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miR-19a-mediated downregulation of RhoB inhibits the dephosphorylation of AKT1 and induces osteosarcoma cell metastasis

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Abstract

Osteosarcoma is a primary malignancy that develops in bone, along with serious recurrence and metastasis. As an isoform of Rho family GTPases, RhoB could suppress cell proliferation, invasion, and anti-angiogenesis. But it is not clear how RhoB involves in tumor metastasis. Here we found that expression of RhoB was decreased in osteosarcoma primary samples and cell lines. Ectopic expression of RhoB restrains the migration of osteosarcoma cells in vitro and in vivo, and induces osteosarcoma cell apopotsis. Further study showed that RhoB could interact with B55, increase the proportion of B55 in PP2A complex, and then enhance the dephosphorylation of AKT1. Moreover, we demonstrated that miR-19a, which exhibits abnormal expression in highly metastatic osteosarcoma cell lines, could inhibit the expression of RhoB and promote the lung metastasis of osteosarcoma cells in vivo. Our results indicate that miR-19a-mediated RhoB is a critical regulator for the dephosphorylation of AKT1 in osteosarcoma cells. It may have a possible strategy on suppressing osteosarcoma metastasis by miR-19a inhibitory oligonucleotides. The miR-19a/RhoB/AKT1 network may help us to better understand the mechanism of osteosarcoma metastasis.