so altogether 18 CupPrint analyses had been carried out. The dropout of 12 cases is explained by paucity of tumor tissue and by insufficient RNA quality, possibly due to long storage time of tissue samples. Results were evaluated and discussed case-by-case on a consensus conference including two independent referees (Folprecht, Buettner). The information yielded by each method was regarded separately and reviewed by clinical experts based on the individual characteristics of the baseline data and clinical course of each patient.
Results. In 11 cases the results of IHC and CupPrint were concordant and matched also the clinical findings. In 1 of these cases, the results would have been beneficial to the patient, as he could have received a more specific chemotherapy. From the remaining 4 samples 1 can not be regarded as CUP anymore, as both IHC and CupPrint strongly favour the diagnosis of serous ovarian cancer, which would also be consistent with the clinical findings. In 2 cases the CupPrint was more concordant with the clinical findings than IHC. In 2 cases IHC was more concordant with the clinical findings than the CupPrint results.
Conclusions. IHC performed centrally led to more informative results than multicenter IHC. IHC and CupPrint microarray testing showed a high grade of concordance. Combination of the results of both methods led to a better definition of the possibly primary tumor, allowing a more specific therapy in some cases.

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Microarray gene expression analysis of human adrenocortical tumours

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Background: Adrenal tumours are common, occurring in 7% of patients over the age of 50 years. Adrenocortical carcinomas (ACCs), however, are rare, with an incidence of two per million population per year. The management of adrenocortical tumours (ACTs) is complex, compounded by the difficulty in discriminating benign from malignant tumours using conventional histology. The identification of a molecular marker which could reliably distinguish between the two groups would be valuable and would lead to improved clinical management of these patients. The aim of this study was to use microarray gene expression analysis to identify molecular markers which would discriminate between ACCs and adrenocortical adenomas (ACAs).
Materials and Methods: RNA was prepared from 6 normal adrenal cortices, 16 ACAs and 12 ACCs. Only samples with an RNA integrity number of 7.5 or greater were used. The samples were hybridised to Affymetrix HGU133plus2.0 genechips. Data analysis was performed with Partek and Affylmgui softwares. Seven genes were selected for validation studies with real time reverse transcription polymerase chain reaction (qPCR). Of these, three genes were also validated by immunohistochemistry (IHC).
Results: Using a cutoff of B > 2 and M > 2 or <−2, 217 genes were found to be significantly differentially expressed between ACCs and ACAs. Of these genes, 120 were unpregulated while 97 were downregulated. On qPCR, all seven candidate genes selected were significantly differentially expressed in ACCs compared to ACAs. All three candidate genes selected for IHC also differed significantly in their protein expression in ACCs when compared to ACAs and normal adrenal cortex.
Conclusion: We identified seven genes which were significantly differentially expressed between ACCs and ACAs using microarray gene expression profiling and confirmed the expression of these genes with qPCR and IHC. With further studies, these genes will provide greater insight into the pathogenesis of ACTs as well as having the potential to be reliable discriminators between ACCs and ACAs.

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Serum adipokine levels in colorectal cancer patients

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Purpose: Leptin, a product of the ob gene involved in the control of food intake and energy expenditure, may act as a potent mitogen and anti-apoptotic cytokine in colon cancer cell lines and promotes the invasiveness of familial adenomatous colonic cells. Adiponectin, in turn, may exert protective actions through its anti-proliferative and anti-angiogenetic effects. Despite a significant amount of in vitro data, direct and convincing evidence about their role in the development of colorectal cancer (CRC) is not available. Thus, the aim of this study was to evaluate the possible associations between leptin, adiponectin and clinicopathological variables of CRC.
Methods: Baseline serum leptin (DBC Inc.), adiponectin (BioVendor Inc.), TNF-alpha (R&D Systems) and carcinoembryonic antigen (CEA, Abbott Labs.) levels were analyzed in 90 patients with histologically diagnosed primary (Stages A: 7, B: 34, C: 19 and D: 13, with a single resectable liver metastasis) or metastatic (liver: 8, peritoneum: 5, lung: 1 and multiple: 3) CRC treated at “Tor Vergata” Clinical Center and followed for a median period of 3 years. The study was performed under the appropriate ethics approvals, and informed consent was obtained from each patient.
Results: Serum leptin and adiponectin levels in patients with CRC were 8.8 ng/ml [median, interquartile range (IQR): 3.7−17.6) and 8.06 μg/ml (IQR: 5.66−9.34). Of interest, median leptin (10.9 ng/ml), but not adiponectin levels of metastatic CRC were higher than those observed in primary CRC patients (7.7 ng/ml, $p = 0.034$). Leptin inversely correlated with adiponectin ($p = 0.002$) and directly correlated with TNF levels ($p < 0.05$) in all patients. In metastatic CRC only the correlation with TNF was retained. Of interest, 47% of non metastatic CRC had leptin levels above the median compared with 71% of metastatic patients ($p = 0.07$). Median follow-up of metastatic CRC patients was shorter (12.6 months) in patients with high leptin levels compared to those with normal levels (21.7 months, $p = 0.07$). Cox proportional hazard regression model including age, sex, leptin, adiponectin, TNF and CEA levels showed that leptin was an independent predictor for overall survival in metastatic CRC (Cox-Mantel test 2.03, $p = 0.042$).
Conclusions: These results suggest that serum leptin levels might have a role in the biology of CRC and may be regarded as a useful prognostic indicator in metastatic disease.

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Cetuximab-induced thymidylate synthase inhibition is associated with EGFR expression

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The monoclonal antibody cetuximab directed against the epidermal growth factor receptor (EGFR) is an attractive agent for targeted therapy in advanced colorectal cancer (CRC), especially when combined with 5-fluorouracil (5-FU)-based chemotherapy. However, the mechanisms of cetuximab activity as chemosensitizer remain poorly understood. Using proteome-fluorescence-based technology we found that cetuximab is able to suppress the expression of thymidylate synthase (TS) which is involved in the mechanism of 5-FU action. Caco-2, HRT-18, HT-29, WiDr and SW-480 CRC cells were found to express different levels of EGFR. SW-620 was used as EGFR-negative cell line. Only in EGFR-expressing cells cetuximab is able to inhibit TS expression. Combination treatment with cetuximab and 5-FU revealed an antitumor response that is closely correlated with the level of EGFR expression. Moreover, no correlation was seen between constitutive TS expression, cetuximab-induced TS downregulation and response either to 5-FU alone or in combination with cetuximab. We demonstrated that only high level of EGFR expression is important for the synergistic effects between cetuximab and 5-FU in the investigated cell lines and may represent a potential marker of response to cetuximab/5-FU-based chemotherapy in patients with advanced colorectal cancer.
This study was supported in part by the Austrian National Bank, project No. 11681, and the Austrian Cancer Society/Tyrol.

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Prognostic significance of Ki-67 expression in sporadic desmoid tumor

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Background: This study is conducted to evaluate the treatment outcome of sporadic desmoid tumor patients, and its association with Ki-67 expression.
Materials and Methods: From April 1999 to July 2005, 44 patients were pathologically diagnosed with primary sporadic desmoid tumor at Seoul National University Hospital. Among these, we analyzed the medical records of 38 patients and performed immunohistochemical staining for Ki-67 expression. Tumors were located in extra-abdominal areas (23 cases), abdominal walls (11 cases), and intra-abdominal areas (4 cases). Clinical or pathologic tumor sizes ranged from 1 to 13.5 cm in largest linear dimension