Aptamer-based methods for biosensing of estrogen receptors and human epidermal growth factor receptor 2 in breast cancer

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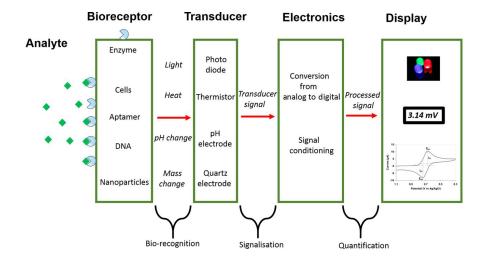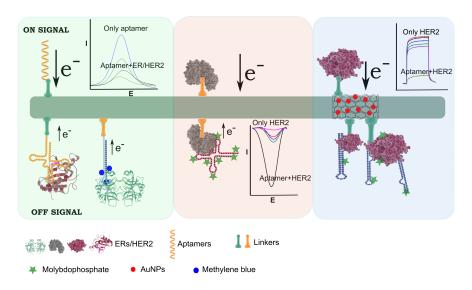[2]Apeejay Stya University

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Abstract

Breast cancer is a common malignancy and a leading cause of cancer related mortality among women. Early diagnosis and better prognosis are vital to improve breast cancer outcomes and survival rates. Clinical assessment of the expression levels of biomarkers including estrogen receptors (ERs) and human epidermal growth factor receptor 2 (HER2) had been beneficial in assisting the prognosis and deriving treatment regimes. Conventionally, these biomarkers were detected mostly using antibody-based methods. However, recent advances in identifying aptamers as antibody substitutes have favoured development of aptamer-based sensing platforms for rapid, cost-effective, and point-of-care testing applications. The last decade witnessed substantial use of aptamers in cancer diagnosis. This review provides a thorough update of recent developments in aptamer-based detection of human estrogen receptors (ERs) and epidermal growth factor receptor 2 (HER2) in breast cancer. The widely used tissue and serum-based biomarkers of breast cancer are introduced, and the conventional methods of ERs and HER2 detection are discussed. Electrochemical and optical methods of aptasensing strategies based on "on/off", "target sandwich", "nanomaterial beacons" and AuNP-based localized surface plasmon resonance (LSPR) approaches are then elaborated. Finally, a perspective for futuristic remote health care monitoring of breast cancer patients using smart wireless nano-aptasensor is provided.

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Analyte   **Bioreceptor**   **Transducer**   **Electronics**   **Display**

Bioreceptor	Transducer
Enzyme	Photo diode
Cells	Thermistor
Aptamer	pH electrode
DNA	Quartz electrode
Nanoparticles	

Light   *Heat*   *pH change*   *Mass change*

Transducer signal

Conversion from analog to digital

Signal conditioning

Processed signal

3.14 mV

Bio-recognition   Signalisation   Quantification

ON SIGNAL

Only aptamer

Aptamer+ER/HER2

OFF SIGNAL

Only HER2

Aptamer+HER2

Only HER2

Aptamer+HER2

ERs/HER2   Aptamers   Linkers

Molybdophosphate   AuNPs   Methylene blue

Gold nanorod (GNR)

Na_2PdCl_4 / Ascorbic acid

GNR@Pd SS

SH / Aptamer

HRP

GNR@Pd SSs—Apt—HRP

Gold electrode

DNA tetrahedron

BSA

HER2

H_2O / H_2O_2 → HQ(red) / BQ(ox)

DPV

with HER2

without HER2

HRP (horseradish peroxidase)

BSA (bull serum albumin)

HER2 (human epidermal growth factor receptor 2)

recycling

HER2

Host-Guest recognition

o-PD / H_2O_2

3

(1)

Templated sequence

G-rich sequence

I → AgNO₃ / NaBH₄ → II → HER2 → III

HER2-binding aptamer

dark Ag NCs   light Ag NCs   HER2

DNA2

(2)

980 nm   546 nm   FRET

980 nm   546 nm   546 nm   No FRET

UCPs   CEA Protein

CNPs   CEA Aptamer

(3)

A

Dye-SiNP → PEG-OH → PEG-SiNP → Avidin → Avi-SiNP → Biotin-HER2 aptamer MUC1 aptamer → Dual-SiNP

B

Streptavidin-MB → Biotin-HER2 aptamer MUC1 aptamer → Dual-MB

HER2 (+) or MUC1 (+) Breast cancer → Dual-SiNP → Fluorescence

HER2 (−) and MUC1 (−) Breast cancer → Dual-SiNP → No fluorescence

(4)

GO   Nanoprobe

Nucleus

AF405-labeled P1   FAM-labeled P2   Cy3-labeled P3

Cy5-labeled P4   AFP   HER2   VEGF₁₆₅   CEA

A

ERα-RNA aptamer   NaCl

Dispersed AuNPs

NaCl

Dispersed AuNPs

ERα

ERα-aptamer complex

Aggregated AuNPs

B

Au   +   HER2 binding aptamer   1   →   Au   2

No HER2+ NaCl Salt   2

NaCl Salt

HER2   3

4