The AptaReport

"Forget Antibodies. Use Aptamers!™

May 2013

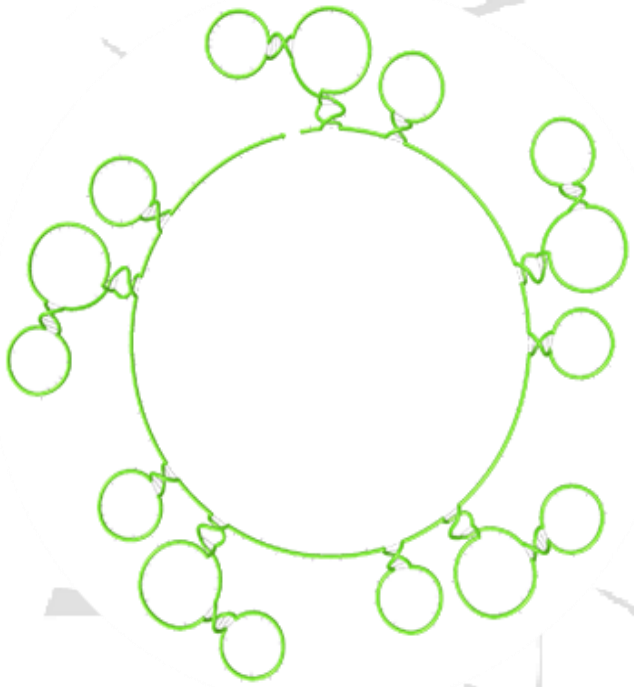

Figure 1— Rolling circle amplification generates a strand of DNA containing many aptamer sequences.[1]

DNA "Tentacles" used to Capture Lymphoma Cells[2]

Dr. Jeffrey Karp of the Center for Regenerative Therapeutics at Brigham and Women's Hospital in Boston turns to nature for the answers to tough biomedical questions. The question he addressed, was how to capture trace amounts of lymphoma cells from patients' blood samples. Inspiration came from a gelatinous pest sometimes painfully encountered at the beach. With its long tentacles, the jellyfish is able to scour the vast ocean for small morsels. Dr. Karp and his colleagues created their own DNA "tentacles" using a technique called "rolling circle amplification." The team found that by joining the two ends of a DNA molecule together, the enzyme that copies DNA travels in a circle several times before falling off. This product strand contains many repeats of the PTK7 (protein tyrosine kinase) aptamer sequence, which act similarly to the thousands of cellular barbs that line a jellyfish's tentacles (Fig. 1). The effect of each aptamer region is additive, and analysis showed that the long DNA strands bound to cancer cells much more tightly than individual aptamers. Combining a multitude of these strands into a complex DNA network, Dr. Karp was able to capture cancer cells faster, more effectively, and with greater purity than using a single aptamer or antibody. Better cell capture methods could mean earlier detection of relapse in patients whose leukemia is in remission, resulting in quicker treatment and a better prognosis. Furthermore, these aptamer networks can be easily adapted for many other cancer biomarkers.

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COMPANY PROFILE - WHAT IS APTAGEN?

Aptagen, LLC is a biotechnology company offering DNA and RNA, R&D services for use in diagnostics, drug discovery and therapeutics.

Aptagen was formed in 2004. Operations began in 2006. Aptagen is located in Jacobus, PA, a suburb of York, beautifully surrounded by Lake Redman and conveniently situated off of Interstate 83. The facility is a forty minute drive from Johns Hopkins University and Hershey Medical Center.

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Aptasensors Increase Detection of Breast Cancer[3]

In the field of nanotechnology, double-stranded DNA can function as a microscopic version of copper wire by conducting electrons through the stacked bases on the interior of the double helix. J. Thomas *et al*. at Simon Fraser University recently exploited this property to design an aptasensor that mimics a common electrical switch. Researchers introduced an aptamer against the lung cancer biomarker CTAP III/NAP2 into a strand, disrupting the helix and reducing the current flowing through the DNA (Fig. 2). When the target is introduced, the aptamer binds and restores the double helix. The current increases and can be measured using a gold electrode. The resulting aptasensor identified CTAP III/NAP2 with very high sensitivity (~1 nM), registering levels 100-200 fold smaller than those found in blood samples. Moreover, aptamers against other targets can be used to generate similar high-sensitivity aptasensors.

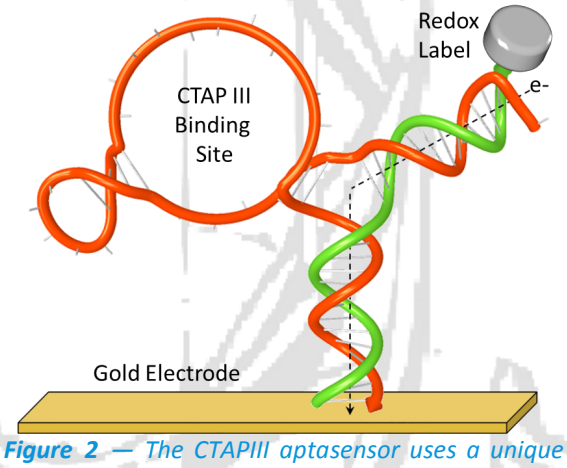

Figure 2 *— The CTAPIII aptasensor uses a unique property of DNA to detect breast cancer biomarkers with high sensitivity.*[1]

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Catalog ID #239, #328, #357, #446

Aptamers Neutralize Rogue Antibodies to Prevent Heart Failure.[4]

Because of the incredible diversity in their variable regions, antibodies bind to a wide variety of targets. Most of the time, these targets are foreign particles such as bacteria or viruses, and antibodies partner with other parts of the immune system to destroy the invading objects. On rare occasions, antibodies target the body's own cells. These "autoantibodies" have been linked to heart failure in patients with Chagas disease, Diabetes, and other disorders. Annekathrin Haberland *et al*. of The Institute of Laboratory Medicine in Germany created an aptamer that binds specifically to the autoantibodies that cause heart failure and not to other beneficial antibodies that thwart diseases. In cell cultures this aptamer blocked the autoantibodies from binding to heart tissue and prevented cell death. It is hoped that one day, aptamers like this one can be administered to patients to neutralize autoantibodies in the bloodstream, not just for heart failure, but also other autoimmune diseases like lupus, rheumatoid arthritis, and type 1 diabetes.

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"Smart Drugs" for Complex Drug Therapy created using Aptamers[5]

Tylenol Arthritis®, Adderall XR®, and Prilosec® are well known extended-release medications that distribute their active ingredients at a controlled rate. Compared to other formulations of the same drug, extended-release medications have reduced side effects and require fewer pills. However, the rate of release is controlled by the pore size or disintegration rate of the tablet or capsule, which are predetermined during the manufacturing process. Complex biological applications such as tissue regeneration and cell differentiation depend upon the precise administration of growth factors at critical times. It would be beneficial to have a delivery system that can regulate the release of several different molecules in real-time. Mark Battig *et al*. has suggested a way of creating these "smart drugs" using aptamers. Once the sequence of an aptamer is known, the complimentary sequence can bind to the aptamer and release the target molecule. Battig *et al*. demonstrated this concept, freeing VEGF and platelet-derived growth factor from an aptamer hydrogel over the course of several days. While this was a proof-of-concept experiment, a patient's own stem cells might one day be transplanted into damaged brain tissue using aptamer-mediated drug delivery to induce the stem cells to develop into healthy neurons.

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Real-Time, Specific Detection of Dopamine using an RNA Aptasensor[6]

In addition to Parkinson's disease, the neurotransmitter dopamine has been linked to a variety of other neurological disorders including attention deficient hyperactivity disorder (ADHD) and schizophrenia. Current detection methods are either too slow to monitor neurotransmitter dynamics in the brain or unable to distinguish dopamine from similar molecules such as catechol or adrenaline. A new RNA aptasensor discovered by Farjami *et al*. is capable of detecting dopamine in complex mixtures with response times of less than a second. Because of their chemical structures, dopamine and some other neurotransmitters are electrochemically active but produce overlapping signals. By trapping an aptamer on the surface of a gold electrode, dopamine is specifically recruited to the electrode, bringing the target close enough to induce an electric current. Farjami's aptasensor recorded physiologically relevant levels of dopamine with no response to several related neurotransmitters. Given further optimization, this aptasensor may one day significantly contribute to our understanding of dopamine dynamics in patients suffering Parkinson's disease and other disorders.

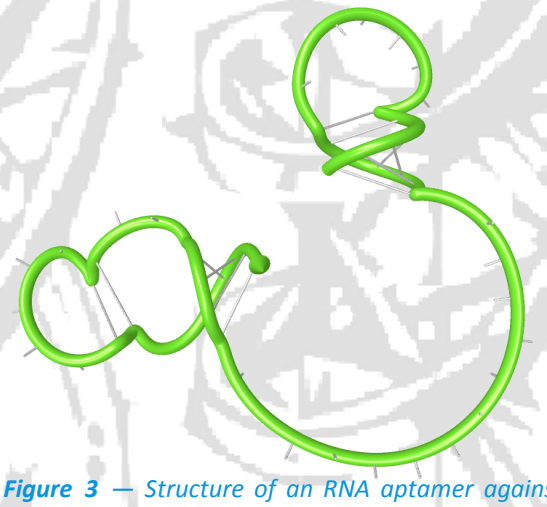

Figure 3 *— Structure of an RNA aptamer against the neurotransmitter dopamine.*[1]

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Catalog ID #095, #401, #402, #403

References:

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