Gene expression profiles of different clinical stages of colorectal carcinoma: toward a molecular genetic understanding of tumor progression.

BACKGROUND AND AIMS:
Colorectal cancer is one of the leading causes of cancer deaths in the Western world. A better understanding of the development and progression of colorectal carcinoma is needed to define novel targets and strategies for treatment. PATIENTS/METHODS:
Gene expression profiles were determined for primary tumors of 10 locally restricted (T3N0M0), 8 lymphatically metastasized (T3N+M0), 7 systemically metastasized (T3N+M1) colorectal carcinomas, and 6 specimens of normal colorectal tissue by histology-guided oligonucleotide microarray analysis. RESULTS: A total of 1,995 genes were differently regulated in primary tumors of colorectal carcinoma compared with normal colorectal tissue. Besides common features of dedifferentiation and different expression of genes involved in cell division, cell adhesion, angiogenesis, signal transduction and metabolism we observed a deregulation of genes with an as yet unclear function. We identified 126 genes that were subsequently up- and 204 genes down-regulated during tumor progression. Furthermore, we found a cluster of five genes exclusively up-regulated in primary tumors of systemically metastasized colorectal carcinomas. A comparison of locally restricted (T3N0M0) and systemically metastasized (T3N+M1) primary tumors showed 50 deregulated genes
with a massive down-regulation of immune-modulatory genes in primary tumors of systemically metastasized carcinomas. Primary tumors of lymphatically (T3N+M0) and systemically metastasized (T3N+M1) carcinomas differed in the expression of 19 genes. CONCLUSION: These results provide an additional step toward the identification of crucial genes for the progression of colorectal cancer and the identification of novel treatment targets or strategies.