The AptaReport™
Newsletter
Spring 2022

Rapid Selection of Single-stranded DNA Aptamers Binding Staphylococcus Epidermidis in Platelet Concentrates

One of the biggest issues in transfusion medicine is bacterial contamination of blood and blood products. It is estimated that 1 in 3000 platelet units are contaminated with bacteria, resulting in life-threatening sepsis in 1 in 20,000 transfusions. There are many procedures to eliminate or reduce contaminating bacteria, but detection can still be an issue. Small amounts of bacteria may not be detectable with current methods, even if they are clinically significant.

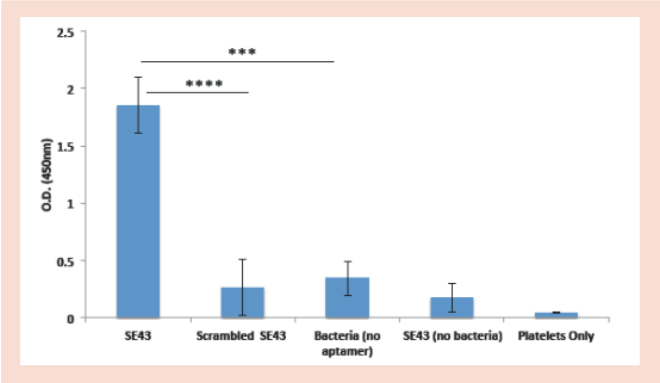


Figure 5 (adapted) from Kaur et al., 2018 This bar graph shows the binding capability of aptamer SE43 to S. epidermis compared to various control groups. SE43 generated the largest response in a colorimetric test, meaning that it binds to the bacterial cell with the most affinity.

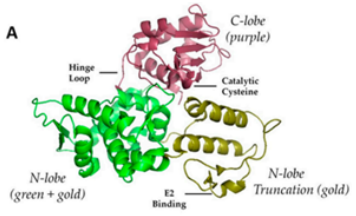
Researchers working on behalf of the United States FDA have developed an aptamer that binds to the common pathogen Staphylococcus epidermis in platelet-concentrate conditions. The aptamer, named SE43, is a 76-base single-stranded DNA oligo. During the SELEX process, the researchers were careful to control for response against plasma proteins. This is important because an aptamer bound to plasma cannot interact with any bacteria targets. SE43 has good binding affinity with S. aureus and it had better affinity in platelet concentrate compared to a typical buffer solution. The aptamer is still in early stages of research, but it shows promise. The final goal would be to incorporate SE43 into filtration devices that could remove small numbers of contaminating bacteria. If widely put into practice, this method could save dozens of patients from fatal infections each year.

*Reference:Apta-Index™ ID# 7247 -H.R.

Selection and Characterization of a DNA Aptamer Specifically Targeting Human HECT Ubiquitin Ligase WWP1

Ubiquination is the post translational process of binding and activating a pattern of ubiquitin to any given protein. Ubiquitin (Ub) is a small protein found across all systems in all living organisms, a rather ubiquitous distribution, hence the catchy name. Ub is responsible for signal regulation regarding protein function and degradation. Fundamentally, when you change the pattern of Ub bound to it, you tweak the protein's "run" program. We understand the basic mechanics of this system but cannot yet actually read and write such programs. Ubiquitination requires each Ub to interact with three successive enzymes (specialized proteins that encourage certain reactions to occur): an activation enzyme (E1), conjugation enzyme (E2), and ligase enzyme (E3). The E3 enzymes are the most diverse and the most studied, identifying binding sites on a protein substrate (or prior activated attached ubiquitins) and matching each Ub to an appropriate target site.

Figure 1 (adapted) from Tucker et al., 2018 Structure of WWP1 HECT domain target and selected pool. (A) WWP1 HECT structure as generated by pyMOL with functionally important regions labeled;



One E3 of note is the WW HECT domain-containing Ub protein ligase 1 (WWP1), which is an oncoprotein. This means, when WWP1 binds ubiquitins to a given protein, the ubiquicode will transform that bound protein into a tumor. WWP1 also programs that protein to degrade. Suffice to say, many scientists are attempting to find a way to moderate, block, or inhibit this process. One promising way involves using aptamers to promote bone deposition by regulating specialized cells that form new bone called osteoblasts to treat osteoporosis.

Aptamers hold the promise of tailor-made therapeutic tools to control protein expression. One of the proteins that WWP1 ubiquinates—and degrades—is Runt-related transcription factor 2 (Runtx2). Runtx2 controls osteoblast differentiation and mineralization (depositing healthy new bone tissue). So, developing an aptamer—called C3A—that binds to WWP1 would block the ubiquination of Runtx2, lead to less Runtx2 degradation, and allow for increased bone deposition.

*Reference: Apta-Index™ ID# 7246 -J.B.

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Selection and Preliminary Application of a Single Stranded DNA Aptamer Targeting Colorectal Cancer Serum

Colorectal cancer ranks second among all malignant cancers in the United States. Early diagnosis and treatment are crucial to improving patients' survival rates with colorectal cancer. At present, the early diagnosis of colorectal cancer depends mainly on endoscopies and tumor markers in the serum. Given that serum is the best specimen for in vitro diagnosis of cancer, detecting tumor markers in serum is a relatively good, non-invasive way for the clinical diagnosis of colorectal cancer. Currently, researchers use antibodies to recognize tumor markers in the serum of colorectal cancer patients. However, drawbacks to this method include complicated synthesis routes, high costs, and relatively weak selectivity and affinity, leading to low accuracy in recognizing colorectal cancer. There is still a great need to develop simple diagnostic tools with high accuracy to recognize colorectal cancer based on patient serum.

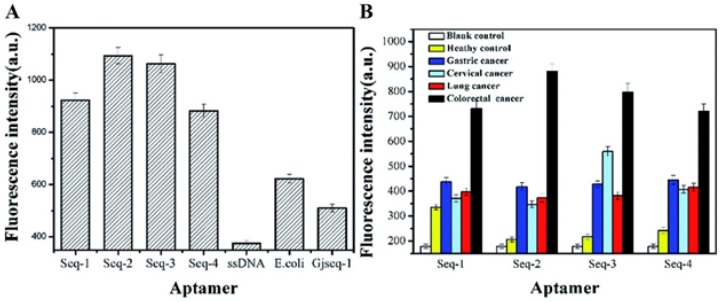


Figure 3 (adapted) from Li et al., 2019: Selectivity analysis of aptamer candidates based [on] fluorescence. (A) [T]he evaluation [of] the selectivity of these aptamer sequences with three control aptamer pools toward colorectal cancer serum. (B) The four aptamer candidates tested with multifarious serum proteins. Error bars represent standard deviation from triplicate analysis.

In this study, an efficient SELEX technique using single-walled carbon nanotubes was developed to identify highly specific DNA aptamers that bind to tumor markers found in the serum of colorectal cancer patients. Their strategy identifies four aptamers with highly selective affinity directly screened from colorectal cancer serum, and the approach does not need high instrument requirements. Aptamer Seq-2 can strongly bind the colorectal cancer serum, weakly bind the non-colorectal cancer serum, and even more weakly bind the healthy serum. Therefore, aptamer Seq-2 presents enormous potential in developing tumor diagnostic kits.

*Reference: Apta-Index™ ID #7248 O.D.

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

Ovarian cancer affects hundreds of thousands of people every year, and the development of early treatment and diagnostic tools has been key in our fight against it. Researchers at McGovern Medical School in Houston, Texas have developed just such a tool: a new method for developing aptamer-based diagnostics to quickly find those who have ovarian cancer and get them treated as soon as possible. This tool, called Morph-X-Select, is a morphology-based aptamer selection method. Such a method allows cancer researchers to develop specific aptamers for tumor sites within larger tissue samples. This novel method of selection starts the same as other tissue-based selection methods. However, it makes use of a laser microdissection device which lets researchers cut around the tumor sites within a particular tissue sample and extract any aptamers that are bound to that region of interest. By using this highly accurate system of extraction, cancer cell diagnostics can be developed by first generating aptamers that are incredibly specific to tumor regions within the body.

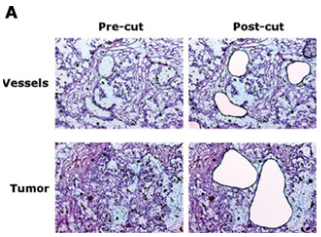
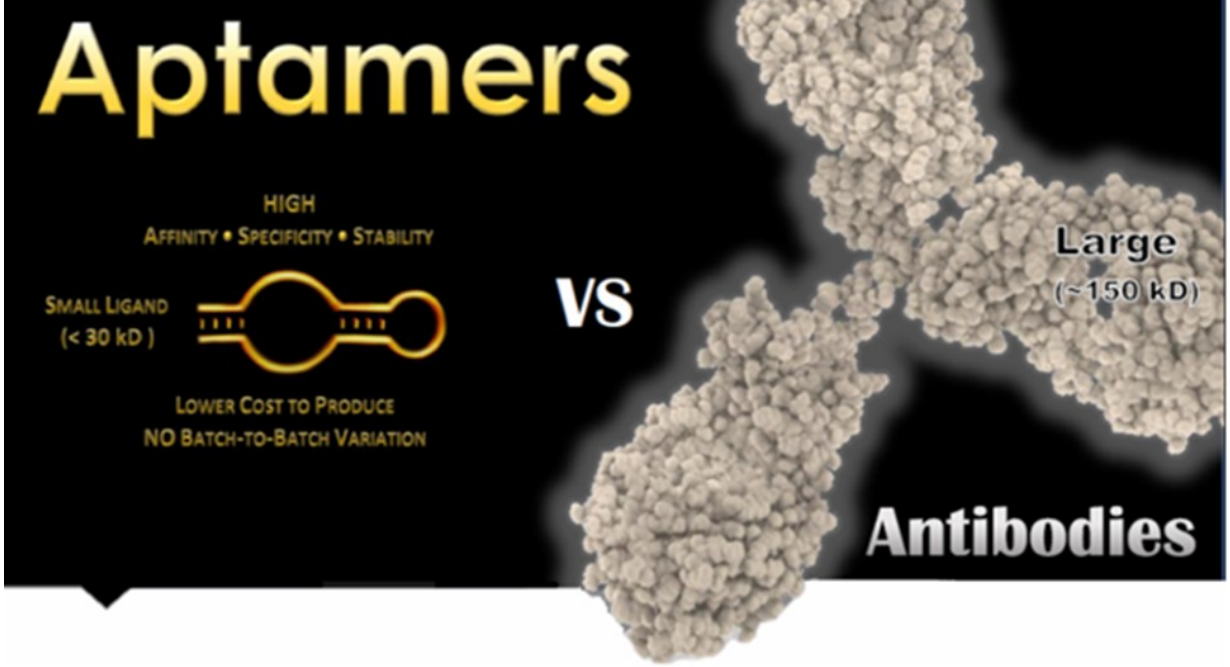


Figure 2 (adapted) from Wang et al., 2016: The Morph-X-Select procedure. This figure shows the tissue samples before and after the laser microdissection. Morph-X-Select allows for the extraction of aptamers bound to a region of interest within tissue samples.

Furthermore, the team behind Morph-X-Select utilized ovarian cancer patient tissue samples to generate aptamer T3 and V5, which bound to ovarian tumor cells and tumor vessels, respectively. Through various fluorescence-based assays, these aptamers were found to be highly specific to the targeted tumor tissue. Additionally, the aptamers showed no response to healthy ovarian tissues. Overall, the success of the T3 and V5 aptamers show that the Morph-X-Select method is a repeatable and individual method for creating tumor-recognizing aptamers.

*Reference: Apta-Index™ ID #7244 #7245 -D.W.



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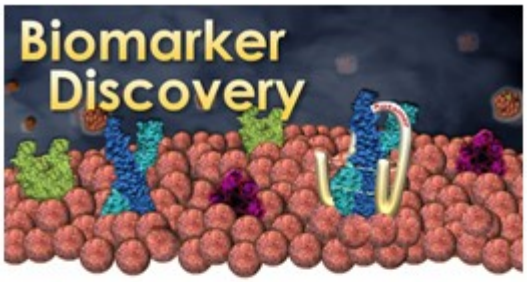

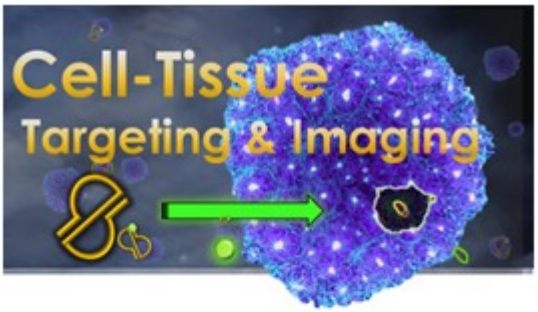

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