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Novel nanotechnology approach to target cancer disease by switching an alternative splicing ALEXANDER KAZANSKY, IVAN MENDEZ, KAREN MARTIROSYAN, University of Texas at Brownsville — High levels of activated STAT5B, a specific member of the STAT family, are intimately associated with prostate tumor progression, while the naturally occurring truncated form of STAT5B acts as a tumor suppressor. We have demonstrated that the truncated isoform of STAT5 is generated by insertion of an alternatively spliced exon and results in the introduction of an early termination codon. Recently, we have also demonstrated the feasibility of using steric-blocking splice-switching oligonucleotides (SSOs) with a complimentary sequence to the targeted exon-intron boundary to enhance alternative intron/exon retention. In this work we report the efficacy of the steric-blocking by splice-switching oligonucleotide (SSO) conjugates with pH insertion peptide (pHLIP) to block alternative splicing of STATs mRNA in vitro and in vivo. This technology would allow opening new pathways for chemotherapeutic disease intervention strategies based on the combination of pHLIP nanotechnology and a novel approach of switching expression from a proto-oncogene to a tumor suppressor.

Alexander Kazansky
University of Texas at Brownsville

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