Polymorphisms in ATP-binding cassette transporter genes and interaction with diet and lifestyle factors in relation to colorectal cancer in a Danish prospective case-cohort study - DTU Orbit (03/01/2019)

Polymorphisms in ATP-binding cassette transporter genes and interaction with diet and lifestyle factors in relation to colorectal cancer in a Danish prospective case-cohort study

The ATP-binding cassette (ABC) transporter family transports various molecules across the enterocytes in the gut protecting the intestine against potentially harmful substances. Moreover, ABC transporters are involved in mucosal immune defence through interaction with cytokines. The study aimed to assess whether polymorphisms in ABCB1, ABCC2 and ABCG2 were associated with risk of colorectal cancer (CRC) and to investigate gene-environment (dietary factors, smoking and use of non-steroidal anti-inflammatory drugs) and gene-gene interactions between previously studied polymorphisms in IL1B and IL10 and ABC transporter genes in relation to CRC risk. We used a Danish prospective case-cohort study of 1010 CRC cases and 1829 randomly selected participants from the Danish Diet, Cancer and Health cohort. Incidence rate ratios were calculated based on Cox’ proportional hazards model. None of the polymorphisms were associated with CRC, but ABCB1 and ABCG2 haplotypes were associated with risk of CRC. ABCB1/rs1045642 interacted with intake of cereals and fiber (p-Value for interaction (Pint) = 0.001 and 0.01, respectively). In a three-way analysis, both ABCB1/rs1045642 and ABCG2/rs2231137 in combination with IL10/rs3024505 interacted with fiber intake in relation to risk of CRC (Pint = 0.0007 and 0.009). Our results suggest that the ABC transporters P-glycoprotein/multidrug resistance 1 and BRCP, in cooperation with IL-10, are involved in the biological mechanism underlying the protective effect of fiber intake in relation to CRC. These results should be replicated in other cohorts to rule out chance findings.

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