2nd URSI AT-RASC, Gran Canaria, 28 May – 1 June 2018

Terahertz Chemical Mircroscope for Detecting Cancer Cells

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Breast cancer is the most common cancer among women, and second lethal only after lung cancer [1]. 90% of breast cancer deaths are due to metastasis of cancer cells that take place in the early stages in the patients. Unfortunately, the biology and the mechanism of metastasis is still inadequately understood, but circulating tumor cells (CTCs) are known to be keys to gaining insights into the metastatic process. CTCs are cells that shed from the primary tumor to the blood stream. Many methods have been developed to detect CTCs in the circulation, but there is still a need for effective and highly sensitive methods to detect human CTCs in blood.
In this study, we developed two novel aptamers (MAMB1 and MAMA2) against mammaglobin B (MGB2) and mammaglobin A (MGB1) proteins, which are breast cancer and CTCs biomarkers, respectively. This was achieved by using a combination of regular Systematic Evolution of Ligand by Exponential enrichment (SELEX) [2] against the recombinant form of these proteins, and a cell based- SELEX against MCF7 and MDA-MB-415 breast cancer human cell lines for MGB2 and MGB1, respectively. The selected aptamers were tested for their binding affinity to target cancer cell lines by determine their dissociation constant values. Furthermore, the selectivity of these aptamers against other cancer and normal cell lines was investigated. The binding of both aptamers to their target breast cancer cells was investigated in plasma and blood environments using flow cytometry. In addition, the potential use of both aptamers in breast CTC detection was studied in spiked breast cancer cells in blood. The binding of both aptamers to breast cancer cell lines were then tested for the first time using the Terahertz Chemical Microscopy (TCM) [3].

The results obtained by this study showed that the selected aptamers bind to their target breast cancer cell lines with high affinity (low nanomolar K_d values) and specificity. They also bind to their free recombinant target proteins and show minimal non-specific binding to normal and other cancer cell lines. Moreover, both aptamers recognized breast cancer cells in plasma and blood environments as well as in spiked breast cancer cells. TCM results showed that both aptamers recognized their breast cancer cells compared to the control, and showed binding even at low cell numbers. Overall, the results obtained here indicate the excellent potential to use both aptamers with the TCM to detect metastatic breast cancer and breast CTCs.

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3. T. Kiwa *et al.*, “Work function shifts of catalytic metals under hydrogen gas visualized by terahertz chemical microscopy”, Opt Express. **20**, 11637-11642 (2012).