T4:105

Differentially expressed microRNAs in osteosarcoma

Jan Smida[1], Daniel Baumhoer[2], Kristian Unger[3], Kathrin Poos[4], Eberhard Korsching[4], Michaela Nathrath[5]

[1)] CCG Osteosarcoma, Germany [2)] Pathology, University Hospital Basel, Switzerland [3)] Rad. Cytogenetics of HMGU, München [4)] Bioinformatics, University Münster [5)] Pediatric Oncology, Klinikum Kassel, Germany

Osteosarcomas are genetically complex tumors with abundant structural and numerical alterations. The molecular pathogenesis of the disease is, however, still poorly understood. Besides various oncogenes and tumor suppressor genes, deregulated microRNAs (miRNAs) are known to affect osteosarcoma development and biology. MicroRNA-expression profiling has been recently established as a method to unravel the impact of miRNA-involvement in malignancies in general, whereas deregulation of a single miRNA can have major impact on a multitude of genes.
We investigated six osteosarcoma cell lines for genome-wide miRNA expression and correlated our findings with gene expression profiles to identify biologically active miRNAs. Cultured osteoblasts (hFOB 1.19) and mesenchymal stem cells (L87/4) were used as normal references.
Focussing only on miRNAs that were deregulated in the majority of osteosarcoma cell lines, we identified several miRNAs with oncogenic and tumor suppressor properties, including various members of the oncogenic miR-17-92 cluster. In addition, several genes involved in differentiation, cell cycle control and apoptosis were found be deregulated in osteosarcoma cell lines, most likely due to altered miRNA expression patterns. In order to evaluate these results and to confirm their functional significance in vivo, we analyzed the expression levels of ca 30 miRNAs of interest in a collective of 35 osteosarcoma biopsy samples. We identified several candidate miRNAs that can be used as biomarkers to discriminate responders to chemotherapy and reflecting the metastatic potential in osteosarcoma.
Our findings indicate a crucial impact of deregulated miRNAs with consecutive changes in gene expression in osteosarcomas and strongly suggest pathogenetic and potentially therapeutic implications of miRNA expression.

E-mail (main author): smida@helmholtz-muenchen.de