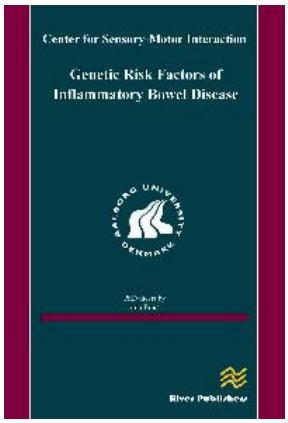

Genetic Risk Factors of Inflammatory Bowel Disease

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Description:

Crohns disease and ulcerative colitis are two related diseases that together are grouped as chronic inflammatory bowel diseases. Studies indicate that several interacting factors are involved in disease aetiology. Among these inherited genetic susceptibility, environmental factors and the immune system. The prevalence of inflammatory bowel disease show wide geographical variation.

The CARD15 gene encoding a protein recognising molecular patterns from bacterial cell walls was the first gene found to confer susceptibility of Crohns disease, but not ulcerative colitis. The recent years genome wide association studies have revealed several new susceptibility genes of both Crohns disease and ulcerative colitis, some of them are shared. Many of the susceptibility genes show great ethnic variation. Three common CARD15 variants are less prevalent in Scandinavia compared with other European countries, and the variants are absent in Asian populations. Great ethnic differences exist in environmental exposures also, and this ethnic variation further complicates the finding of true genetic and environmental risk factors of chronic inflammatory bowel disease. The most intensively investigated environmental exposure is tobacco smoking. Smoking has been shown to predispose to Crohns disease, whereas current smoking is a protective factor of ulcerative colitis.

In the present case-control study we investigated the prevalence of three common CARD15 variations in the Danish population. Two of the three common CARD15 variations were associated with Crohns disease, but were in general rare compared with other European countries.

Increased intestinal permeability has been demonstrated in patients with chronic inflammatory bowel disease. A large group of enzymes, grouped as xenobiotica metabolizing enzymes, are involved in detoxification of substances potential of interrupting the epithelial barrier. These enzymes are highly polymorphic displaying changes in enzymatic activity. We investigated selected functional polymorphisms in xenobiotica metabolizing enzymes to see whether they were associated with chronic inflammatory bowel disease in Denmark, but the results revealed no association between the genetic polymorphisms and disease. A modifying effect of smoking on genotype was found for a few polymorphisms, revealing a different disease association between smokers and non-smokers. I.e. we found a strengthening of the protective effect smoking has developing on ulcerative colitis from a genetic polymorphism encoding an enzyme with no activity.
In conclusion we found the CARD15 variants to be associated with Crohns disease, but the variants are relatively rare in the Danish population. In general we may conclude that polymorphisms in xenobiotica metabolizing enzymes do not seem to play an important part in aetiology of chronic inflammatory bowel disease. Research has shown the enzymes to be involved in the metabolisation of medicine used to treat patients with chronic inflammatory bowel disease. This could mean that genetic polymorphisms in xenobiotica metabolizing enzymes may become relevant in medical treatment of the patients.

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