Ameloblastin Induces Tumor Suppression and Chemosensitivity in Osteosarcoma

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OBJECTIVE: Ameloblastin (AMBN) is the most abundant non-amelogenin enamel matrix protein. Also, AMBN is expressed in the bone tissue and promotes osteogenesis. But AMBN function in osteosarcoma (OS) is still unknown. Here, we aim to elucidate that AMBN possess tumor suppressive role and enhances chemosensitivity to doxorubicin treatment in OS.

STUDY DESIGN: Immunohistochemical analysis of AMBN expression in thirty-seven OS tissue samples, *in vivo* mice xenograft model, *in vitro* experiments (western blot, wound healing assay, soft-agar colony formation assay and FACS analysis) were performed.

RESULTS: (1) In immunohistochemical analysis of OS cases, AMBN expression was correlated with lower frequency of pulmonary metastasis and better prognosis. (2) *In vivo*, AMBN stable 143B-Luc cells showed the inhibition of tumor growth and pulmonary metastasis. (3) *In vitro*, AMBN stable 143B-Luc cells induced apoptosis, chemosensitivity to doxorubicin and suppressed colony formation ability, migration via the inactivation of Src-Stat3 pathway.

CONCLUSIONS: We demonstrate that AMBN has a novel tumor suppressive role and induce chemosensitivity to doxorubicin via Src-Stat3 inactivation in OS, which indicates that AMBN has a potential to be used as a therapeutic target of OS.