The AptaReport™
Newsletter
SUMMER 2019

Capture of Metastatic Breast Cancer CTCs by Cell-Specific Aptamers

Breast cancer is the second most common form of cancer among women, comprising 30% of newly diagnosed cancers. Metastatic breast cancer will be the cause of the majority of breast cancer related deaths. The development of metastases occurs as a result of the presence of circulating tumor cells (CTCs) in the blood. Once in the blood, CTCs are able to travel from the primary tumor in the breast to other bodily tissues. CTCs become present in the blood during stage 1 cancer, but do not form metastases until later stages of cancer development. A method of early breast cancer detection can be derived from the recognition of CTCs during early cancer stages, before other symptoms develop.

a.

b.

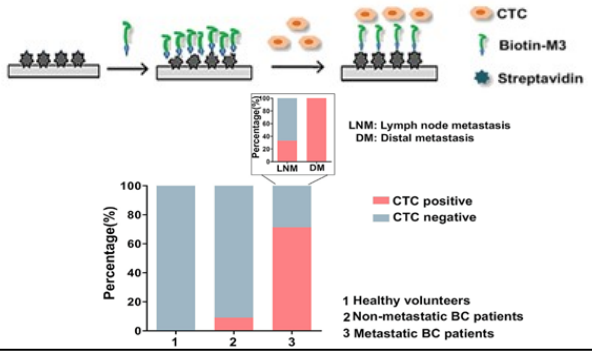

Figure (adapted) part a: workflow of CTTC capture by biotinylated M3 aptamer. Part b: Analysis of CTC capture by developed aptamer probe in healthy, non-metastatic, and metastatic cancer patients.*

Wan-Ming Li et. al. proposes a method of capturing CTCs, specifically those with a metastatic phenotype. They generated aptamers that specifically bound to high metastatic MDA-MB-231 cells, which ensured that they were able to avoid the capturing of CTCs that do not form metastases, while focusing on those that are able to migrate and invade foreign tissues. The use of aptamers for the capture of metastatic breast cancer cells is advantageous because of the high specificity to functional CTCs and provides high affinity to the target cells, a necessity for detection in the blood.

*Reference: Apta-Index™ ID #647 -C.G.

Aptamer Sandwich Assay for Cancer Biomarker Thymidine Kinase 1 (TK1)

Thymidine kinase 1 (TK1) is a protein that aids in cell replication. In the presence of many cancers, blood TK1 level is found in elevated concentrations. Nazari et al. propose a sandwich assay to detect the TK1 biomarker with two TK1 binding DNA aptamers which they have selected for. Based on their research, this aptamer-based assay has similar limits of detection compared to conventional methods (ELISA), except in the case of breast cancers, while also being easily producible and accurate. Therefore, this technique can possibly be utilized or incorporated into current procedures (lateral flow, biosensor systems, ELISA, etc.) for early diagnosis of various cancers.

*Reference: Apta-Index™ ID #645 & ID #646 -J.S.

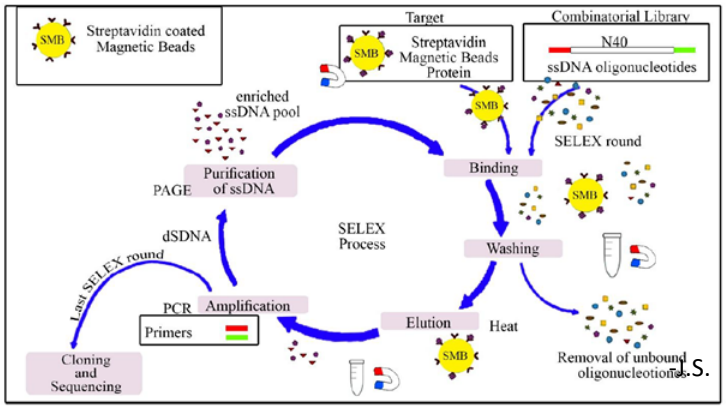

Figure (adapted) : SELEX protocol diagram underwent to obtain the two TK1 binding aptamers.*

J.S.

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Aptamers Engineered to Control Gene Expression within Artificial Cells

In vitro aptamer development has become more precise with better specificities and binding affinities allowing for complex applications. A team in Japan led by Yohei Yokobayashi has applied a SELEX developed aptamer as a riboswitch within an artificial cell, essentially a liposome with selectively added cellular components. The developed cell responds to histamine levels and according to the gene inserted by the team the cell can respond by fluorescence, cargo release, or self-destruction.

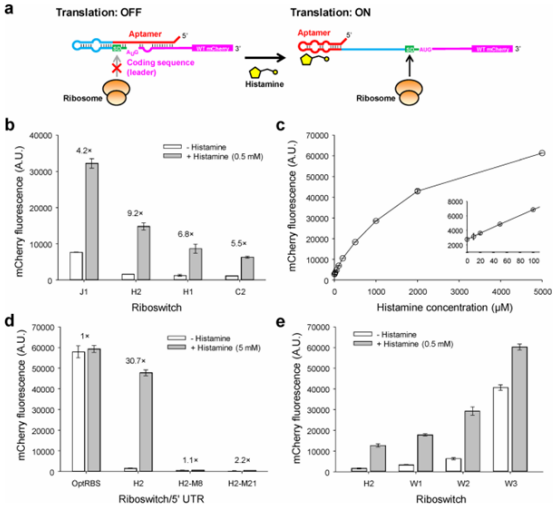

Figure (adapted): Part a: Aptamer-mediated histamine-dependent control of the mCherry fluorescent reporter gene. Part b: mCherry expression of multiple riboswitch variants in the presence of histamine. Part c: Dose-dependent reaction of the selected H2 riboswitch. Part d: Response of various H2 mutant riboswitches. Part e: Assessment of the designed stem region through mutational analysis.*

The approach the team used is based on bacterial riboswitches which control expression of a gene through conformational shifts. The RNA aptamer developed through SELEX prevents translation through its folded structure when histamine is absent. When histamine is present and bound by the aptamer the subsequent conformational shift allows expression of the gene product. This is the first such case of detection of biologically important small molecules by artificial expression systems and the team hopes to further develop this system to deliver drugs locally to relevant areas at relevant times.

*Reference: Apta-Index™ ID #648 -E.F.

Stem-loop Fluorescent Aptamers Adapted for In-vivo RNA Detection

Extracellular RNA sequences can serve as biomarkers for several forms of cancer. However, clinically available *in-vivo* RNA sequence detection methods are neither universal nor sensitive enough to be diagnostically functional. With this in consideration, scientists at the University of Tokyo have developed programmable RNA probes using destabilized versions of the broccoli and baby spinach fluorogenic aptamers. Upon hybridization with the target sequence, the aptamer undergoes a conformational change that stabilizes the fluorophore binding region and dramatically amplifies fluorescence. After optimizing the fluorophore binding region, aptamers were synthesized that bound with and detected RNA biomarkers for breast, squamous and colorectal cancer at concentrations as low as 5nM. Further experimentation with yeast RNA suggested that these aptamers had specificity for their target sequence, but the authors are skeptical that they could discriminate between single base pair mutations.

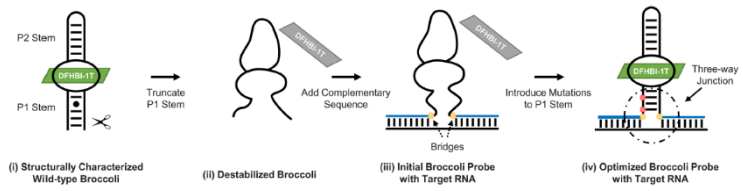

Figure (adapted): Figure 1: RNA complementary to the programmable flanking regions stabilize the central region adapted from the DFHBI-1T fluorophore binding Broccoli aptamer to induce fluorescence. (Adapted from Furuhata et al.)*

Unfortunately, this is critical for such a tool to be a diagnostically useful probe for biomarkers of early stage cancers. Furthermore, the limit of detection must be stretched to 500 pM to match the concentration range of extracellular RNA in blood. Chemistries and selection methods of aptamers are rapidly improving, and other stem-loop fluorogenic aptamers could be similarly adapted, suggesting the near-future possibility of real-time multicolor imaging of RNA in cellular media. Such a development would be a revolutionary new tool for early diagnosis of cancer and for the study of genomics as a whole.

*Reference: Apta-Index™ ID #649 -N.H.

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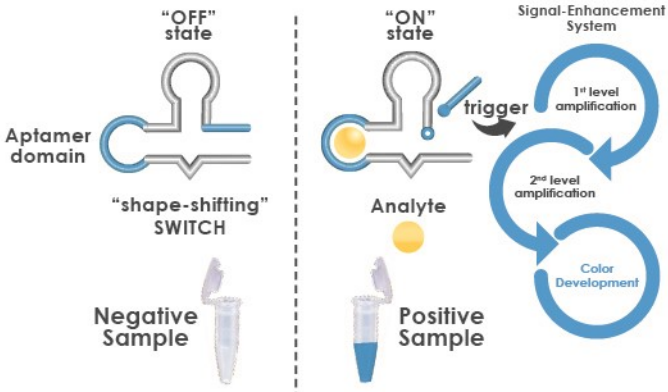

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HIGH Selectivity	+	++++	++++
Unknown Biomarkers		++++	++++
Small Target Selectivity	+	++++	++++
Difficult Target Selectivity		++++	++++
One-Step Detection			++++
In-Solution Detection			++++

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