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Revealing micro RNAs in malignant progression of oligodendrogliomas

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MicroRNAs (miRNAs, miRs) are short non-coding regulatory RNA molecules found ubiquitously in living beings. Recently, miRNAs have also been implicated in oncogenesis, acting as tumor suppressors or oncogenes. Hitherto, the role of miRNAs in CNS tumors has been intensively investigated in glioblastomas and medulloblastomas, but there are few data regarding the role of miRNAs in oligo dendrogliomas. We performed a systematic evaluation of miRNAs and mRNAs expressions in a series of oligo dendrogliomas of different grades of malignancy to determine miRNAs and putative target genes that are differentially expressed in grade III oligo dendrogliomas. Total RNA was extract from 14 cases of bona fide grade II and III oligo dendrogliomas naïve of treatment (7 cases per grade) after tumor micro dissection. For each case, the expression of miRNAs (100 ng) and mRNAs (200 ng) was evaluated using microarray-based expression profiling platforms (723 transcripts and 41,000 genes, respectively). Samples of temporal white matter from patients operated for epilepsy were used as controls (n=15). The study was approved by Ethical Committee. Fifteen and 20 miRNAs were significantly over- and under expressed in anaplastic oligodendrogliomas, respectively. However, after matching with the expressions of putative target-mRNAs disclosed by microarray, we were able to validate 8 out of 10 miRNAs by RT-qPCR (assays in duplicate). Among the hypo-expressed miRNAs, we found some miRs that were previously described in cell differentiation of embryonic stem cells (miR27a, miR-30a/PDGFA and miR24/HDAC2) as well as miR193a-3p and miR30c/RARB. Conversely, among the hyper-expressed miRNAs, we validated the microarray data of miR301/BCL-2 and miR378/FGF2, and PPP4R4 and CD44. Nonetheless, we were able to identify and validate some oncogenic miRNAs and putative target-mRNAs that can be operating in malignant progression of oligodendrogliomas. The biological roles of these miRNAs are being addressed through functional assays in primary cell lines of gliomas.

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