applied LOOCV, we were able to correctly predict the tumor behavior (T-level down-sizing) in 83% of patients ($p = 0.02$). We then observed that after a median follow-up of 34.5 months, all five patients with metastatic disease belonged to the group of non-responders. We again applied LOOCV and correctly predicted all five patients with recurrence. Furthermore, all 11 patients who were predicted to remain cancer free showed no evidence of recurrence.

Conclusion: Our results suggest that pretherapeutical gene expression profiling may assist in response prediction of rectal adenocarcinomas to preoperative CT/RT and in prediction of disease free survival if validated in larger independent studies.

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P68. GENE EXPRESSION SIGNATURE OF COLORECTAL CARCINOGENESIS

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Background: Colorectal carcinomas develop through the sequential stages of increasing morphological and molecular alterations. While the correlation of tumor phenotype with associated genomic alterations has been firmly established, the correlation with global gene expression profiles is less.

Methods: We analyzed tissue samples from 36 patients to identify sequential alterations of the genome and transcriptome that define the transformation of normal epithelium and the progression from adenomas to invasive disease.

Results: Comparative genomic hybridization (CGH) revealed patterns of stage specific, recurrent genomic imbalances. Gene expression analysis on 9K cDNA arrays identified 58 genes to be differentially expressed between normal mucosa and adenoma, 116 genes between adenoma and carcinoma, and 158 genes between primary carcinoma and liver metastasis ($p < 0.001$). Our analysis revealed a direct correlation of chromosomal copy number changes with chromosome-specific average gene expression levels.

Conclusion: Increasing genomic instability, a recurrent pattern of chromosomal aberrations and a specific gene expression pattern correlate with distinct stages of colorectal cancer progression. Chromosomal aneuploidies exert a direct effect on average expression levels of the genes residing on the aneuploid chromosomes, thereby contributing to a massive deregulation of the cellular transcriptome. The identification of novel genes and proteins might deliver relevant molecular targets for diagnostic and therapeutic interventions.

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P69. Ki-67 AUTO-ANTIBODIES IN COLORECTAL CANCER PATIENTS

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Background: Antibodies against the human nuclear antigen pKi-67 (Ki-67, MIB-1) are routinely used in oncology as immune-histological proliferation marker. PKi-67 is exclusively expressed in all active phases of the cell cycle (G1,S, G2, Mitosis). The Ki-67 index (relative number of positive stained nuclei) serves as an independent prognostic marker for certain tumor entities. We investigated whether colorectal cancer patients express auto-antibodies against pKi-67 and whether this has a prognostic relevance.

Methods: Auto-antibodies were detected by Western blot stainings from SW480 nuclear extracts with 36 pre- and 65 post-operative sera of colorectal cancer patients' sera. Sera of 20 voluntary healthy donors served as negative control. The same samples were simultaneously tested for p53 auto-antibodies.

Results: Thirteen percent of the sera proved to be positive for pKi-67 auto-antibodies while the control sera were completely negative. p53 auto-antibodies could be found in 53% of the patient sera. 75% anti-pKi-67 positive samples were also anti-p53 positive. For both antigens we found less positive antibodies in post-operative sera (pKi-67: 9%; p53: 42%) than in pre-operative sera (pKi-67: 19%, p53: 61%). There was, however, no significant correlation between pKi-67 positive sera and tumor stage (I: 13%, II: 4%; III: 23%; IV: 13%), grading or patient's prognosis. Remarkably, there is a significant ($p = 0{,}023$) correlation of pKi-67 positive sera of colon cancer patients (77%) in comparison to rectal cancer patients (60%).

Conclusion: PKi-67 auto-antibodies could be diagnostically valuable in the early detection of neoplasia and could be used as potential markers for recurrent or metastatic disease.

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P70. TRANSCRIPTIONAL AND MOLECULAR REGULATORS OF THE UROKINASE-RECEPTOR-(u-PAR)-GENE: FIRST ANALYSIS OF INDEPENDENT PROGNOSTIC RELEVANCE IN RESECTED COLORECTAL CANCER

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Purpose: Prognostic studies on transcription factors acting at specific promoter elements have never been performed so far. In previous studies we showed that the invasion-related gene *u-PAR* is regulated especially via an AP-2/Sp1(-152/-135)-, and an AP-1-promoter motif(-190/-171), mediating *u-PAR*-induction by