Introduction: Colorectal cancer (CRC) is the forth most common cancer in the world. Epigenetic alterations are described in tumorigenesis. DNA methylation is the most frequent epigenetic change and is widely studied in most tumors. CRC screening by colonoscopy can decrease the risk of death; however is an invasive method with a low adhesion by the physicians and asymptomatic patients. Epigenetic alterations found in tumor tissue, can be detected in free circulating tumor DNA (ctDNA), obtained from blood plasma. The ctDNA may be a molecular marker for precocious diagnosis of cancer. Aim: to compare the levels of DNA methylation genes in normal and tumor tissues with those in blood to identify potential epigenetic biomarkers that may be useful in diagnosing of colorectal cancer

Methods: The CRC group consisted of patients with colon or rectal cancer. Tumors tissues and blood were collected during surgical resection of the tumor. The control group consisted of patients with normal colonoscopy. Blood and colon biopsy had also been collected from this group. Candidate genes were screened using the Methyl-Profiler™ PCR Array System (SABiosciences) in CRC tissue compared to normal biopsy. Two genes, APC (adenomatous polyposis coli) and DKK2 (dickkopf Wnt signaling pathway inhibitor), were selected for the study. DNA methylation of these genes was studied in CRC tissues, in normal mucosa, and in ctDNA in plasma by High Resolution Melting (HRM) analysis.

Results: 112 patients were included, 68 were controls and 46 CRC patients. Among the CRC patients, 28 had colon cancer and 18 rectal cancer. According to TNM classification, 2 were stage I, 20 stage II, 18 stage III and 2 stage IV. The methylation profiles were divided into three subgroups: <0% unmethylated; 1–25% methylated; >25%, hypermethylated. The DKK2 cut-off methylation index was -4.1% with a sensitivity of 89.1% and specificity of 86.8%. The cut-off for APC gene methylation was -19.4% with a sensitivity of 34.8% and specificity of 83.8%. The APC and DKK2 genes showed higher methylation profiles in the CRC group (p < 0.001). The methylation profile of the genes did not significantly differ between stages II and III. In the plasma, the qualitative methylation profile of ctDNA for the APC gene showed no statistically significant difference between the groups (p = 0.800), whereas the ctDNA DKK2 methylation profile was more frequent in the CRC group (p = 0.025).

Conclusion: DNA methylation of DKK2 and APC are most common in colorectal cancer tissue. ctDNA methylated of DKK2 gene may be an epigenetic marker for diagnosis of colorectal cancer.