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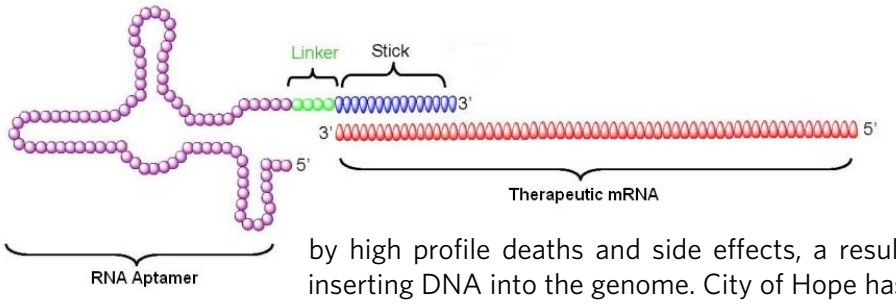
City of Hope
NATIONAL MEDICAL CENTER AND
BECKMAN RESEARCH INSTITUTE

Aptamer-mRNA Conjugates for Targeted Protein Expression



DESCRIPTION

Gene therapy is an exciting method for treating diseases, with hundreds of clinical trials completed and underway. Still, no gene therapy has yet been FDA approved and progress remains hindered by high profile deaths and side effects, a result of using viral vectors and permanently inserting DNA into the genome. City of Hope has developed a new platform technology to compete that is safer and more easily reversed. Like gene therapy, the method induces cells to produce their own therapeutic proteins, but this technology does so using mRNA rather than DNA. Because mRNA degrades, therapy can be terminated without irreversible changes to patient DNA. mRNA is delivered via conjugation to a small molecule aptamer that binds to cell-specific membrane protein; this precisely and safely delivers mRNA to target cells, without relying on the often non-specific nature of viral vectors. Upon binding, cells uptake mRNA conjugates via endocytosis and begin protein synthesis.

Because it can be adapted for many applications, this technology has virtually infinite potential. Genetic disorders like Cystic Fibrosis, where a mutated gene produces only nonfunctioning protein, could be treated by delivering mRNA with the correct nucleotide sequence, thereby enabling cells to synthesize a working protein. Sickle Cell Anemia, in which mutant hemoglobin yields often lethal complications, could be treated by delivering both an aptamer-siRNA to silence mutant protein synthesis and, simultaneously, an aptamer-mRNA for normal hemoglobin to restore a normal red blood cell phenotype. Various cancers and viral infections, including HIV, might be treated with mRNA that codes for apoptotic proteins, directing affected cells to self-destruct. Alternatively, mRNA could induce diseased cells to express antigens that engage the immune system to fight cancer or infections. Not limited to therapeutics, mRNA for bioluminescent or other marker proteins offer many diagnostic applications for this platform as well.

KEY ASPECTS

- Platform technology for deli very of mRNA to targeted cells
- Alternative to gene therapy that does not rely on viral vectors, producing safer, transient expression of therapeutic proteins
- Applications in genetic disorders, viral infections, cancer, and diagnostics

INTELLECTUAL PROPERTY

Title	US Provisional Application	Filed
Aptamer-mRNA Conjugates for Targeted Protein or Peptide Expression and Methods for their Use	13/494,880	6/12/2012

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