Mela NO MORE: Creating Novel and Potent siRNA-based Biotherapies for the Treatment of Melanoma

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The prevalence of tanning and UV-overexposing activities continues to enthrone skin cancers as the most common type of cancer affecting humans. The deadliest and most aggressive form of these carcinomas is melanoma, whose lethal reputation is due to the disease's resistance to current chemotherapies. The present study builds upon the conclusion that the phosphorylated form of the enzyme LysRS is a promising therapeutic target for melanoma as a coactivator of MITF, the master regulator of the tumorigenic cascade. This work designed and synthesized a novel class of biological anticancer treatments targeting noncanonical LysRS that were predicated on RNAi interference. Homologous siRNAs that were complementary to the LysRS gene sequence were designed for treatment, while analogous siRNAs encoding a scrambled LysRS gene sequence were used as a negative control. Western Blot analysis was employed to confirm that a panel of melanoma cells contained high endogenous variability of LysRS and MITF, and the cell lines were either transfected with the homologous or analogous siRNA constructs tagged with Luciferase. To prevent the total knockdown of LysRS—which is vital to cell viability—phospho-null mutant forms of LysRS were introduced into the cell lines. Strikingly, SYBR® Green quantitative PCR showed that the cell lines treated to the homologous siRNA construct had a >75% reduction in LysRS mRNA expression. Moreover, a Luciferase bioluminescence assay showed that tumorigenesis was significantly reduced in those cell lines treated with the homologous siRNA construct. Thus, the siRNA-based biotherapies developed in this research offer a potent, specific, and toxicologically safer treatment for melanoma that can be an efficient alternative to presently deleterious chemotherapies.

Awards Won:

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