Aim: 5-Fluorouracil (5-FU) is the most commonly used anticancer drug for colorectal cancer (CRC). Initially, we aimed to compare expression of 5-FU metabolic enzymes genes: thymidylate synthase (TS), thymidin phosphorylase (TP) and dihydropyrimidine dehydrogenase (DPD) in colorectal cancer and normal colon mucosa. We have tried to prove the correlation of the mRNA levels in fresh frozen tissues and protein expression using immunohistochemistry in paraffin-embedded colorectal cancer and adjacent normal tissues. Finally, we aimed to clarify the prognostic and predictive value of the expression of the 5-FU metabolic enzyme genes in patients with early colorectal cancer.
(...)
Results: We have found significantly higher DPD mRNA levels in normal colon tissue than in tumor tissue (p=0,03), but no significant differences in TS mRNA (p=0,34) and TP mRNA (p=1,0) levels in tumor and normal tissue. Immunohistochemically we have determined significantly higher TS expresion in tumor than in normal tissue (p=0,02) and significantly higher TP expression in stroma

cancer tissue than in normal tissue (p<0,001). No linear relationships were found between mRNA expression and protein TS and TP expression (p=0,28 resp. p=0,87). High TP mRNA expression associated with worse prognosis (p=0,05 HR 4,1), also high protein expression of TP and low protein expression of TS associated with trends to worse prognosis in patients with stage II and III CRC (p=0,08 HR 3,1 resp. p=0,07 HR 0,2). High protein expression of TP in stromal tissue associated with trends to worse prognosis in patients treated adjuvant chemotherapy with 5-fluorouracil (p=0,06). In contrast there were no significant differences between TS mRNA, TP mRNA, protein TS high and low expression groups in disease–free and overall survival rates.