# The AptaReport™

Forget Antibodies. Use Aptamers!

FALL 2015


## DNA Aptamers Target Human Brain Tumor Cells

Glioblastoma is a highly aggressive and difficult to treat form of brain cancer, killing most patients with the disease within two years of diagnosis. Possessing both the natural resilience that is the defining characteristic of most cancers and protection from most currently available treatments by concealing itself in brain tissue, it is difficult to target, and even more difficult to stop. Without an effective means of distinguishing glioblastoma cells from normal brain tissue at a molecular level, therapeutic drugs are rendered ineffective. To resolve this problem, scientists at the Fujian Medical University developed an aptamer to target human glioblastoma cells. The aptamer, dubbed GBM128, binds specifically to human glioblastoma cells contained in clinically obtained tissue, but not to normal glial cells, or to cells from other cancer cell lines. Additional cleavage studies conducted by the scientists found that the GBM128 aptamer bound to membrane proteins of the glioblastoma cells rather than binding through an internalization mechanism, allowing for the potential of easier identification of those proteins in future studies. The GBM128 aptamer demonstrates the ability for aptamers to be used not only as tools of detection, but also as identification of unknown proteins and cells, and presents the possibility of using aptamers as an instrument to guide therapeutic drugs to specific targets.

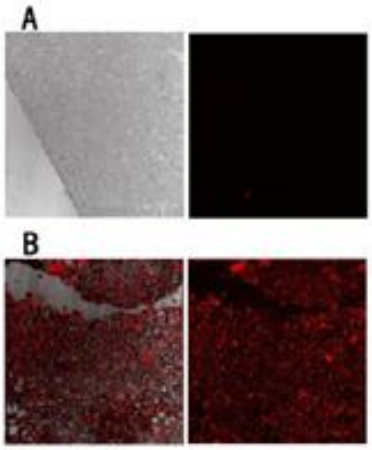


**Figure 1**— Using selected aptamers to recognize FFPE normal or glioma tissue selections. FFPE tissue selections were incubated with cy5-labeled aptamers. 1A=Normal brain tissue, 1B=Gioblastoma tissue*

-C.B.

*Reference: Apta-Index™ ID #509, #589

## Novel Aptamers Cross the Blood Brain Barrier

The blood-brain barrier (BBB) is a crucial component of the body that helps to regulate brain homeostasis and protect the brain from unwanted compounds carried in the blood. An elaborate network of adheren and tight junctions between neighboring endothelial cells greatly limits the ability of therapeutic drugs to penetrate this barrier in order to treat neurological disorders. Typically, for a compound to cross the BBB, it will be lipophilic and have a molecular weight of less than 400 Da; conditions that are difficult to meet with therapeutic drugs. Cheng et al. from the University of Iowa have discovered a library of aptamers capable of crossing the BBB after injection into peripheral vasculature. Aptamers were injected into the tail vein of test mice and were later found within the brain endothelia and parenchymal cells within three hours. This is noteworthy because the molecular mass of most aptamers fall within the range of 5-15 kDa, far above the conventional size threshold that would allow penetration of the BBB. While further studies need to be performed to analyze the exact method of aptamer uptake to the brain, Cheng et al. propose that the aptamers become internalized by the BBB endothelial cells before entering the brain. This novel approach demonstrates that relatively large molecules such as aptamers can penetrate the BBB, and allows for the potential utility of aptamers as a vehicle to transport therapeutic drugs to the brain through peripheral vasculature.

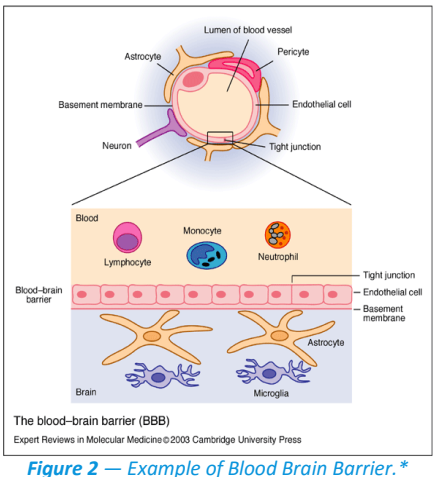


***Figure 2** — Example of Blood Brain Barrier.**

-C.B.

*Reference: Apta-Index™ ID #564, #566, #568


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## Aptamer Photoregulation

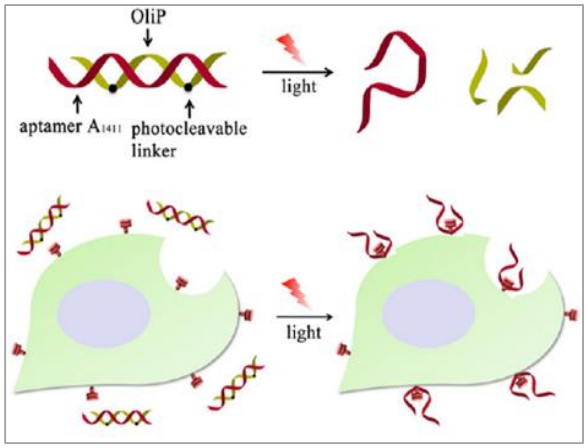


***Figure 3*** *— Photocleavable Linker Illustration.**

The high affinity and specificity of aptamers allows for them to be utilized in a variety of applications. In particular, aptamers appear to be promising methods for the delivery of diagnostic and therapeutic agents. However, some therapeutics can have unfavorable results, as often seen in cancer treatments. Nucleolin is a cell membrane protein that is overexpressed in many types of cancer cells. A photo-triggerable oligonucleotide was designed to be complementary to $AS_{1411}$, the DNA nucleolin aptamer. This oligo was designed to contain certain photo-cleavable bonds, meaning that it will only be able to hybridize to the aptamer in the absence of light. In the presence of light, these bonds break and the aptamer is now free to bind to the cell surface. This allows for the accumulation of aptamers to be limited only to the desired tissue or organ, based simply on the presence or absence of light. The development of this technology creates a spatiotemporal regulation of the delivery of therapeutics via aptamers.

-M.H.

*Reference: Apta-Index™ ID #290

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## Scientist Develop RNA Aptamer to Diagnose Staphylococcus Aureus

*Staphylococcus Aureus* is a gram positive bacterium that is perhaps best known for its antibiotic resistant strains: Methicillin and Vancomycin Resistant *Staphylococcus Aureus* (MRSA and VRSA, respectively). As a gram positive bacterium, *Staph Aureus possesses* a cell wall composed of peptidoglycan and teichoic acids that protects it from its environment, and can contribute to antibiotic resistance. Because early detection of bacterial infection - particularly by an antibiotic resistant strain - is essential to successful treatment, scientists at the University of Dankook, Korea, have tested aptamers as a potential diagnostic tool. Using the teichoic acids that contribute to the formation of the bacterium's cell wall as a target, the scientists were able to identify an RNA aptamer that can successfully bind to *Staph Aureus* specifically. In addition, by modifying the RNA aptamer's pyrimidines the scientists were able to stabilize its structure and increase its resistance to RNases that would degrade it. This new aptamer is a potential candidate for use as a diagnostic tool, and will help to pave the way for the future of aptamers in medical diagnostic testing.

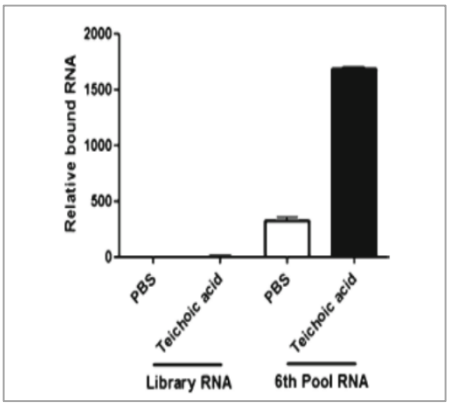


***Figure 4*** *— Enrichment of selected RNA aptamer pool. Library RNA or RNA from the sixth selected aptamer pool was incubated in empty wells. The amount of bound RNA was assessed by real-time PCR and its represented as relative to the amount of library RNA bound to the empty well. Each value represents the mean of three independent measures with standard deviation.**

-M.H.

*Reference: Apta-Index™ ID #593

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