Hypericin inhibits melanoma bone metastasis and osteolysis

by modulating the tumor-bone microenvironment

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BACKGROUND: Bone metastasis is a poor prognostic indicator in melanoma. Agents that prevent bone loss could be used to develop an alternative therapy for bone metastasis. RANKL, a member of the tumor necrosis factor superfamily, has been shown to play a significant role in cancer-associated bone loss. In this study, we examined the efficacy of the natural compound hypericin (HP) in reducing melanoma-induced osteolysis.

HYPOTHESIS: Hypericin could inhibit melanoma-induced bone metastasis.

METHODS: TRAP staining, CCK-8, flow cytometry, western blotting, Migration and invasion, luciferase reporter assay were performed in vitro as well as establishing intratibial xenograft model of breast cancer bone metastasis in vivo.

RESULTS: HP inhibited melanoma cell migration and invasion. HP prevents melanoma-induced osteolysis by suppressing RANKL-mediated and melanoma cell-induced osteoclast differentiation. Molecular analysis revealed that HP prevented osteoclast function by inhibiting RANKL-induced ERK signaling pathway. We also examine HP's anti-metastatic properties by using a well-defined mouse model of osteolytic bone metastasis. HP inhibits the ability of tumour cells to metastasize to bone and that as such, prevents tumour cell-induced decreases in bone strength. Thus, HP is a potent inhibitor of melanoma-induced bone metastasis.