M65 were compared with Wilcoxon test. Means of the difference between M30 and M65 values before and after chemotherapy were calculated then prognostic significance of these increments for survival was evaluated by univariate and multivariate. Logistic regression analysis was performed to predict response to chemotherapy.
Results: Serum M30 and M65 levels were significantly found to be increased after chemotherapy (M30, pre- 582.7±111.5 U/L vs. postchemotherapy 983.3±214.1 U/L, p = 0.01; M65, pre- 2061.7±431.2 U/L vs. postchemotherapy 2646.3±433.1 U/L, p = 0.003). Means of the difference M30 and M65 levels before and 48 hours after chemotherapy were 400.5±190 U/L [(M30-difference) M30-D)] and 584.6±335.4 U/L (M65-D), respectively. Patients whose serum M30-D ⩽400.5 U/L had better median PFS and OS times than patients with M30-D >400.5 U/L (PFS, 7 vs. 3.1 months, p = 0.004 and OS, 8.2 vs. 4.1 months, p = 0.002). In addition, median PFS and OS intervals in patients with serum M65-D >584.6 U/L were significantly worse than those of patients whose M65-D was lower than or equal to 584.6 U/L (PFS, 7 vs. 4.7 months, p = 0.004 and OS, 8.2 vs. 4.7 months, p = 0.002). Patients with increased M30-D and M65-D had better tumour response compared to patients with low M30- and M65-D (p = 0.02 and p = 0.006, respectively). In the logistic regression analysis, only M65-D was significantly found to be an independent factor in predicting response to chemotherapy (p = 0.018, OR:1.4). However, prognostic significance of M30 and M65 levels before and after chemotherapy could not be proved in the multivariate analysis.
Conclusions: These results showed for the first time that both M30 and M65 in serum samples of patients with advanced gastric cancer were elevated 48 hours after chemotherapy and these were poor prognostic factor for PFS and OS of patients. Moreover, increased plasma M65 level after chemotherapy can be predict tumour response.

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MUC4 Expression as a Prognostic Factor in Gastric Cancer − Clinicopathologically Significant Only in the Intestinal Phenotype

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Background: Gastric cancer is histologically classified into two types, intestinal and diffuse type, based on the gland formation tendency. Mucins are high molecular weight glycoproteins that play important roles in carcinogenesis and tumour invasion. Claudins are the proteins that participate in the formation of tight junctions. Tight junction proteins are believed to be involved in the regulation of proliferation, differentiation, and other cellular functions. Expression of mucin and claudin family in gastric cancers has been studied by many laboratories, but the results are conflicting. Therefore, we investigated the potential of MUC and claudin family to be used as a prognostic marker in gastric cancer according to histologic subtype.
Methods: Three-hundred sixty-five gastric adenocarcinoma patients who underwent surgical resection and had not received any pre- or -post surgery therapy, were selected for this study. Among the 365 gastric cancer samples tested here, 124 (34%) were early gastric cancer, and 241 (66%) were advanced. Intestinal type was 68.7% and diffuse type was 30.7%. We made tissue microarrays with paraffin-embeded formalin fixed blocks of gastric cancer and these microarrays were evaluated for phenotypic expression of MUC1, MUC4, Claudin 1, 3, 4, 5, 7 and 10 using anti-human rabbit or mouse polyclonal antibody. The expression levels were correlated with key clinicopathologic features and patient outcomes.
Results: There was no significant difference of MUC and claudin expression between early and advanced gastric cancer. Gastric cancer patients with increased MUC4 and claudin 10 expression were significantly associated with better overall survival (p = 0.049, 0.012). When we evaluated accoding to the histologic type, only significant in the intestinal type (p = 0.032). High expression of claudin 1 was associated with better disease free survival. In early gastric carcinoma, high expression of claudin 5 was significantly correlated with poor disease free survival (p = 0.045), but in advanced gastric carcinoma, high expression of claudin 5 was not correlated with poor disease free survival. Low expression of claudin 10 was significantly correlated with poor overall survival (p = 0.021).
Conclusion: Our present findings show that the increased expression of MUC4 could be used as a good prognostic marker in intestinal type gastric cancer. Overexpression of claudin-10 is a prognostic indicator of prolonged survival of patients with early and advanced gastric cancer.

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The Role of Vascular Endothelial Growth Factor (VEGF) and VEGF-receptors Genotyping in Guiding the Metastatic Process in Radically Resected Gastric Cancer Patients

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Background: In radically resected gastric cancer the possibility to predict the site of relapse could be clinically relevant for the selection of post-surgical management. We previously demonstrated that tumour integrins genotyping is involved in determining the metastatic sites. Preclinical studies suggested that tumour angiogenesis may also be crucial for the metastatic process of gastric cancer cells. We then investigated the role of VEGFs and VEGF receptors genotyping in determining either peritoneal carcinosis or hematogenous metastases in radically resected gastric cancer patients.
Patients and Methods: Genotyping for VEGF-A, VEGF-C and VEGFR-1,2,3 was carried out on pT4a radically resected gastric tumours recurring with either peritoneal-only carcinosis or hematogenous metastases. Tumour genotyping for integrins was also performed according to our previous findings.
Results: 101 patients fulfilled the inclusion criteria: 57 with peritoneal carcinomatosis only and 44 with hematogenous spread only. At multivariate analysis, intestinal histology and the AC genotype of rs699947 (VEGFA) showed to independently correlate with hematogenous metastases, whereas diffuse histology and the AA genotype of rs2269772 (ITGA) independently correlated with peritoneal-only diffusion (p = 0.001) (Table 1).
Conclusions: Our results seem to indicate that combining information from genotyping of rs699947 (VEGFA, AC), rs2269772 (ITGA, AA) and tumour histology could allow clinicians to individuate gastric cancer at high risk for recurrence either with peritoneal or hematogenous metastases. The selection tool deriving from this analysis may allow an optimal use of the available treatment strategies in these patients.

Table 1

	rs10434 (VEGFA, G > A)			
	GG	**GA**	**AA**	**ND**
Peritoneal carcinosis, n (%)	16 (28)	30 (53)	5 (9)	6 (10)
Hematogenous metastases, n (%)	11 (25)	20 (46)	12 (27)	1 (2)
p	n.s.	n.s.	0.0282	
	rs699947 (VEGFA, A > C)			
	AA	**AC**	**CC**	**ND**
Peritoneal carcinosis, n (%)	9 (16)	17 (30)	26 (45)	5 (9)
Hematogenous metastases, n (%)	5 (11)	26 (59)	11 (25)	2 (5)
p	n.s.	0.006	n.s.	
	rs7993418 (FLT1, A > G)			
	AA	**AG**	**GG**	**ND**
Peritoneal carcinosis, n (%)	34 (60)	16 (28)	1 (2)	6 (10)
Hematogenous metastases, n (%)	21 (48)	13 (29)	7 (16)	3 (7)
p	n.s.	n.s.	0.0259	

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Genetic Polymorphism of Biotransforming Enzymes and Risk of Pancreatic Cancer

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Background: The incidence of pancreatic cancer (PC) in the Czech Republic is highest in the world. Both genetic and enviromental factors may be involved in pancreatic carcinogenesis. Genetic and enviromental factors may also interact, e.g. when polymorphism of biotransforming enzymes is associated with increased susceptibility enviromental chemical mutagens. PC remains an incurable disease in most patients. Preventive strategies aim to identify the population at risk that could be followed more closely in screening programs. In addition, elimination of enviromental risk factors or chemopreventive strategie could be studied in high risk population. The present study was focused on gene polymorphisms in biotransforming enzymes in PC patients.
Materials and Methods: 278 PC patients and 403 healthy controls were studied. Gene polymorphisms of following biotransforming enzymes was investigated: CYP1B1, EPHX, NQO1 GSTP1, GSTT1 and GSTM1. DNA was amplified by PCR, subsequently split by restriction enzymes, and the