ELEVATED LEVELS OF PLATELETS AND MDM2 EXPRESSION ARE CONTRIBUTING FACTORS TO FACILITATING THE METASTASIS OF OSTEOSARCOMA

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Osteosarcoma (OS) is the most common form of primary bone cancer and the 6th leading cause of cancer in pediatric patients. A chart review of OS patients treated at this institution suggests that a high platelet count at diagnosis is significantly ($p=0.023$) and inversely associated with the first year of survival. As the effects of platelet interaction with OS have been extensively researched and suggest that platelets may facilitate tumor metastasis, and the most important prognostic factor for OS patient survival is metastasis to the lungs, we hypothesized that platelets increase metastasis to the lungs and reduce survival. Therefore, we sought to determine whether increasing platelet numbers in a well characterized OS mouse model would decrease survival and/or increase metastasis to the lungs. We found that thrombopoietin (TPO) treated mice, had increased platelet numbers, died earlier than placebo treated controls, and that lungs from TPO treated mice contained a small number of large tumor cells (most metastatic lesions were 2-4 cells), whereas lungs from placebo treated controls showed no signs of metastases. Next, an OS tissue microarray (TMA) was built from OS patients seen at our institution over the past 10 years. Mdm2, p53, TPO, and c-mpl expression were evaluated by immunohistochemical (IHC) staining followed by quantitation using the Aperio Imaging system and analysis software. C-mpl (TPO receptor) expression was higher in the metastatic than the primary tumors, suggesting that platelets may contribute to the metastasis of OS. Elevated levels of Mdm2 correlated with metastasis and lower levels of p53, as detected by IHC. In conclusion, both the mouse model and the human OS data were similar, suggesting that both platelets and Mdm2 promote metastases in OS.

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