Therapeutic applications of SAMMSON IncRNA inhibition in uveal melanoma

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Uveal melanoma is the most common intraocular malignancy in adults. The lack of an effective treatment results in a median survival time less than one year for patients with metastatic disease. Recently, our lab identified the melanoma-specific long non-coding RNA (IncRNA) SAMMSON as a novel therapeutic target in skin melanoma. Analysis of a PAN cancer RNA-sequencing dataset revealed consistent expression of SAMMSON in uveal melanoma tumors. Although SAMMSON expression was lower in uveal compared to skin melanoma, over 90% of uveal melanoma tumors showed detectable SAMMSON expression. Further analysis also revealed SAMMSON expression in conjunctival melanoma, another form of ocular melanoma. To evaluate the therapeutic potential of SAMMSON inhibition in uveal and conjunctival melanoma, we treated a panel of representative cell lines with SAMMSON-specific antisense oligonucleotides (ASOs) and observed a strong reduction in cell viability, accompanied by induction of apoptosis. These effects were dependent on ASO dosing and were validated using 8 independent SAMMSON-targeting ASOs and various ASO chemistries. ASO-treatment of a uveal melanoma PDX model further confirmed the observed phenotype. In line with the function of SAMMSON in modulating mitochondrial metabolism, SAMMSON knock down resulted in a decreased mitochondrial oxidative phosphorylation. Together, our results demonstrate the efficacy of SAMMSON inhibition as a novel treatment option for uveal melanoma patients.