Summary
The level of MMP-7, TIMP-1 and MMP-2 mRNA expression was significantly higher in the tumour tissue of colorectal carcinoma than in normal colorectal tissue. It could be possible to inhibit matrix metalloproteinases activity using appropriate antibodies, which could have therapeutic effect on tumour tissue and its vicinity. Some of the preparations are being tested (Bay 12-9566 /Bayer/, BB94 /British Biotechnology/). We have not proved correlation between expression of these genes and disease stage and diagnosis. We have succeeded to prove that if the surgical principles for colon resection performed due to colorectal carcinoma are observed, the resection line does not show any signs of the presence of tumour cells –
mRNA for CEA is not present. The level of mRNA for TIMP-1 is present in the resection line at lower levels than in tumour tissue, and this is due to the role that TIMP- 1 plays in the colon. Its level increases not only in all tumour diseases, but also in inflammatory diseases of the colon. The question whether the expression of mRNA for TIMP-1 is also increased outside the resection line and therefore it is a reaction of the colon as an organ will be subject
to further research, as will be a potential comparison with samples of colon unaffected by tumour or inflammation. Although the role of TIMP-1 as a prognostic marker remains a subject for further studies, all available studies suggest that the use of TIMP-1 in colorectal carcinoma screening is unsuitable due to the significant non-specificity of this marker.
Two different methods for determination of mRNA in peripheral blood were used. We have not succeeded to detect neither mRNA for CK 20 or CEA using first method (isolation of free RNA from plasma). We have not succeeded to detect mRNA for CEA using second method
(isolation of RNA from cells attached on Millipore membrane), but we have succeeded to detect mRNA for CK 20 in 13 samples from 11 patients. No correlation has been observed during evaluation of presence of mRNA for CK 20 in peripheral blood of these patients and
comparison with development of their tumour disease (progression x remission) or omparison with primary tumour staging and grading. Determination of mRNA for CK 20 and CEA in peripheral blood using the above-mentioned methods appears to us as practically not utilisable for clinical purposes. In spite of all optimism of the research group concerning new
methods, the utilisation of current immunoanalytic methods for determination of tumour markers appears as unsubstitutable. We have compared serum levels of tumour markers in control group of healthy persons and in patients with acute inflammatory disease and also in patients with benign disease of GIT (Crohn's disease). A statistically significant difference was observed especially in proliferative marker thymidine kinase (TK) and in cytokeratins TPA and TPS, significantly higher values of TK were observed in patients with benign disease of GIT. This result is consistent with scientific literature. Prognostic relevance of CEA has been proved in our cohort of patients. Significant correlation between elevation of preoperative CEA values and overall survival was determined using both laboratory and
optimised cut off. In case of laboratory cut off, the determination of TPA was important for overall survival and in case of optimised cut off the determination of CA 19-9 was important, that is again consistent with results of literature from some authors. (7, 8, 31) However, longer
follow up will be necessary for evaluation of relevance of these markers. In case of survival without any signs, the best result was obtained again in preoperative CEA values, which significance was confirmed not only using univariate, but also multivariate analysis while using laboratory cut off. Patients with preoperative CEA elevation had 11 times higher
probability of progression than patients with normal values. In our cohort of patients, the postoperative CEA values reacted best to the resection therapy by decrease. No change between preoperative and postoperative values of CA 19-9 tumour marker has been observed. On the contrary, significant increase in postoperative values of TPS tumour marker, which was followed in our cohort after the surgery, was observed. It was most probably connected with separation processes after performed surgery. It can be concluded that for control of surgical treatment success is most suitable to follow preoperative and postoperative CEA values. The highest sensitivities have been obtained in tumour marker TPS (83%) with 95% specificity, sensitivities of classic tumour markers CEA and CA 19-9 were significantly lower (41% or 25%, respectively). These numbers are rather surprising mainly because of low sensitivity of classic tumour markers. It can be explained by cohort characteristics, where patients with locally advanced colon disease (grade I-III, it means at the most with locoregional lymph nodes affected with tumour) entered study. Distal metastases into the liver were found only in two patients during operation. Furthermore it is the character of recurrences, where locoregional recurrence occurred in more than 50%. The results
should be carefully interpreted due to the small number of relapses with regard to short follow up. Nevertheless, TPS seems to be promising marker for follow up of patients with colorectal carcinoma. Therefore, the combination of CEA and TPS appears to be ideal.