Therapeutic DNAzyme-Nanoparticle Conjugates for Gene Regulation

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Technology description

Market Summary

Recent clinical successes with diseases like chronic myelogenous leukemia and Parkinson's disease have renewed interest in gene therapies. DNAzyme-nanoparticle based therapeutics capture an important niche within this market because they function under a unique RNAi-independent mechanism different from that used by siRNA/shRNA (and siRNA/shRNA nanoparticle conjugates). Importantly, off target side effects are minimized, allowing for a broader range of disease targets, including genes that either involve or regulate the dicer complex.

Technical Summary

DNAzymes are short DNA sequences that catalytically cleave mRNA at a single programmable site. They represent an emerging technology in therapeutic gene regulation and hold potential advantages over siRNA/shRNA due to their innate ability to catalytically cleave mRNA without the need for hijacking the RISC (RNA-induced Silencing Complex) machinery of the cell. The efficacy of DNAzymes is limited by two factors: the inherent instability of foreign DNA within cells and site-specific delivery.
To address these two key challenges, Dr. Salaita's lab has created hybrid DNAzyme-gold nanoparticles using the well characterized '10-23' DNAzyme as an example. The '10-23' DNAzyme consists of a 15-base enzymatic core flanked by two arms that can be tuned to any sequence targeting a purine-pyrimidine junction, and functions as a site- and sequence- specific RNAase. In this technology, DNA oligonucleotides containing the catalytic sequence of '10-23' DNAzyme are conjugated to the surface of the gold particles through a thiolated linking group. The optimized hybrid molecule has been shown to be approximately one order of magnitude more catalytically active and five times more resistant against nuclease degradation than the DNAzyme alone. Although this example employs the '10-23' DNAzyme, ultimately this technology can be applied to all other DNAzymes and ribozymes to design novel therapeutic agents targeting specific diseases or infections.

Application area

Catalytic DNA molecules (DNAzymes) conjugated to gold nanoparticles for use as therapeutics to treat cancers, infections or other applications of gene therapy.

Advantages

DNAzyme-gold nanoparticles regulate gene expression through an RNAi independent mechanism.
Each DNAzyme-gold nanoparticle is more catalytically active than a free DNAzyme molecule.
Gold nanoparticle conjugation protects DNAzymes against nuclease degradation and extends their half-life and activity.
DNAzyme gold nanoparticles are non-toxic and readily enter cells without transfection agent.
DNAzyme-gold nanoparticles are a highly tailorable platform that allows for molecular targeting, drug loading for synergistic treatment, and imaging.
Gold nanoparticles are non-toxic and are already used to treat rheumatoid arthritis; therefore, DNAzyme gold nanoparticles have potential for immediate market impact for in vivo applications.

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