: 0.21–0.68] and AA (rs2243193) [11% vs. 20.4%, P = 0.002, OR = 0.48, 95% CI: 0.29–0.80] in UC patients as compared to healthy controls. On the other hand, the TC (rs2243191) genotype was found to be increased in UC patients compared to healthy controls [53.1% vs. 43.5%, P = 0.01, OR = 1.47, 95% CI: 1.05–2.06]. In the subgroup analysis, no differences were found between the IL-19 genotypes and the clinical characteristics of UC.

**Conclusions:** IL-19 polymorphisms (rs2243188, rs2243191 and rs2243193) were associated with UC.