

Analysis of global gene expression profiles and invasion related genes of colorectal liver metastasis



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(Francis Lubowitz)

ANALYSIS OF GLOBAL GENE EXPRESSION PROFILES AND INVASION RELATED GENES OF COLORECTAL LIVER METASTASIS

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Epubli. Taschenbuch. Condition: Neu. Neuware - Liver is most frequently populated by metastases and may therefore serve as a model organ for studying metastatic invasion. For this reason, it was the aim of this thesis to understand the gene expression profiles and identify metastasis and invasion related genes in liver metastasis model. Differential gene expression was examined in three systems: A syngeneic mouse model (CT26/Balb/C mouse), a xenograft model (LS174T/nude mouse) and five clinical specimens. Gene expression profiles of a syngeneic mouse model and human clinical specimen revealed that the invasion front should be considered as a whole to find more overlapping potential target genes. Global gene expression studies on the host part of the invasion front revealed a pronounced overexpression of hepatic stellate cell activation markers at single gene level in this region demonstrating the feasibility of a differential gene expression approach on a genome wide scale. Global gene expression studies focusing on the tumor cells in vitro, in vivo and tumor part of the invasion front revealed an overall increase of cellular specialization from in vitro to invasion front. In addition to the secreted angiogenic cytokines, beta-catenin gene was elevated 9.6 fold in invasion front compared to in vitro. Evaluation of transcriptional up-regulation of beta-catenin by promoter activity showed an 18.4 fold increase in the tumor cells of the invasion front as compared to the tumor cells in the inner parts of the tumor indicating a transcriptional mechanism of beta-catenin regulation in addition to the well described post-translational regulatory mechanisms. In summary, application of high throughput Oligonucleotide microarray analysis in combination with real time PCR technology allowed the identification of genes, which might play a role in proliferation, invasion and angiogenesis of tumors in colorectal liver metastasis. 124 pp. Englisch.

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