The Role of PAG1 and the SFKs in Neuroblastoma Tumor Formation and Invasion

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Neuroblastoma is a lethal and commonly metastatic childhood cancer that arises when neural crest cells fail to differentiate properly during embryonic development. A group of cell-signaling proteins called the SRC Family Kinases (SFKs) appear to be key regulators of cell outcomes such as migration and adhesion that are important aspects of cancer metastasis. PAG1 is an important regulator of SFK activity as it localizes both the SFKs and CSK, their inhibitory protein, to the plasma membrane. A soft agar assay was conducted where cells were placed in an agarose solution for a week in order to measure tumor formation. It was hypothesized that SFK inhibition would decrease tumor formation, PAG1KD would increase tumor formation, and SFK inhibition paired with PAG1KD would decrease tumor formation. The PAG1KD cells exhibited increased tumor formation and produced visibly larger tumors in both trials. The effect of PP2 and SU6656, two SFK inhibitors, on tumor formation was insignificant suggesting that SFK inhibition does not affect tumor formation. Future research will include more trials of the soft agar assay and completion of an invasion assay using agarose and gelatin to further investigate the role of PAG1 and the SFKs in cancer cell invasion. This study provides insight about the role of the SFKs and PAG1 in tumor formation and cell-cell adhesion. Understanding the signaling proteins that regulate adhesion and tumor formation could allow for better treatment and prediction of cancer metastasis.

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