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Advances in Clinical Diagnosis through Electrochemical Aptamer Sensors

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Aptamers are oligonucleotides, such as ribonucleic acid (RNA) and single-strand deoxyribonucleic acid (ssDNA) or a peptide molecule that can bind with a specific target molecule with high affinity and specificity which is due to the formation of specific three-dimensional structures. Since the discovery of aptamers, scientists have used aptamer in the fabrication of various kind biosensors such as; electrochemical, optical, fluorimetric etc. Aptamers have been considered as a bio-material in diagnostics and also as therapeutic tool in the development of new drugs, drug delivery systems. Other advantages of aptamers are that they can be regenerated, highly stable to external factors, and does not require animal models for production [1]. Out of various kinds of clinical detection assays generally an electrochemical methods is more fascinating because it offers high sensitivity, compatibility with novel microfabrication technologies, miniaturization, and low cost. Therefore, in recent times various electrochemical aptasensors have been fabricated using several techniques such as; electrochemical impedance spectroscopy, potentiometry, and other electrochemical techniques [2-8]. Kim et al. selected DNA aptamers that specifically bind to estradiol through the SELEX (Systematic Evolution of Ligands by Exponential enrichment) process from a random ssDNA [8]. In this study, the DNA aptamer was immobilized on the gold electrode and estradiol was detected using a redox mediater where the sensitivity and selectivity of the detection was drastically increased. In an another study, Zhu et al. [9] successfully developed a new highly sensitive, selective, and label free sensor for the detection of anticancer drug "daunomycin" using a cancer cell surface lipid molecule "phosphatidylserine" and aptamer co-immobilized onto the nanocomposite conducting polymer film [7]. This sensor was 190 times more sensitive than the then reported any other daunomycin detection system. The strategy described in this work has many attractive features, such as: simplicity, rapidity, no requirement for a specific label (*i.e.*, a fluorescent or reactive moiety), low-cost and hence could be a useful method in medical diagnosis.

Aptamers have not only been utilized for the detection of biochemical molecules rather it has been very well explored for the detection of cancer cells. Zhu et al reported a novel method to detect human epidermal growth factor receptor 2 (HER2) and HER2- overexpressing breast cancer cells using an electrochemical immunosensor combined with hydrazine and aptamer-conjugated gold nanoparticles (AuNPs) conjugate [10]. The conjugate selectively deposited the silver ion only on the immunocomplex and hence helped in the highly selective bioimaging of cancer cells by bare eye and under optical microscope in a very short time. This method exhibited an excellent diagnosis method for the ultrasensitive detection of SK-BR-3 breast cancer cells in human serum samples. In another study, a novel electrochemical aptamer sensor for the detection of acute blood cancer, Burkitt's lymphoma has been reported (Figure 1). In this case, cancer cell is firstly captured by an aptamer probe, and the cell-aptamer complex was analyzed by an electrochemical detection process through the alkaline phosphatase-catalyzed silver deposition reaction [11]. It is expected that this aptamer based detection is simple and cost-effective, and exhibits excellent compatibility with miniaturization technologies in future.

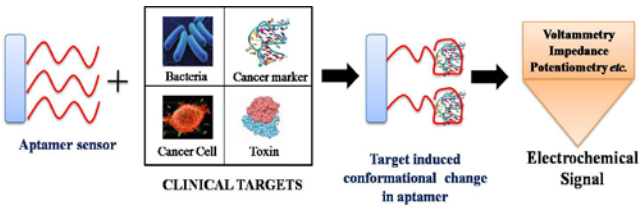

Figure 1: Schematic diagramofan aptamer sensor, various kinds of clinically important target molecules, and detection using electrochemical techniques.

A part of electrochemical detection methods, aptamer has also been coupled with microfluidic device for the extraction and detection of various biomolecules and cancer cells. This integrated technology is extremely advance in clinical analyses and it could be a next generation point-of-care assay system. In a study, a microfluidic device for specific extraction and thermally activated release of analytes using nucleic acid aptamers has been reported [12]. The device primarily consists of a microchamber packed with aptamer-functionalized microbeads as a stationary phase, and integrated with a micro heater and temperature sensor. The device functioning has been verified by performing the extraction of a metabolic analyte, adenosine monophosphate coupled with thiazole orange, with high selectivity. In another case, circulating cancer cells were isolated from whole blood using an aptamer mediated micropillar-microfluidic device [13]. The special geometry of the micropillar array in the device resulted in the high-performance circulating cancer cell isolation. This microfluidic device enabled the isolation of as few as 10 tumor cells/1 mL of whole blood within half an hours. The advantages of such aptamer mediated device over the other methods include rapid analysis, no pre-treatment of blood samples, and low detection limit. Consequently, this aptamer-coupled microfluidic device has a potential to be used for clinical applications such as cancer diagnosis, prognosis, and monitoring the progress of therapeutic treatment.

In conclusion, electrochemical aptamer based methods have been very well developed in clinical diagnostics and therapeutics. Various kind of novel sensor fabrication approaches and new aptamer design will be extremely helpful for highly sensitive and selective analysis of clinical analyte in future.

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