Bivalent aptamer-dual siRNA chimera effectively suppresses prostate cancer

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Technology description

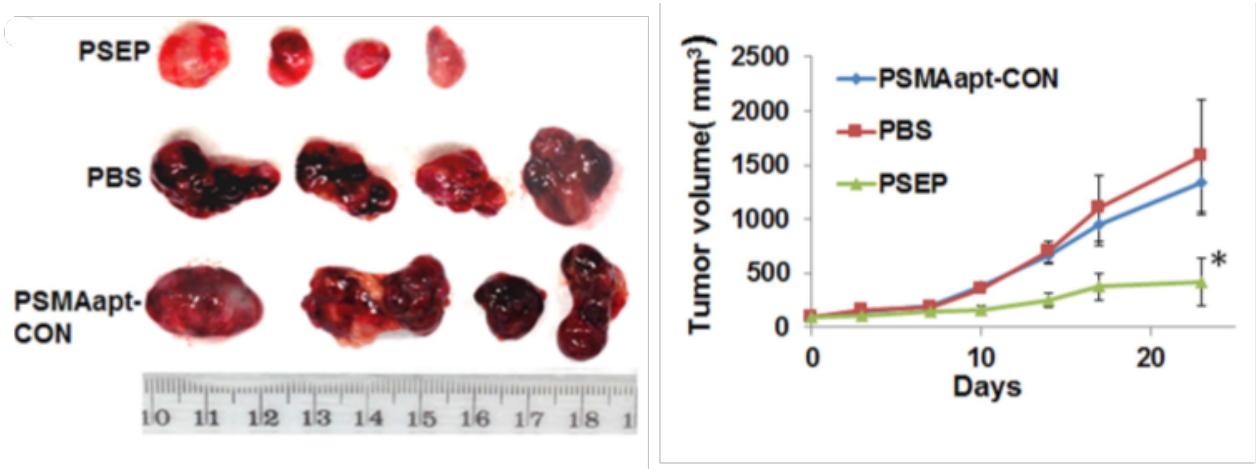

Fig 1. Systemic administration of bivalent aptamer-siRNA chimera suppressed tumor growth and reduced tumor associated angiogenesis.
PSEP: bivalent aptamer-siRNA chimera, PSMAapt-CON: scrambled siRNA.

Current State of the Art

Both aptamer and RNAi therapies are promising treatments for a wide range of diseases. Anti-VEGF aptamer was approved by FDA in 2017 for treating wet (age-related) macular degradation. The only FDA approved RNAi therapy is Patisiran for treating hereditary transthyretin amyloidosis with neuropathy. Aptamer and RNAi therapies in cancer are being tested in clinical trials, but the efficacy is not conclusive.

Problems with the current state of art

RNAi therapy is limited to liver disease because the current siRNA delivery system only targets the liver. Aptamer is a new delivery vehicle that transport siRNAs to specified cells including cancer cells by targeting specific membrane proteins. In addition, the aptamer-RNAi system prevents siRNAs from degradation and does not induce an innate immune reaction. However, the efficiency of the aptamer-RNAi system is limited by its low circulation half-life and quick renal clearance.

Advantages

Our invention utilizes bivalent aptamer-dual siRNA chimeras, targeting both EGFR and survivin in prostate cancer. The bivalent siRNA chimeras increased in vivo circulation half-life and reduced renal clearance in vivo. In both in vitro and in vivo studies, bivalent aptamer specifically binds to prostate-specific membrane antigen and degraded EGFR and survivin, leading to cell death and reduced angiogenesis in prostate cancer. As a result, the bivalent siRNA system improves the specificity and sensitivity of the aptamer-siRNA system in treating prostate cancer.

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