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A Low-Cost Paper-Based Electrochemical Aptasensor for HER-2 Detection Using $Ti_3C_2T_x$ MXene

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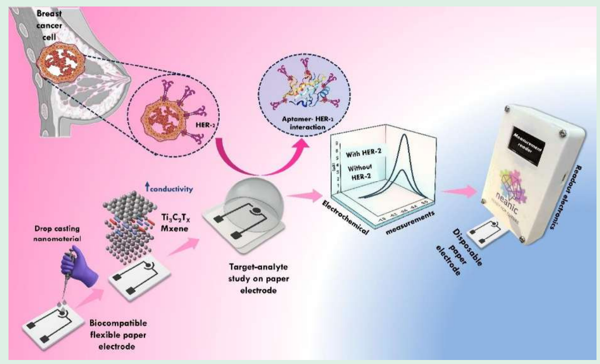
ABSTRACT: Breast cancer remains a leading cause of mortality among women worldwide, emphasizing the need for early, rapid, and cost-effective diagnostic tools. In this study, we report a low-cost, paper-based electrochemical aptasensor for the specific detection of human epidermal growth factor receptor 2 (HER-2), a critical biomarker associated with breast cancer progression. The sensor was fabricated on a carbon screen-printed paper electrode (CSPPE) modified with $Ti_3C_2T_x$ MXene, a two-dimensional transition metal carbide providing excellent conductivity and abundant surface sites for aptamer immobilization. The HER-2-specific aptamer was covalently attached onto the MXene surface via EDC-NHS coupling, and methylene blue (MB) served as a redox mediator to monitor binding events. The developed biosensor exhibited excellent analytical performance, achieving a wide linear detection range from 10 fg/mL to 100 μg/mL, a limit of detection (LOD) of 9.3 fg/mL, a limit of quantification (LOQ) of 28.4 fg/mL and a sensitivity of 10.05 μA/fg/mL/mm^2. Furthermore, the aptasensor demonstrated high selectivity, reproducibility, and operational stability, maintaining its sensing performance for up to one month under ambient storage conditions. The integration of MXene's superior electrical conductivity with a disposable paper-based platform presents a highly promising approach for point-of-care HER-2 detection, contributing toward accessible, rapid, and cost-effective breast cancer diagnostics.



KEYWORDS: *Breast cancer, Paper-based electrodes, MXene, Electrochemical aptasensor, Cost-effective approach*

1. INTRODUCTION

Breast cancer remains the most frequently diagnosed malignancy among women globally, accounting for approximately 25% of all cancer cases each year and posing a major public health challenge that affects patients, families, and healthcare systems worldwide.[1] Early detection and timely treatment significantly improve survival outcomes, as advanced stages are often associated with metastasis and poor prognosis.[2,3] However, current diagnostic tools such as mammography, biopsy, ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) are often costly, time-consuming, and limited in detecting early stage tumors.[4,5] Therefore, there is a strong demand for affordable, rapid, and sensitive diagnostic methods for early breast cancer screening.

Breast cancer classification relies on the expression of molecular biomarkers such as human epidermal growth factor receptor 2 (HER-2), progesterone receptor (PR), and estrogen receptor (ER).[6] Among these, HER-2 overexpression occurs in about 20−30% of breast cancers and is associated with aggressive tumor growth and poor prognosis.[7] Elevated levels of HER-2 extracellular domains (ECD) can also be detected in patient serum,[8,9] offering a minimally invasive approach for disease monitoring. Although fluorescence in situ hybridization (FISH) and immunohistochemistry (IHC) are widely used.[10−13] They require skilled personnel, involve invasive sampling, and may yield inconsistent results.

Electrochemical biosensors have emerged as promising diagnostic tools due to their simplicity, portability, cost-effectiveness, and rapid response.[14] They provide real-time quantitative detection of cancer biomarkers with high sensitivity and selectivity. Several HER-2 electrochemical sensors have been reported.[15−18] However, many still face limitations related to detection range, reproducibility, and fabrication cost. Incorporating nanomaterials into sensor design enhances performance by improving charge transfer, increasing surface area, and facilitating biomolecule immobilization.[19−22] Among these materials, $Ti_3C_2T_x$ two-dimensional (2D) transition metal carbides and nitrides known as MXenes,[23−25] particularly have attracted significant attention

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