the case-control studies in an independent family based population, METHODS: We obtained a whole genome search was performed in a larger group of IBD affected relative pairs to see Validates Previous Linkages

Validates Previous Linkages

A permutation based probability test was used to calculate association independent of linkage chromosomes hut only a number of susceptibility regions have been replicated: 16oen

CONCLUSION: We have confirmed the association of the TNF -1031 polymorphJsm with Crohn's

results from a case control study, IBD families were genotyped and the transmission disequilib-

Expression of the TNFα gene in mediating inflammation. Previous genetic linkage studies have identified a susceptibility locus on the

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in the case-control or PDT analysis for CD11a and CD11c was observed. Conclusions: The 4G/4G polymorphism of the PAl-1 gene plays a critical role in the thrombin gene were assessed by PCR. Plasma PAl-1 antigen was quantified by ELISA. Results: In patients with CD the multivariate analysis showed that the 4G/4G genotype is an independent predictor of penetrating phenotype (p: 0.005, relative risk: 6.30, 95% CI: 2.22-22.9), along with male sex (p: 0.004, relative risk: 6.15, 95% CI: 1.7-22.9), and age >2 years (p: 0.009, relative risk: 6.32, 95% CI: 1.58-25.0). IBD-related complications were also more frequent in patients with the 4G/4G genotype (43.4%) than in patients with the 4G/5G genotype (22.2%) or the 5G/5G genotype (28.8%) (p: 0.026). Fifteen patients had a history of arterial (n: 5) or venous (n: 9) thrombosis. The 4G/4G genotype was more frequent in IBD patients with arterial thrombosis (83.3%) than in patients with venous thrombosis (6%, p: 0.010) and more frequent in patients without thrombosis (44.4%, p: 0.006) than in patients with thrombosis (21.1%, p: 0.001). The 4G allelic frequency was higher in IBD patients with arterial thrombosis (0.83) than in patients without thrombosis (0.59, p: 0.038) or controls (0.47, p: 0.016). A weak but significant correlation was observed between plasma PAI-1 antigen and disease activity (r: 0.36, p<0.0001). Plasma PAI-1 antigen was higher in patients with the 4G/4G genotype and thrombosis (36.2±3 mg/mL) than in 4G/4G patients without thrombosis (22.4±1.8 mg/mL, p: 0.013). Conclusions: The 4G/4G polymorphism of the PAI-1 gene plays a role as a disease modifier for CD, with the 4G/4G genotype being an independent risk factor for the development of a penetrating phenotype. This fact may be taken into account in the therapeutic options for patients with CD. In addition, the 4G/4G genotype is associated with the occurrence of arterial thrombosis in patients with IBD. This finding may be useful for identifying a subgroup of IBD patients which may benefit from prophylactic antithrombotic therapy.

2329
Localization of a Recessive Locus in the SAMP/Yit Model of Crohn's Disease
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Background: Various epidemiologic and genetic studies support a role for genetic factors in susceptibility to Crohn's disease (CD). Since Ashkenazi Jews have a 10-fold greater risk of developing the disease than their non-Jewish neighbors we sought to determine whether there might be susceptibility genes unique to this population by performing linkage analysis on a population comprising entirely of Ashkenazi Jews. Methods: A genome-wide screen of an Israeli Jewish population was performed. These 170 patients consisted of 105 affected relatives pairs consisting of 56 sib-pairs, 31 cousin-cousin pairs, 15 uncle/parent-nieces/nephews, and 3 grandparent-grandchild pairs. Of these 170 affecteds, 101 have an age-of-onset >21,79. For genotyping the ABI medium density linkage mapping panel which consists of 15-20 dinucleotide repeats per chromosome with an average heterozygosity of 0.79 and an average distribution of 9.2 cm was used. Results: We have, to date, screened our patient population for linkage to markers on four chromosomes, 1, 5, 6, and 14. These chromosomes were initially selected because others have obtained suggestive evidence for linkage to these four chromosomes in predominantly non-Jewish populations. The genotyping data was then subjected to non-parametric multipoint linkage analysis using Genehunter 2.0. There was no evidence of linkage on chr 1 or only slight evidence of linkage on chr 5 at DSS424 (p = 0.018); this is near the region of suggestive linkage previously observed by others. For chr 6 we observed modest evidence of linkage at DSS1610 (p = 0.02) which is near the HLA region where evidence of linkage has also previously been observed. However, the strongest evidence for linkage was observed on chr 14 at D14S46 (p = 0.007). Although there have been two other reports of possible linkage to CD on chr 14, the previously reported linkage was observed for markers at 14q11-12 while the linkage we observe is on the 5' end of the chromosome not observed any similar results in the 14q11-12 part. Conclusion: These studies suggest that there may be unique susceptibility genes in the Ashkenazi Jewish population that is responsible for their increased risk to CD.