Introduction: The aim of this study was to evaluate the role of genetic and lifestyle factors in the risk of onset and progression of colorectal and pancreatic cancer. The first part deals with the etiological factors and the importance of polymorphisms in biotransformation enzymes and genetic alterations in the gene *CHEK2* in the origin of these malignancies. In the second part, the ABC transporter genes were analyzed as potential prognostic and predictive markers of a treatment's outcome. **Materials and methods:** The polymorphisms and other genetic alterations were detected using real-time PCR, allelespecific PCR and PCR-RFLP methods in DNA which was extracted from the blood of patients. The frequency of polymorphisms was evaluated and their importance was assessed with regard to the available epidemiological data. Gene expressions were determined by qPCR in paired samples of tumor tissue and adjacent non-tumorous parenchyma. **Results:** A majority of the observed polymorphisms failed to show a relationship between their presence and the risk of any of these malignancies. *CYP2A13* variant allele*7 coding inactive enzyme was found in 7 of 265 controls and in none of 235 pancreatic carcinoma patients. In contrast, *GSTP1*-codon 105 Val variant allele and *GSTT1-null* genotype were associated with an elevated pancreatic cancer risk (OR=1.38; 95%CI=0.96-1.97 and OR=1.56; 95%CI=0.93-2.61, respectively). A combination of *GSTT1-null* and *GSTP1*-codon 105 Val variants further increased the risk of pancreatic cancer (OR=2.50; 95%CI=1.20-5.20). In the group of patients with colorectal cancer, the *GSTT1-null* genotype in combination with the *GSTM1-null* genotype was associated with a slightly increased risk (OR=1.58, 95% CI=1.01-2.47) and the actual deletion of *GSTM1* increased the risk of colorectal cancer after adjusting for other observed factors (OR=1.30, 95% CI=1.01-1.68). By comparing the expression levels of all 49 members of the human ABC transporters in pancreatic tumor samples with nonmalignant pancreatic tissue, we found that 11 genes were significantly upregulated and 4 genes downregulated ($p<0.05$) in adenocarcinoma tissue. The observed increased expression of *ABCB2*, *ABCB3*, *ABCB4*, *ABCC1*, *ABCC5* in tumor tissue is consistent with their previously demonstrated multidrug resistance phenotype. Downregulation of *ABCA3* ($p=0.002$), *ABCA5* ($p=0.010$), *ABCC6* ($p<0.001$) and *ABCC7* ($p=0.016$) in pancreatic cancer tissue has not yet been published. **Conclusions:** Our results indicate that polymorphisms in genes coding for biotransformation enzymes may influence the risk of malignant disease of the pancreas and colon in the Czech population. The results of the pilot study on the expressions of ABC transporters in pancreatic cancer tissues showed signifiant differences in transcript levels of these membrane proteins that are crucial for the transport of chemotherapeutic agents outside of tumor cells. However, analyses on larger sets of patients are necessary to verify and confirm these results.