Absence of association between cyclin D1 (CCND1) G870A polymorphism and age of onset in hereditary nonpolyposis colorectal cancer.

CCND1 encodes cyclin D1, which plays an important role in the G1 to S phase transition of the cell cycle. A common polymorphism (c.G870A) increases alternate splicing. Hereditary nonpolyposis colorectal cancer (HNPCC) is caused by mutations in mismatch repair (MMR) genes, mainly MSH2 and MLH1, and shows a wide range in the age of its onset (AO), suggesting the existence of other modifying genetic factors. To date, two studies have investigated the association between CCND1 G/A variation and AO in HNPCC with contradictory results in 86 and 146 MMR mutation carriers, respectively. To clarify the role of the CCND1 G/A variation in HNPCC, we performed a study in 406 individuals carrying exclusively clear cut pathogenic mutations in MSH2 or MLH1. We did not observe a significant difference in genotype frequencies of affected and unaffected mutation carriers and healthy controls. A significant association between CCND1 genotypes and AO was found neither in the global comparison (log-rank, P = 0.2981; Wilcoxon, P =0.2567) nor in a multivariate Cox regression analysis (hazard ratios 1.111, 95%CI 0.950-1.299, P = 0.188 and 1.090, 95%CI 0.868-1.369, P = 0.459 for the additive and dominant effect, respectively). We conclude, that the
CCND1 G870A sequence variation is not a genetic modifier of the phenotype of HNPCC.