SCREENING FOR COLORECTAL CANCER AND THE ASSOCIATION OF SINGLE NUCLEOTIDE POLYMORPHISMS AT THE GSTM1, CHR8 AND FOXO1 GENES

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Introduction: Colonoscopy is the mainstay of screening for colorectal cancer (CRC) but is relatively expensive and intrusive. We have previously reported a relationship between a single nucleotide polymorphism (SNP) at the TGFBR1 locus and CRC (ASCO 2013, abstract e14591). Here we extend the analysis to a total of 34 germline SNPs. Further associations would be expected to improve SNP typing as part of a screening protocol.

Methods: Blood samples were taken from 185 CRC patients and 93 healthy controls from a North European (Caucasian) population. After gDNA extraction, selected sequences were amplified by PCR followed by melting curve analysis. The association between allele frequency for the various SNPs and CRC status was evaluated by logistic regression. Applying a Holm-Bonferroni correction for multiple comparisons, the critical value for the smallest P becomes 0.05 divided by 34, i.e. 0.00147; for the second smallest P, 0.05/33 = 0.00152 and so on.

Results: The association with colorectal cancer was clearly statistically significant for five variants: TGFBR1 A > G rs3343448, GSTT1, INSR rs12459488, telRNA rs12696304, (P < 0.00005 in each case); LRRC31 rs16847897 (P = 0.0002) and GSTM1 (P = 0.0005). Associations for two further markers (CHR8 G > A rs7014346, P = 0.0066, and FOXO1 rs2721068, P = 0.0083) were suggestive but not conclusive. The association for GSTM1, CHR8 and FOXO1 are shown here for the first time; those for TGFBR1, GSTT, INSR, telRNA and LRRC1 confirm our results previously reported. For the other 21 SNPs results were not clearly significant.

Conclusion: SNP type is a potential genetic marker for CRC susceptibility. We suggest that subjects be offered a test for variants in the TGFBR1, GSTT, INSR, telRNA, LRRC1 and GSTM1 (and perhaps CHR8 and FOXO1) genes. In case of a positive result, subjects should be informed that they are at risk of CRC and strongly encouraged to have a colonoscopy, perhaps even before 50 years of age. For this suggestion to become a definite recommendation, a cost effectiveness analysis of SNP typing (although such typing is inexpensive) and a prospective study of colonoscopy and SNP typing, should be carried out.