MicroRNA: from basic research
to therapeutic applications

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MiR-29b-1 expression impaired Cancer Stem-Like properties of human osteosarcoma 3AB-OS cells in vitro

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Osteosarcoma (OS) is the most common type of bone cancer, with a peak incidence in the early childhood. Emerging evidence suggests that treatments targeting cancer stem cells (CSCs) within a tumor can halt cancer and improve patient survival. Although microRNAs are frequently dysregulated in human cancers, if they influence OS malignancy and whether or not targeting CSC-associated microRNAs inhibit OS progression remain unclear. Recently (1), we described a predictive network for two downregulated miRNA family (lct-7/98 and miR-29a,b,c) and their upregulated anticorrelated miRNAs. Here, we investigated in vitro the role of miR-29b-1 in regulating cell proliferation, clonogenic growth and chemoresistance of 3AB-OS CSCs. We found that the exogenous overexpression of miR-29b-1 in 3AB-OS CSCs reduces both cell growth in two- and three-dimensional culture systems and clonogenic growth. Furthermore, ectopic expression of miRNA-29b-1 reduced resistance to chemotherapy agents as paclitaxel, doxorubicin, cisplatin and etoposide. Next, we explored the molecular mechanisms responsible for the observed functions of miR-29b-1. Predicted target genes of miR-29b were retrieved using publicly available databases. Among these predicted target genes we selected MSTN, NMYC, CCND2, E2F1 Bcl-2 and IAP2, because they are overexpressed in 3AB-OS cells. Real-Time-PCR and western-blot analyses have also shown that enhanced expression of miR-29b-1 diminished the endogenous expression of these genes and proteins, suggesting that miR-29b-1 could negatively regulate these targets. These results support the hypothesis that miR-29b-1 might be a key negative regulator in 3AB-OS CSCs, suggesting that developing miR-29b-1 as a novel therapeutic agent may offer benefits for OS treatment.