Advanced Biosensing for Early Detection of HIV

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Abstract. Early detection of the Human Immunodeficiency Virus (HIV) has, over the years, been very critical in ensuring effective intervention and, concurrently, controlling the rates of transmission. However, there are serious challenges to a set of conventional diagnostic methods, especially in that window period, the period in which the concentration of the virus may remain low enough to be missed. This paper reviews how such a diagnosis could be achieved using biosensors. Biosensors are made up of detection elements and biological detection elements. These put together can achieve high sensitivity and specificity in the detection of HIV biomarkers. These biomarkers are at low levels. This review is focused on a few biosensing strategies, electrochemical and optical biosensors, and AuNPs and CNTs integration nanomaterials that can be employed to enhance biosensors. It should also consider the point-of-care testing that is called for in resource-constrained areas around the world. The survey indicates that biosensors tend to be more effective than traditional methods in the early detection of HIV infection. Those are quicker and more accurate results that these devices used to produce effective outcomes.

Keywords: Biosensing, HIV, early detection.

1. Introduction

Human Immunodeficiency Virus Infection, or HIV, is still one of the major health problems in most parts of the world. According to the World Health Organization, it is estimated that 38 million people all over the world suffer from HIV infection in 2020, and 1.5 million cases are diagnosed every year [1]. Despite the advances of ART, wherein it is no longer considered a life-threatening but rather a chronic condition, early diagnosis remains a challenge. HIV may be latent in form within host cells and remain almost undetectable by standard diagnostic modalities, more so during the early beginnings of infection within the three-month window period. The risk for transmission here is that even if patients are infected with the virus, this far away from the infection site they may not show a plus sign of the illness. Biosensors being devices can help solve this challenge. Biosensors have been defined as devices that incorporate biological recognition elements and a biological detector that together are used in detecting biological phenomena of interest. These hold high potential for early detection of HIV infection since they can combine sensitivity and specificity, even the capturing of low concentrations of infection biomarkers at early stages. This essay will discuss the search for early stages of HIV infection and penetration into state-of-the-art biosensing technologies.

2. HIV and the Window Period

One recognizes it as a retrovirus because it will only attack those parts of the immune system that target the CD4+ T-cells, which are important in initiating an immune response [2]. After entry into the host cell, the virus HIV degrades its RNA genome into host cell DNA. It is in this form that HIV can remain inert, residing within latent reservoirs of encoding immune cells in the body that have become infected with HIV viruses but do not produce new particles [3]. It is practically impossible to find the virus at this stage, as it is very little, and in some cases, normal assessment such as an antibody-based test is likely to yield invalid outcomes. The window period is the period between the earliest infection and the time that the standard HIV tests would expect to provide a reliable positive result.

This is the period when infected persons show no symptoms yet are dangerously infectious. One of the biggest challenges in handling HIV and AIDS is the window period after one has been infected with the virus. The window period, it is said, lasts for about 2-8 weeks until antibodies against HIV can be measured [4]. Such delay may prove to be important in timely intervention. Although NATs can detect viral RNA and allow diagnosis much sooner, most of these methods are prohibitively expensive, labor-intensive, and require a lot of special equipment [5]. Thus, there is a biosensor with the ability to detect low concentrations of HIV biomarkers in the early stages of infection. This can allow currently used HIV Detection Methods.

3. Antibody-Based Tests

The most common HIV detection is an antibody test, which focuses on the presence of antibodies to HIV, either in the blood or in saliva.

These tests are relatively cheap, widely available, and mostly sensitive after the window period. However, they have certain shortcomings during the period of early infection, as it takes time for the immune system to build up and produce a detectable number of antibodies. A study showed that in the early stages of the disease - from stages I to II of the HIV infection - antibody tests are unreliable and can give false negatives as high as 30% [4]. Tests that can be applied for antigens, for instance, the p24 antigen test detects the presence of the p24 antigen. This antigen is produced in the early days of infection with HIV. These tests potentially allow for earlier detection than tests that rely on detecting antibodies to HIV, which may not be developed for several weeks after infection. However, once antibodies form against the virus, the p24 antigen disappears from the blood, so this type of testing only allows for a very small window period, approximately 2-3 weeks post-infection [5].

Nucleic acid tests have the potential to detect HIV RNA, thus allowing an infection to be identified as early as 10-12 days after exposure--considerably earlier than other methodologies [6].

However, NATs are very expensive and require specialized laboratory equipment and therefore cannot be useful in low-resource settings of screening. Despite the accuracy high cost and complexity, they limit their accessibility, especially in low- and middle-income countries where HIV infection rates are often the highest [1].

Combination tests, also known as fourth-generation assays, simultaneously detect both HIV antibodies and the p24 antigen. This leads to greater sensitivity and a relatively reduced window period compared to tests that rely on antibodies alone. These can detect the presence of HIV within 2-4 weeks of exposure [7]. Even so, while they represent an advance over earlier methods, combination tests are still sensitive enough to detect HIV during this acute phase of infection.

4. The Promise of Biosensors in HIV Detection

Biosensors have great potential and promise to revolutionize diagnostics in HIV by offering rapid, sensitive, and cost-effective detection of HIV biomarkers. Unlike the conventional methods, biosensors are designed to detect multiple biomarkers at the same time factor which improves diagnosis accuracy even during the window period.

The above attributes make electrochemical biosensors one of the promising technologies for HIV detection considering their high sensitivity, low cost, and ease of miniaturization.

These sensors detect the presence of biomarkers indicating HIV through changes in the electrical signals produced within reactions between the target molecule and the transducer. An example could be an electrochemical biosensor that utilizes antibodies or aptamers to bind to either proteins or nucleic acids of HIV, which would yield an electric signal that one could easily recognize. In one study, the usage of an electrochemical biosensor for the detection of the p24 antigen was shown to have a detection limit as low as 10 pg/mL, which is way below the threshold needed for the p24 tests. The sensor was able to detect HIV during the early stages of infection and thus offered a promising alternative to standard ELISA tests [8].

Optical biosensors make use of light-based detection methods to identify HIV biomarkers. These sensors normally rely on changes in the optical properties of a transducer. For example, fluorescence, absorbance, or a surface plasmon resonance when a target molecule binds to the detection element. The optical biosensors are highly sensitive; moreover, some of them can detect multiple targets simultaneously [9]. A good example is that Shan et al., in 2013, presented the SPR biosensor for detecting HIV antigens and antibody interactions.

The SPR biosensor gave the results of real-time detection of HIV-1 at lower concentrations of 1 ng/mL and considerably improved the sensitivity compared to conventional diagnosis of the disease,as shown in fig 1 [10]. In this regard, the detection of HIV has become much easier and more advanced after nanomaterials were applied to biosensors. Such nanomaterials possess certain unique properties, including great surface area, excellent electrical conductivity, and biocompatibility, which have made them useful candidates to enhance the performance of biosensors. For instance, AuNP-based biosensors have been utilized for the detection of both DNA and RNA of HIV antigens with high sensitivity. One of the studies elaborates on the application of AuNPs in the colorimetric biosensor for the detection of HIV. The sensor could detect DNA of HIV at low concentrations of 0.1nM [11]. The detection of HIV, particularly in developing countries, may be greatly improved by point-of-care diagnostics. Biosensors engineered for point-of-care use are lightweight and easy to handle and operate. They also deliver quick results without needing high-level laboratory equipment.

These devices play a critical role in accessing HIV testing in far-flung areas and among poor nations. Peeling et al., 2017, have identified that a microfluidic-based POC biosensor, chip is capable of detecting both antibodies from HIV and syphilis with high sensitivity. The chip shows results in less than 20 minutes and costs less than $1 per test, hence is a very cost-effective solution for diagnostics related to HIV in low-resource settings [12]. Challenges in Biosensing for Detection of HIV Despite the promise, challenges are associated with developing one effective biosensor for HIV detection in its early stages. One of the main challenges of HIV biosensing is concerned with the question of high sensitivity and specificity.

HIV is in low concentration during the initial stages of infection, hence the difficulty in detecting biomarkers at a concentration that may be too low to be compared to the threshold limit of conventional biosensors [13].

The high degree of genetic variability in HIV, along with its rapid mutation rate, complicates the task of developing a universal biosensor that can detect all viral variants. In addition to these, various research groups have reverted to the use of multiplexed biosensors that can detect more than one HIV biomarker. These biosensors target several viral proteins, nucleic acids, and host immune responses; hence, they are likely to result in higher accuracy and reliability for early-stage detection of HIV infection [14]. Biocompatibility and stability are the two most influencing factors on biosensor performance.

Functionality of biosensors should not degrade in complex biological fluids such as blood and saliva. While nanomaterials offer many advantages, they sometimes possess cytotoxicity and immunogenicity, which can severely limit their application in clinical use. About the challenges mentioned above, biocompatible coatings or surface modifications are being developed to further enhance the in-vivo stability and safety properties of biosensors. For example, PEG coatings have been used to improve the biocompatibility of AuNP-based biosensors by reducing toxicity and prolonging stability in biological fluids. Whereas biosensors have enormous advantages concerning sensitivity and speed, device development and deployment costs may remain a limitation for their use, especially in low-resource settings. Most of these advanced biosensors are based on expensive materials or complicated fabrication techniques, limiting their scalability and accessibility in the regions hardest hit by HIV infection [15]. For this reason, scientists try to develop biosensors using cheap materials and simple manufacturing techniques to make the manufacturing process as low-cost and easy as possible.

Among others, recently, paper-based biosensors have emerged as a promising solution for relatively inexpensive diagnostics of HIV. These biosensors use cellulose paper as a substrate with a tremendous reduction in production cost while maintaining high sensitivity and specificity [16].

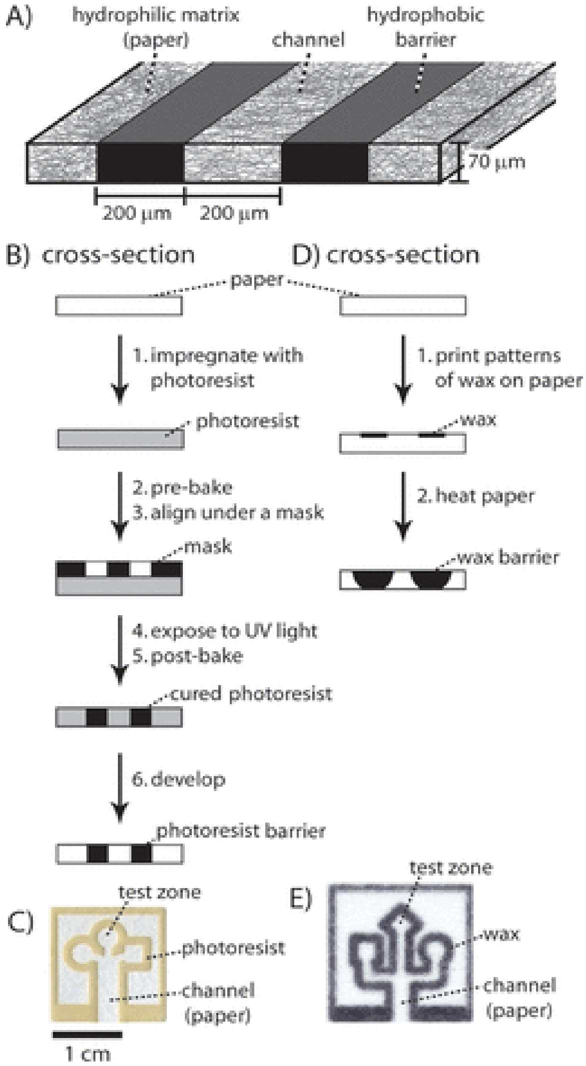

Figure 1. Schematic of AuNP-based biosensor for the detection of HIV DNA [10].

Future Direction and Innovation in HIV Biosensing CRISPR-Cas technology, initially for gene editing, has lately undergone some modifications to be applied in biosensing. These CRISPR-based biosensors would be useful, with high precision for the detection of specific nucleic acid sequences, thereby being suitable for diagnostics in HIV. For instance, CRISPR-Cas12a has been applied to develop a nucleic acid detection platform recognizing HIV RNA with sensitivity within less than an hour. This technology can help realize the rapid diagnostic performance of HIV at low costs with high sensitivity.

Wearable biosensors form another exciting part of HIV detection. These devices offer continuous biomarker monitoring in real time; therefore, they offer great potential in the early detection and ongoing monitoring of HIV status. For example, biosensors using sweat have been developed to detect the biomarkers of HIV infection and other diseases through a non-invasive method. Such integration of these biosensors into wearable devices, such as watches, illustrates that individuals at risk of HIV could be offered continuous monitoring with early treatment.

The integration of AI and machine learning into biosensing platforms could have the potential for improved precision and efficiency in HIV diagnostics. Large, pre-existing datasets from biosensors can be analyzed by AI algorithms to pick up on patterns that would otherwise be missed using traditional methods. For example, AI may analyze the output from multiplexed biosensors to identify signs of HIV infection earlier and more precisely than any one biomarker test.

5. Conclusion

High-performance biosensor development for early detection of HIV infection represents a huge field of biomedical science. Because HIV remains a global concern over health, mostly within resource-poor countries, a biosensor can be highly capable of enhancing sensitivity, selectivity, and availability of diagnostics for HIV. Though there are persistent challenges regarding sensitivity, biocompatibility, and cost issues, continuous improvements with the use of nanotech, CRISPR-based biosensors, and integration of AI may revolutionize HIV diagnostics. Biosensors focus on early detection during the window period of HIV, enabling early intervention and treatment, and reducing morbidity for the patient while reducing rates of transmission. With this field constantly in development, this marriage of biosensing technologies into medical practices is bound to eventually discard traditional methods of diagnosis and introduce a new era of precision medicine for HIV and other infectious diseases.

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