The cGAS-STING Pathway in Rhabdomyosarcoma and Osteosarcoma

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Annually, about 15,000 people in the US are diagnosed with sarcoma. Rhabdomyosarcoma (RMS) and osteosarcoma (OS) are the most common sarcomas in children and adolescent young adults. Survival rates of primary RMS and OS are near 70% but drop to less than 30% if the patient has metastases. Alternative treatments to surgery and chemotherapy are needed to improve survival. Cryoablation, a process using ultra-cold temperatures to freeze and destroy tumor tissue, has been proposed as one option. Cryoablation induces the release of immune activation molecules from dying tumors that can activate the cGAS-STING pathway and boost anti-tumor immunity. Previously, we showed that dendritic cells, one type of immune cell, were activated by cryoablated tumor cells. Previous studies also show that cryoablation may activate cGAS-STING pathway signaling in RMS tumors. To determine the applicability of cryoablation, I performed a gene expression analysis using a Galaxy pipeline on RMS and OS patient RNA-seq data from the GEO database to determine the expression of cGAS-STING pathway signaling molecules. This analysis showed that primary RMS samples had significantly higher transcript expression of the cGAS-STING pathway molecules while primary OS samples had significantly lower expression than normal tissue. I also found that metastatic RMS and OS samples tend to show higher expression of the pathway transcripts than primary samples. These data suggest that cryoablation may be more effective in RMS rather than OS as well as in metastatic rather than primary tumors. These results can be applied practically in future cryoablation test studies to determine if it is a possible alternative treatment for RMS and OS.

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