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MicroRNA profiling in human medulloblastoma.

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Medulloblastoma is an aggressive brain malignancy with high incidence in childhood. Current treatment approaches have limited efficacy and severe side effects. Therefore, new risk-adapted therapeutic strategies based on molecular classification are required. MicroRNA expression analysis has emerged as a powerful tool to identify candidate molecules playing an important role in a large number of malignancies. However, no data are yet available on human primary medulloblastomas. A high throughput microRNA expression profiles was performed in human primary medulloblastoma specimens to investigate microRNA involvement in medulloblastoma carcinogenesis. We identified specific microRNA expression patterns which distinguish medulloblastoma differing in histotypes (anaplastic, classic and desmoplastic), in molecular features (ErbB2 or c-Myc overexpressing tumors) and in disease-risk stratification. MicroRNAs expression profile clearly differentiates medulloblastoma from either adult or fetal normal cerebellar tissues. Only a few microRNAs displayed upregulated expression, while most of them were downregulated in tumor samples, suggesting a tumor growth-inhibitory function. This property has been addressed for miR-9 and miR-125a, whose rescued expression promoted medulloblastoma cell growth arrest and apoptosis while targeting the proliferative truncated TrkC isoform. In conclusion, misregulated microRNA expression profiles characterize human medulloblastomas, and may provide potential targets for novel therapeutic strategies. (c) 2008 Wiley-Liss, Inc.

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