The Effect of the Tumor Microenvironment and RK-33 Treatment on Macrophage Infiltration in Sarcoma Mouse Tumors

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Pediatric sarcomas comprise approximately 10% of childhood solid tumors, with metastatic disease yielding survival rates as low as 20-25%. Despite many efforts, advancements in survival outcomes for metastatic sarcomas remain limited. This study investigates the role of the tumor microenvironment and the potential of RK-33, a DDX3 inhibitor, to influence macrophage infiltration and improve therapeutic outcomes for patients with metastatic sarcomas. One way to determine the metastatic potential of a tumor is to assess its macrophage infiltration. Macrophages range from M1, which are pro-inflammatory and help prevent metastasis, to M2, which exhibit pro-tumor activity and contribute to metastasis. In this study, macrophage infiltration was measured by performing immunofluorescence staining. Macrophage infiltration was measured by quantifying the amount of staining found within the area of the stained tissue. Compared to subcutaneous tumors, orthotopic tumors showed higher overall macrophage infiltration, specifically M2 macrophage infiltration, indicating pro-tumor activity. These results highlight the metastatic tendency of orthotopic tumors and indicate that the tumor microenvironment plays a crucial role in the metastatic potential of a tumor. Additionally, both orthotopic and subcutaneous tumors treated with RK-33 showed higher M1 macrophage infiltration than non-treated samples, with little to no increase in M2 macrophage infiltration. This increase in immune activation converts the tumor microenvironment from immunologically "cold" to "hot," enhancing anti-tumor immunity and mitigating metastasis. These findings highlight the potential of RK-33 to target the tumor microenvironment and improve survival rates for patients with metastatic sarcomas.

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