Polymorphisms in NFKB1 and TLR4 and Interaction with Dietary and Life Style Factors in Relation to Colorectal Cancer in a Danish Prospective Case-Cohort Study

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Maintenance of a balance between commensal bacteria and the mucosal immune system is crucial and intestinal dysbiosis may be a key event in the pathogenesis of colorectal cancer (CRC). The toll-like receptor 4 (TLR4) is an important pattern-recognition receptor that regulates inflammation and barrier function in the gut by a mechanism that involves activation of the nuclear factor-kappa B (NF-kappa B) transcription factor. Dietary and life style factors may impact these functions. We therefore used a Danish prospective case-cohort study of 1010 CRC cases and 1829 randomly selected participants from the Danish Diet, Cancer and Health cohort to investigate three polymorphisms in NFKB1 and TLR4 and their possible interactions with diet and life style factors in relation to risk of CRC. Homozygous carriage of the variant allele of the TLR4/rs5030728 polymorphism was associated with increased risk of CRC (incidence rate ratio (IRR) = 1.30; 95% confidence interval (CI): 1.05-1.60; P = 0.02 (gene-dose model); IRR = 1.24; 95% CI: 1.01-1.51; P = 0.04 (recessive model)). Del-carriers of the NFKB1/rs28362491 polymorphism had a 17% (95% CI: 1.03-1.34; P = 0.02) increased risk of CRC compared to homozygous carriers of the ins-allele. However, none of these risk estimates withstood adjustment for multiple comparisons. We found no strong gene-environment interactions between the examined polymorphism and diet and life style factors in relation to CRC risk.

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