The AptaReport™
Newsletter
Spring 2025

Pressure overload-induced heart failure can be prevented and reversed by osteopontin RNA aptamer

Osteopontin (OPN) is an extracellular signaling molecule that shows increased activity in stressed myocytes and fibroblasts. In patients with heart failure, OPN level increases and acts as a predictor of 4-year mortality.

Current therapies for pathologic hypertrophy could be reduction of associated signaling pathways by blocking the activities of upstream cell membrane receptors and ion channels. Shehadeh et al. used an RNA aptamer to target cardiac OPN protein to see whether tuning down OPN pathologic signaling has any beneficial therapeutic effects on cardiac dysfunction.

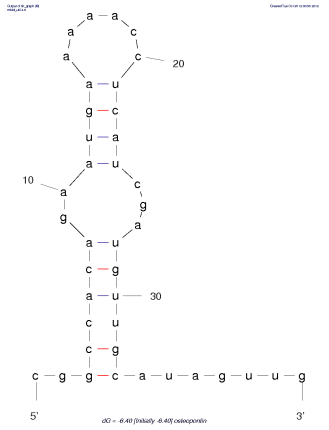

Figure 1. Predicted structure of aptamer OPN-R3. Note that secondary structure may be inaccurate due to changes resulting from interactions with the target.

Using a mouse model of pressure overload and treating with an OPN Aptamer two months after surgery, it was demonstrated that OPN aptamer reversed cardiomyocyte hypertrophy and cardiac fibrosis. This was confirmed by results such as blocked downstream signaling (PI3K and Akt phosphorylation), reduced expression of extracellular matrix (Lum, Col3a1, Fn1) and hypertrophy (Nppa, Nppb) genes, as well as prevented cardiac remodeling and dysfunction after pressure overload.

Thus this study demonstrated that tuning down cardiac OPN signaling by an OPN RNA aptamer could be an effective approach for improving cardiac function, preventing cardiac hypertrophy and fibrosis, and reversing pressure overload-induced heart failure.

*Reference: Apta-Index™ ID# 7737

-H.P.

Aptamer-based detection of foot-and-mouth disease virus using single-stranded DNA probe

Foot-and-mouth disease (FMD) is a veterinary disease that is projected to cost the US billions of dollars in annual financial loss. FMD's deadliness lies in its ability to spread quickly, mainly among cloven-hoofed animals. Having an accurate, reliable diagnostic tool on hand is critical for early detection. Nordin et al. have created that tool by synthesizing aptamers that bind to the VP2 region of the FMD viral capsid protein. They call them aptamers T1, T2, and T3, with T2 having the best binding for all kinds of FMD serotypes. This means that no matter the slight variations of the proteins on the shell of the virus, aptamers are flexible enough to bind and target FMD viruses.

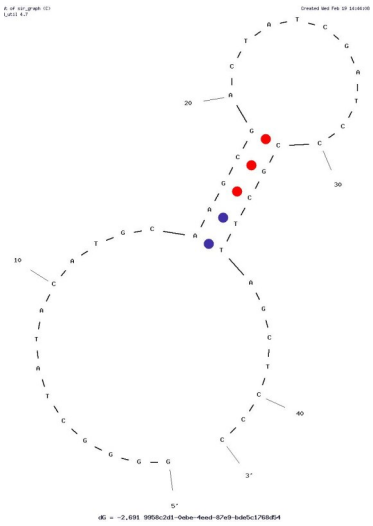

Figure 1. Predicted structure of aptamer T2. Note that secondary structure may be inaccurate due to changes resulting from interactions with the target.

The assay to determine aptamer's binding, ELASA, is relatively simple to perform and resulted in high binding affinities of the aptamers to FMD viruses with Kd constants ranging from 3 nM to 35 nM. Therefore, future studies integrating aptamers with biosensors or lateral flow assays could be critical in reducing the impact of a FMD outbreak across the globe.

*Reference: Apta-Index™ ID# 9138

-P.A.

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ATLAS-seq: A Breakthrough in TCR Discovery for Immunotherapy

Identifying effective antigen-reactive T-cell receptors (TCRs) is crucial for advancing T cell-based immunotherapies. Traditional methods, such as MHC multimer staining, focus on high-affinity interactions but often fail to select TCRs with strong activation potential. ATLAS-seq (Aptamer-based T-Lymphocyte Activity Screening and SEQuencing) offers a revolutionary approach by isolating and characterizing activated T cells based on their ability to secrete interferon-gamma (IFNγ), a key marker of immune response.

This microfluidic-based technology encapsulates individual T cells and antigen-presenting cells in droplets, preventing external interference and ensuring precise cytokine detection. ATLAS-seq uses an aptamer-based fluorescent sensor, enabling real-time monitoring of T-cell activation. The platform integrates single-cell RNA and TCR sequencing, allowing for analysis of functional TCRs.

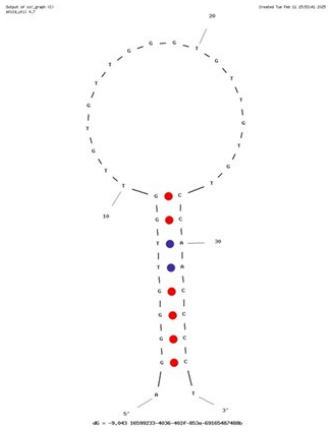


Figure 3. Predicted structure of IFNγ aptamer. Note that secondary structure may be inaccurate due to changes resulting from interactions with the target.

In studies screening TCRs reactive to cytomegalovirus (CMV) and prostate-specific antigen (PSA), ATLAS-seq identified clonotypes with superior activation & lower cytotoxicity compared to traditional selection methods. These TCRs had higher cytokine secretion and greater efficiency in eliminating target cells, making them promising for immunotherapies.

ATLAS-seq holds tremendous potential where precise TCR selection is essential. By prioritizing functional efficacy over binding affinity, this technology marks a significant advancement in engineering potent TCR-based therapies.

With its ability to enhance TCR discovery, ATLAS-seq paves the way for more effective, personalized immunotherapies, offering new hope for patients with treatment-resistant diseases.

*Reference: Apta-Index™ ID# 9256 -S.P.

Aptamer BC 007 - Efficient binder of spreading-crucial SARS-CoV-2 proteins

The COVID-19 pandemic caused by the SARS-CoV-2 virus has underscored the need for effective therapeutic interventions. Aptamers, single-stranded nucleic acid molecules capable of high-affinity binding to specific targets, have emerged as promising antiviral agents. In this study, Weishoff et al. investigated the aptamer BC 007 for its ability to bind and neutralize key SARS-CoV-2 proteins crucial for viral replication and host cell entry. The study evaluates BC 007's binding affinity to two essential SARS-CoV-2 proteins: the RNA-dependent RNA polymerase (RdRp), responsible for viral genome replication, and the receptor-binding domain (RBD) of the spike (S) protein, which mediates viral entry into host cells.

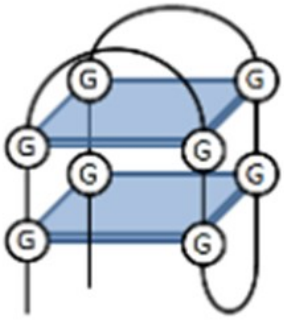
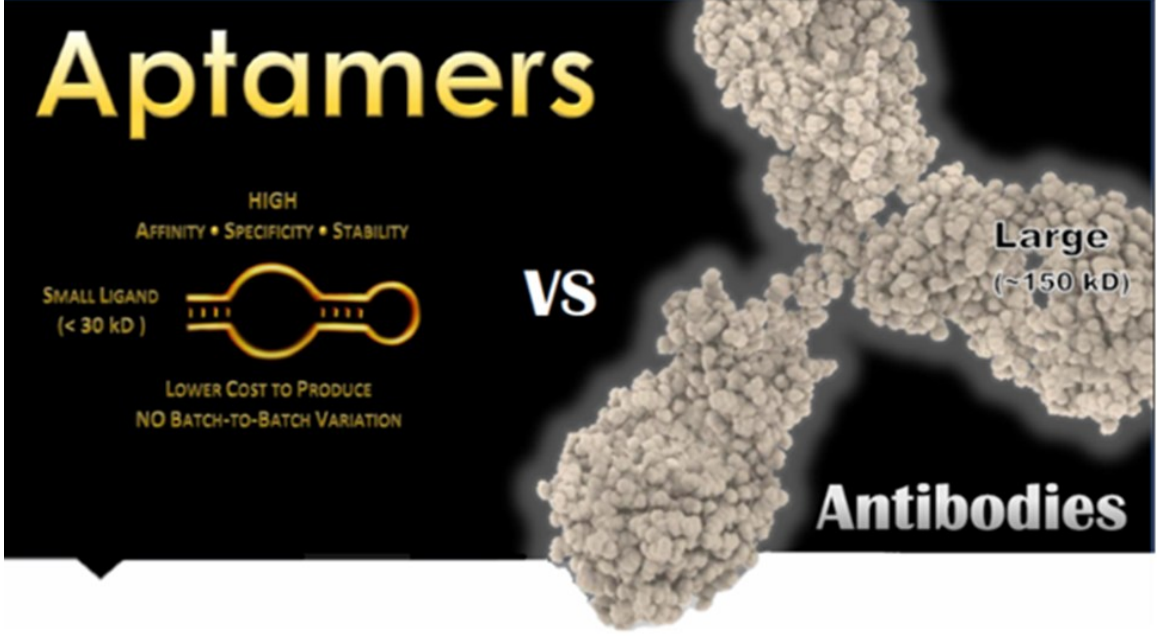


Figure 3. Predicted structure of aptamer BC007. Note that secondary structure may be inaccurate due to other modifications and/or changes resulting from interactions with the target.

In vitro assays demonstrated BC 007's strong and specific binding to both targets, with functional analyses revealing that BC 007 effectively inhibited RdRp activity, impairing viral RNA synthesis. Concurrently, its binding to the RBD of the S protein prevented viral attachment and entry into host cells. These findings indicate that BC 007 may serve as a dual-action antiviral agent capable of simultaneously inhibiting SARS-CoV-2 replication and transmission. This study provides compelling evidence that BC 007 effectively binds and neutralizes key SARS-CoV-2 proteins, presenting a promising therapeutic strategy against COVID-19. Its dual-targeting mechanism highlights its potential utility in antiviral treatment regimens. Further in vivo studies and clinical trials are necessary to validate efficacy and explore its broader therapeutic applications.

*Reference: Apta-Index™ ID #9134 -F.L.T.



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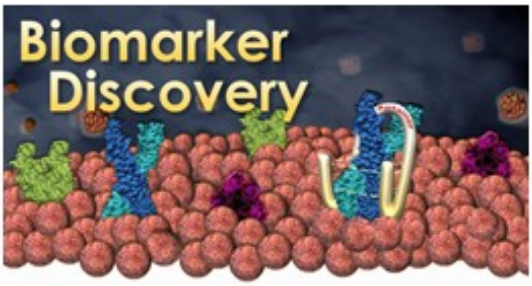

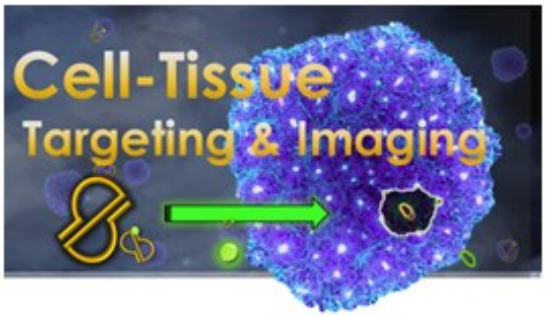

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