High ABCC2 and Low ABCG2 Gene Expression Are Early Events in the Colorectal Adenoma-Carcinoma Sequence

Development of colorectal cancer (CRC) may result from a dysfunctional interplay between diet, gut microbes and the immune system. The ABC transport proteins ABCB1 (P-glycoprotein, Multidrug resistance protein 1, MDR1), ABCC2 (MRP2) and ABCG2 (BCRP) are involved in transport of various compounds across the epithelial barrier. Low mRNA level of ABCB1 has previously been identified as an early event in colorectal carcinogenesis (Andersen et al., PLoS One. 2013 Aug 19; 8(8): e72119). ABCC2 and ABCG2 mRNA levels were assessed in intestinal tissue from 122 CRC cases, 106 adenoma cases (12 with severe dysplasia, 94 with mild-moderate dysplasia) and from 18 controls with normal endoscopy. We found significantly higher level of ABCC2 in adenomas with mild to moderate dysplasia and carcinoma tissue compared to the levels in unaffected tissue from the same individual (P = 0.037, P = 0.037, and P<0.0001) and in carcinoma and distant unaffected tissue from CRC cases compared to the level in the healthy individuals (P = 0.0046 and P = 0.036). Furthermore, ABCG2 mRNA levels were significantly lower in adenomas and carcinomas compared to the level in unaffected tissue from the same individuals and compared to tissue from healthy individuals (P<0.0001 for all). The level of ABCC2 in adjacent normal tissue was significantly higher than in tissue from healthy individuals (P = 0.011). In conclusion, this study found that ABCC2 and ABCG2 expression levels were altered already in mild/moderate dysplasia in carcinogenesis suggesting that these ABC transporters are involved in the early steps of carcinogenesis as previously reported for ABCB1. These results suggest that dysfunctional transport across the epithelial barrier may contribute to colorectal carcinogenesis.

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