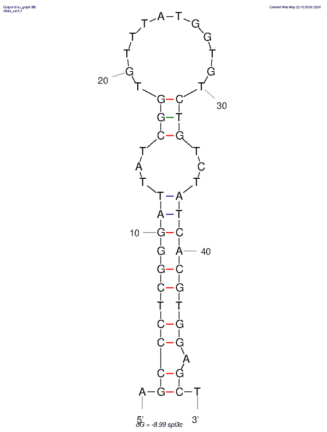
The AptaReport™
Newsletter
Summer 2024

Regulation of Cellular Signaling with an Aptamer Inhibitor to Impede Cancer Metastasis

The spl3c aptamer, developed to explore CKAP4 upregulation, can hinder tumor metastasis. CKAP4, a protein involved in cell migration and adhesion, interacts with β1 integrin and DKK1. The spl3c aptamer disrupts these interactions, inhibiting cancer cell migration and invasion. Research shows that spl3c, a truncated version of its parent spl3, maintains high affinity for CKAP4. Experiments demonstrated its strong binding to CKAP4 in both cell membranes and cytoplasm. By preventing the internalization and recycling of α5β1 integrin, the aptamer weakens cell adhesion and reduces traction force. Additionally, it blocks the CKAP4-DKK1 interaction, inhibiting the PI3K/AKT signaling pathway, which is crucial for cell survival and migration. This blockage reduces AKT phosphorylation, impairing actin cytoskeleton reorganization, essential for cell migration. The study's in vitro findings showed that the spl3c aptamer effectively inhibits cancer cell migration and invasion.

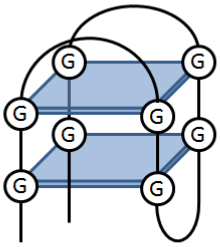


In vivo, treated tumor-bearing mice exhibited reduced tumor volumes and increased E-cadherin expression, indicating enhanced cell-cell adhesion and reduced metastasis.

This research highlights the stability and biocompatibility of spl3c. The results suggest that spl3c could be a powerful new therapeutic tool for targeting CKAP4 in cancer treatment. The study provides a foundation for future research on aptamer-based therapies in clinical settings.

*Reference: Apta-Index™ ID# 8661 -G.B.

A Universal Aptamer for Influenza A Viruses: Selection, Recognition, and Infection Inhibition



A recent study unveiled an innovative approach of using aptamers for the delivery of plant-based compounds, marking a significant advancement in targeted drug delivery. Aptamers have proven to be exceptional targeting agents due to their high specificity, stability, and ease of synthesis. This research showcases how aptamers can enhance the therapeutic efficacy of natural products, addressing long-standing challenges in pharmacokinetics and bioavailability.

One interesting application utilizes the AS1411 aptamer, which targets nucleolin (NCL) with high specificity and affinity for various cancer cells. Although AS1411 is not a new discovery, its utilization as a carrier molecule for drug delivery is groundbreaking. By binding to nucleolin, which is overexpressed on the surface of cancer cells, AS1411 facilitates the targeted delivery of therapeutic agents, enhancing their efficacy while minimizing harm to healthy cells.

The precision of aptamers like AS1411 opens new avenues for developing targeted therapies with minimal side effects. Their potential applications extend to creating highly sensitive biosensors for early cancer detection.

Additionally, aptamer-based drug delivery systems could revolutionize treatment protocols for various cancers, enhancing the efficacy of plant-based compounds known for their therapeutic properties but limited by poor bioavailability. These compounds include terpenes and terpenoids, known for their antioxidant and anti-inflammatory properties; alkaloids, which have potent anticancer and antimicrobial effects; and phenolic compounds, which offer diverse health benefits, including cardiovascular protection and neuroprotection.

*Reference: Apta-Index™ ID# 7675 -D.K.

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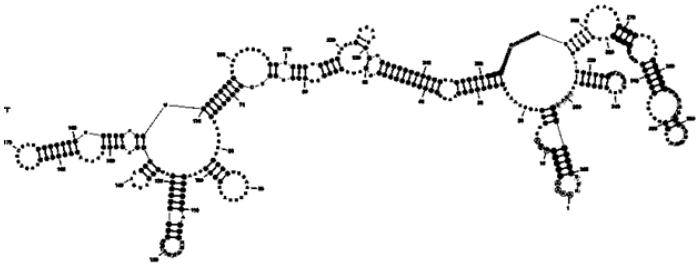
Therapeutic Application of Circular RNA Aptamers in a Mouse Model of Psoraisis

Aptamers can take the form of single-stranded DNA, RNA, or modified RNA molecules. Many aptamers take the form of DNA or modified RNA due to the high occurrence of RNA exonucleases in most environments; these enzymes is to degrade accessible RNA starting at any exposed end, such as what might be present in viruses. However, the presence of this defense system also affects the utility of RNA aptamers, as they have extremely short half-lives in such hostile environments.



Guo et al. have used a strategy to create closed circular RNA, where the targets of exonucleases are linked together so that they cannot be recognized by the enzymes. Additionally, the specific construction method used was able to allow the aptamer to retain its original structure and therefore binding ability while also keeping the aptamer construct from inducing an immune response. As a demonstration of potential applications, Guo et al. applied this approach to a protein kinase R (PKR) aptamer that could interfere with PKR activity, reducing inflammatory signals and psoriasis symptoms. Since high PKR activity is linked to many auto-inflammatory diseases, the ability of this aptamer to regulate PKR could lead to treatment of a wide range of conditions. However, as this mechanism is also required for many normal body processes, additional research is needed to determine if this development will be meaningful in creating a cure for auto-inflammatory diseases.

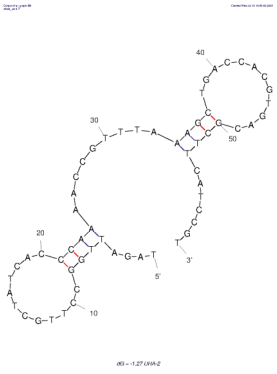
*Reference: Apta-Index™ ID# 8744 -A.L.

Morph-X-Select: Morphology-Based Tissue Aptamer Selection for Ovarian Cancer

Researchers have developed a universal aptamer that can recognize and neutralize multiple subtypes of influenza A viruses (IAVs). This breakthrough aims to address the challenge posed by rapidly mutating viruses that render conventional inhibitors less effective. The aptamer, named UHA-2, was selected using a multi-channel enrichment (MCE) strategy, which enabled it to bind with high affinity to different hemagglutinin (HA) protein subtypes of IAVs, including H5N1, H7N9, and H9N2. This binding ability allows UHA-2 to broadly neutralize various influenza A viruses, such as H1N1 and H3N2, making it a versatile and potent antiviral agent.

Traditional approaches to combating viral infections, such as broadly neutralizing antibodies (bnAbs) and multivalent vaccines, often face limitations related to size, complexity, cost, and the risk of antibody-dependent enhancement (ADE). The UHA-2 aptamer overcomes these hurdles due to its small size, stability, and ease of production. Aptamers are advantageous because they are single-stranded DNA or RNA molecules that can be generated in vitro and possess high affinity for their targets.

The study highlights the innovative SELEX (Systematic Evolution of Ligands by Exponential Enrichment) procedure used to select the UHA-2 aptamer. This involved fabricating a magnetism-controlled microfluidic chip and conducting multiple rounds of selection to enrich for DNA sequences with strong binding capabilities to various HA proteins. The resulting aptamer demonstrated nanomolar affinity for HA proteins and effectively inhibited viral infection in several assays.



*Reference: Apta-Index™ ID # 8739 -J.S.

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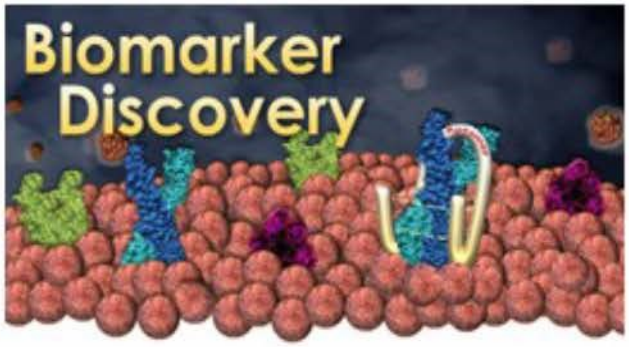

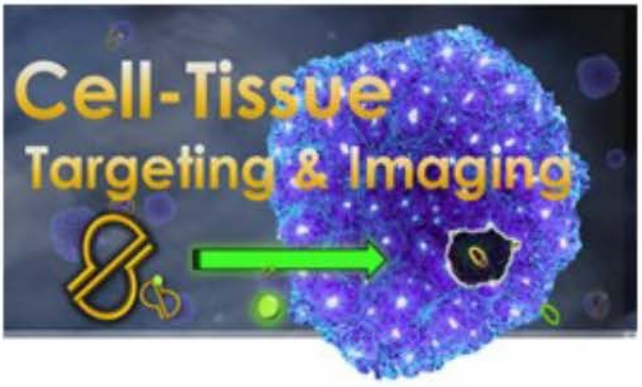

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