Therapeutic applications of *SAMMSON* lncRNA 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 (lncRNA) *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.