Siemens Competition
Math : Science : Technology
Regional Finalist

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Project Title: *Targeted MerTK inhibition improves response of BRAF-mutant melanomas to vemurafenib* (Cancer Biology)

Metastatic melanoma, the deadliest form of cutaneous cancer, causes 10,000 deaths per year in the U.S. Currently, metastatic melanoma is incurable; underlying efforts to identify oncogenic targets in melanoma, such as B-Raf, a serine-threonine kinase mutated in 40% of metastatic melanomas. Although BRAF-mutant melanomas initially respond to vemurafenib, a B-Raf inhibitor, most patients progress within a year, with no viable therapeutic options available. The receptor tyrosine kinase (RTK) MerTK is over-expressed in nearly 50% of melanomas including those with BRAF mutations. MerTK signaling potently activates numerous pathways that increase cancer cell proliferation, survival, and invasion. Therefore, experiments were performed to block MerTK RTK activity in BRAF-mutant melanomas using the inhibitor BMS-777607, or to block MerTK expression using shMerTK. As a single agent, shMerTK or BMS-777607 decreased cancer cell growth. However, the combination of BMS-777607 or shMerTk with vemurafenib, inhibited cell growth to a greater extent than either agent alone. Furthermore, BRAF-mutant melanomas previously selected for acquired resistance to vemurafenib remained sensitive to BMS-777607. These data suggest that MerTK targeting in BRAF-mutant melanomas could be used in combination with vemurafenib to improve outcomes for melanoma patients. Further studies will identify cross-talk between MerTK and B-Raf signaling pathways in melanoma cells.