Performance of epigenetic markers SEPT9 and ALX4 in plasma for detection of colorectal precancerous lesions.

BACKGROUND: Screening for colorectal cancer (CRC) has shown to reduce cancer-related mortality, however, acceptance and compliance to current programmes are poor. Developing new, more acceptable non-invasive tests for the detection of cancerous and precancerous colorectal lesions would not only allow preselection of individuals for colonoscopy, but may also prevent cancer by removal of precancerous lesions. METHODS: Plasma from 128 individuals (cohort I - exploratory study: 73 cases / 55 controls) was used to test the performance of a single marker, SEPT9, using a real-time quantitative PCR assay. To validate performance of SEPT9, plasma of 76 individuals (cohort II - validation study: 54 cases / 22 controls) was assessed. Additionally, improvement of predictive capability considering SEPT9 and additionally ALX4 methylation was investigated within these patients. RESULTS: In both cohorts combined, methylation of SEPT9 was observed in 9% of controls (3/33), 29% of patients with colorectal precancerous lesions (27/94) and 73% of colorectal cancer patients (24/33). The presence of both SEPT9 and ALX4 markers was analysed in cohort II and was observed in 5% of controls (1/22) and 37% of patients with polyps (18/49). Interestingly, also 3/5 (60%) patients with colorectal cancer were tested
positive by the two marker panel in plasma. CONCLUSIONS: While these data confirm the detection rate of SEPT9 as a biomarker for colorectal cancer, they also show that methylated DNA from advanced precancerous colorectal lesions can be detected using a panel of two DNA methylation markers, ALX4 and SEPT9. If confirmed in larger studies these data indicate that screening for colorectal precancerous lesions with a blood-based test may be as feasible as screening for invasive cancer.