A Biopolymer-based Fluorescent Nanobiosensor for Early Breast Cancer Diagnosis

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In 2020 alone, breast cancer accounts for 2.3 million cases and 680,000 mortalities. Early detection has been known to improve overall survival-rate of breast cancer patients. Thus extensive research has been focused on microRNAs (miRNAs) as diagnostic biomarkers, for their regulatory role in post-transcriptional gene-expression. Hybridization chain reaction (HCR) is an amplification strategy that produces long biopolymeric DNA chains from monomeric DNA hairpin probes. Herein, we present a nanobiosensor that integrates fluorogenic silver nanoclusters (AgNCs) into a HCR system to detect miRNA-155, a commonly upregulated miRNA in breast cancer patients. To prepare this biosensor, DNA hairpins were first mixed with miRNA-155 to initiate HCR. Silver salt was subsequently added and reduced to form fluorescent AgNCs. The performance of HCR was validated through gel electrophoresis. The fluorescence of AgNCs was analyzed qualitatively and quantitatively with UV-transilluminator and spectrofluorometer, respectively. The HCR-AgNCs nanobiosensor exhibited a strong fluorescence enhancement in the presence of miRNA-155. In addition, the nanobiosensor was highly sensitive with a wide linear range between 100 fM and 1 μM, and a limit-of-detection as low as 1.13 fM. Besides, the nanobiosensor also displayed high selectivity towards miRNA-155, with capabilities of discriminating single-base mismatch. In real sample analysis, the nanobiosensor showed exceptional reproducibility and stability when tested with diluted human serum samples. In lieu of current breast cancer and miRNA detectors, the HCR-AgNCs nanobiosensor exhibits relatively similar performance at a miniscule fraction of cost, effort and time required. Likewise, the proposed nanobiosensor potentially offers a non-invasive and safer approach towards the clinical detection of miRNA-155 and point-of-care early diagnosis of breast cancer.

Keywords Biosensor; Breast Cancer; Hybridization Chain Reaction; MicroRNA; Silver Nanoclusters