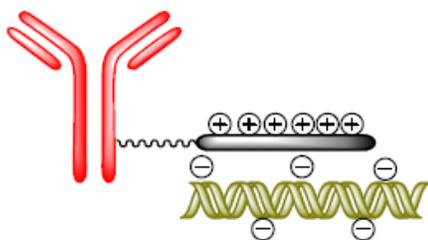
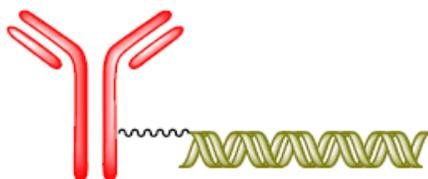


Lewis-Y Specific Antibody-Based Delivery of STAT3-siRNA



non-covalent



covalent

DESCRIPTION

STAT3, a cytokine-activated transcription factor, has been identified as a therapeutic target in countless types of cancers, where a dysfunction in the activation pathway results in overactive STAT3 and is typically indicative of poor prognosis. The use of siRNA to silence STAT3 production holds promise as a therapeutic; however disruption of normal STAT3 activity has been associated with undesirable side effects such as recurrent infection and malformed bone development. Additional safeguards must be implemented to ensure that siRNA therapies do not significantly disrupt normal STAT3 regulation.

City of Hope, in collaboration with the Ludwig Institute, has developed a method that both improves siRNA cell-targeting to avoid the above described side effects as well as increasing the uptake of siRNA molecules into cells. This is accomplished by conjugating siRNA molecules to an antibody that is targeted to a membrane antigen that is

upregulated in tumors such as colorectal adenocarcinomas, squamous cell lung carcinoma, and ovarian carcinoma (i.e. Lewis-Y antigen aka CD174). After the antibody-antigen binding delivers the siRNA to the targeted cells, the siRNA passes through the cell membrane via endocytosis, consequently inhibiting STAT3 production.

KEY ASPECTS

- siRNA cancer therapeutic with improved cell targeting and siRNA uptake by conjugating STAT3-siRNA to cancer-targeting anti-Lewis Y antibodies
- Potential therapeutic for numerous cancers including: Prostate Cancer, Breast Cancer, Renal Cell Carcinoma, Melanoma, Lung Adenocarcinoma

INTELLECTUAL PROPERTY

Title	US Patent Application	Filed
Humanized Lewis-Y Specific Antibody-Based Delivery of Dicer Substrate siRNA (D-siRNA) Against STAT3	13/424,267	3/19/2012

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