Opinion

Electrochemical biosensors for detection of cancer biomarkers

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Cancer is the second highest cause of death in the United States. Early detection of cancer and its treatment leads to saving of lives and the improvement in quality of life. Detection of cancer biomarkers is utilized for a number of reasons. For example, CA15-3/CA27.29 detection and its quantification not only help determination of breast cancer, but it also helps evaluate effectiveness of treatment rendered, and to check for metastasis. Similarly, beta-human chorionic gonadotropin identification and its quantification help determine the stage of choriocarcinoma and also the response to treatment offered to the patient. A partial list of biomarkers that can be analyzed using electrochemical and other detection methods in blood and serum is provided in Table 1.Biosensors contain biologically active element such as an enzyme (also antibody, antigen, cell organelle, whole cell, nucleic acids etc.). The enzyme acts on the substance (target molecule) whose concentration is being measured (such as glucose in blood). The product of the reaction is analyzed using a transducer that generates signal whose detection and measurement helps quantify the amount of the product (such as hydrogen peroxide during glucose determination step). This quantification is then related to the amount of the target molecule (glucose). Transducers are generally electrochemical, optical, piezoelectric, magnetic or optical in nature. The electrochemical detection techniques involve cyclic voltammetry (CV), square wave voltammetry (SQWV), stripping voltammetry (SV), differential pulse voltammetry (DPV), amperometry and galvanometry, potentiometry, conductometry and electrochemical impedance spectroscopy (EIS). In addition, detection methods involve the filed-effect, which employs measurement of current as a result of a potentiometric effect at a gate electrode. For glucose determination electrochemical detectors are found to be most optimal because they have very good sensitivity and reproducibility. In addition, they exhibit linearity and are cost effective, which provides motivation for exploring and developing electrochemical biosensors.

The electrodes employed in electrochemical biosensors along with the type of electrochemical technique employed play a great role in detection of cancer biomarkers. For example, 3D gold nanowire electrodes embedded in polypyrrole (Ppy) employing DPV has been shown to detect PSA concentrations corresponding to less than one femto gram per ml.[1] Glassy carbon electrodes modified with gold nanocrystals can detect NSE – a biomarker for lung cancer at concentrations as low as 0.3 pico gram per ml using cyclic voltammetry.[1] Investigators have employed carbon ionic liquid electrode, which has been modified with multi-walled carbon nanotubes to detect HER2 – a breast cancer biomarker using EIS at nano gram per ml concentration.[1] The electrode surface modification improves the stability of the biological recognition element. Frequently a redox mediator such as ferro/ferricyanide ion is employed to enhance the biosensor sensitivity. In order to make a better prognosis, more than one biomarker needs to be analyzed simultaneously. This problem can be addressed by employing multiplexed electrochemical immunoassays.[2] Multiple working electrodes or single electrode with multi-labeling of antibodies can be used. Microfluidic chips or platforms are being investigated to electrochemically determine multiple biomarkers using electrochemical detection methods.

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Another emerging technology that is drawing attention involves the wireless electrochemical analytical workstations that connect to the Internet.[3] This technology facilitates automation of microfluidic platforms. Commercial, biosensors employing the standard enzyme-linked immunosorbent assay (ELISA) have been available for a number of years.[4] i-STAT is a pioneer in that they have developed the world's first hand-held sensor for clinical assay of blood. The sensor employs many electrochemical detection methods. Other commercial biosensors include devices for detection of cholesterol and various ions in the blood. The growth in electrochemical biosensor development has been growing over the last two decades. Developments in 3D printing, DNA chips, and microfluidic platforms as well as integration involving wireless technology will further fuel interest in electrochemistry-based biosensors for early cancer detection (Table 1).[5]

Table 1 Examples of biomarkers used for cancer detection[5]

Type of cancer	Biomarker
Ovarian	Antigen 15-3 (CA-125)
Prostate	PSA, Sarcosine, CYFRA 21-1
Liver	Alpha-fetoprotein (AFP)
Breast	CA15-3/CA27.29, HER-2/neu
Pancreatic, colorectal	CA19-9
Acute myeloid leukemia	CD 33
Mesothelioma	HAPLN1

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Conflicts of interest

The author declares that they have no conflict of interest.

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