SNS01-T Nanoparticles

National Cancer Institute

Source

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A colloidal mixture of nanoparticles consisting of small interfering RNA (siRNA) targeting the native eukaryotic translation initiation factor 5A (eIF5A), plasmids expressing a pro-apoptotic mutant of eIF5A under the control of a B-cell specific promoter (B29), and a synthetic cationic polymer polyethylenimine (PEI) as a delivery vehicle, with potential antineoplastic activity. Upon administration, the siRNA component of SNS01-T suppresses eIF5A expression, thereby interfering with translation of eIF5A and reducing levels of hypusinated eIF5A in cancer cells. In turn, this inhibits activation of the transcription factor NF-kB and induces apoptosis. In addition, the B-cell specific plasmid component expresses an arginine substituted form of eIF5A, eIF5AK50R, which can not be hypusinated, thus leads to a selective induction of apoptosis in B-cells. The native unhypusinated form of eIF5A is pro-apoptotic and can be modified at the lysine residue, by deoxyhypusine synthase (DHS) and subsequently deoxyhypusine hydroxylase (DHH), to the anti-apoptotic hypusinated form which is associated with tumor cell growth and survival. The delivery vehicle protects the siRNA and plasmid from degradation.