A Novel Approach for HIV Detection Using CANARY Technology Based Biosensor

P Hemanthini, K Preetha, R Sathya, B Padmapriya

Abstract— **AIDS, caused by infection of HIV is an illness that alters the immune system, making people vulnerable to infections and diseases. Rapid tests with oral fluid which has lower antibody concentration and tests done in serum are also proved to be ineffective in some sero-negative patient. The Cellular Analysis and Notification of Antigen Risks and Yields (CANARY) technology can be used for detection of HIV and the task can be accomplished in minutes as the CANARY technology has been proved to detect <50 particles of pathogen in less than 3 minutes in air samples. The specialized receptor protein present on the surface of B cell is specific for HIV antigen thereby increasing the sensitivity and specificity of proposed method. CANARY could provide an excellent first screen for people who may have been exposed to HIV, thus enabling treatment to be started sooner.**

Index Terms— **B cell, CANARY technology, HIV, Sero-negative, specificity.**

I. INTRODUCTION

By the end of 2007, it was estimated that a total of 33.2 million people worldwide are living with HIV and AIDS. HIV has continued to rise, due to population growth. HIV and AIDS negatively affect economic growth which makes it difficult for countries and individuals to initiate adequate and comprehensive responses to the epidemic, due to a weak economic base. HIV infection is acquired through sexual intercourse with an infected partner, exposure to infected blood and blood products, and from an infected mother to her unborn child, in the uterus, during delivery, or from breast milk.

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***P Hemanthini**, Department of Biomedical Engineering, PSG College of Technology., Coimbatore, India, 7402111426.*

***K Preetha**, Department of Biomedical Engineering, PSG College of Technology, Coimbatore, India, 9751265257*

***R Sathya**, Department of Biomedical Engineering, PSG College of Technology, Coimbatore,India,9698715754*

***B. Padmapriya**, Department of Biomedical Engineering, PSG College of Technology, Coimbatore, India, 9443883109,*

Transmission of HIV through body fluids other than blood and genital secretions such as CSF, pleural fluid, and amniotic fluids is also possible. However, HIV transmission resulting from exposure to saliva, urine or sweat is not very likely to happen. Interaction between the viral envelope proteins (gp120) and receptors on the cell membrane is critical for HIV to enter and infect the host cell. High concentrations of the CD4 molecules and co -receptors have been detected on the surface of T -lymphocytes and macrophages and hence they serve at entering sites for HIV. The diagnosis of AIDS is confirmed when a person with HIV develops one or more of a specific number of severe opportunistic infections or cancers. Such conditions include Kaposi's sarcoma, Cryptococcal meningitis, PCP, Toxoplasmosis and CMV retinitis. Now-a-days there are various techniques for HIV detection which includes western blot and ELISA which has some disadvantages like producing false negatives. On the other hand CANARY technology delivers extremely rapid detection of HIV at previously unseen levels of sensitivity and specificity. Accurate results can be obtained in less than 3 minutes by non-expert users.

II. METHODS FOR HIV DETECTION

A. Existing Methods

Since the recognition that HIV is the agent causing AIDS, many tests have been developed to aid in establishing the diagnosis of HIV infection and evaluating the stage of infection [1]. Antibodies to HIV can be measured by a variety of techniques. None of these detect HIV itself, but rather detect an immune response to the virus, and therefore take some time to develop and become reactive (or positive) after HIV infection has been acquired. Antibodies to HIV-1 and HIV-2 are detected by EIA, also known as enzyme-linked immunosorbent assay (ELISA), simple/rapid test devices, and western blot (WB) tests. HIV infection in infants is diagnosed by detecting the presence of viral nucleic acid (i.e. viral RNA or viral DNA) often called nucleic acid testing (NAT).False positive results have been reported in cases of haematologic

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malignant disorders, DNA viral infections, autoimmune disorders, multiple myeloma, primary biliary cirrhosis, alcoholic hepatitis, chronic renal failure, positive RPR (rapid plasma regain) test and false negative results have been reported in cases of window period prior to seroconversion, immunosuppressive therapy, malignant disorders, B-cell dysfunction and bone marrow transplantation, etc. These tests cannot detect HIV infection until antibodies develop, which may take six to 24 weeks after exposure. Hence an advanced technology that efficiently detects the HIV even in the course of window period is needed in order to prevent the transmission of virus in the initial periods when the transmission remains very active [3].

B. CANARY Technology

CANARY uses nature's bio identifiers, B cells, the fastest antigen identifiers known. B cells are a type of white blood cell that binds to and recognizes antigens. The Laboratory genetically engineered B cells bind specifically to antigens of interest and then, within seconds, emits photons that indicate that binding and therefore recognition have occurred [5]. The fundamental components of the CANARY biosensor include genetically engineered B cells that emit photons upon binding to specific bio agents and a photo detector that measures the luminescence. The steps involved in CANARY technology are B cells are first exposed to bio agents in test sample, then the bio agents bind to B-cell antibodies, and the biochemical signal transduction cascade is triggered, resulting in Ca2+ release which makes aequorin emit photons, and finally the emitted photons are detected.

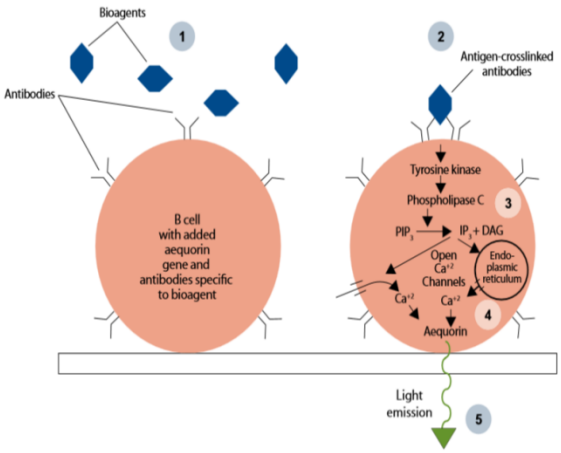

Fig. 1 Principle of CANARY technology

CANARY is the only sensor that makes use of immune cells. Other available sensors are based on immunoassays or PCR (polymerase chain reaction), both of which take much longer and/or are not as sensitive as CANARY. Instead of waiting a few days for test results, with CANARY the results can be obtained in just a minute.

III. B CELL

B cells or B lymphocytes are a type of lymphocytes in the humoral immunity of the adaptive immune system. B cells can be distinguished from other lymphocytes, such as T cells and natural killer cells, by the presence of a protein on the B cells outer surface known as a B cell receptor (BCR). This specialized receptor protein allows a B cell to bind to a **specific** antigen. The principal functions of B cells are to make antibodies against antigens, to perform the role of antigen-presenting cells (APCs) [8]. When a B cell encounters a kind of antigen that triggers it to become active, it gives rise to many large cells known as plasma cells, which produce antibodies.

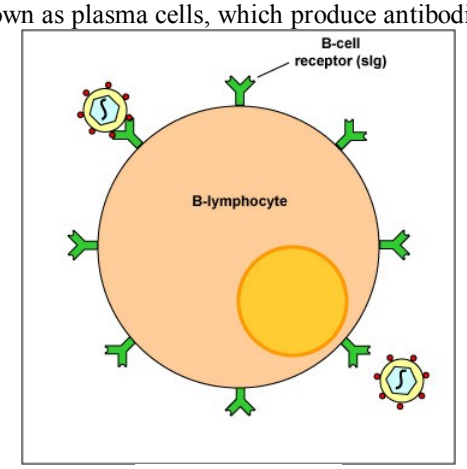

Fig. 2 Structure of B cell

A. HIV-ASSOCIATED B CELL ACTIVATION

HIV infection is associated with severe B cell disturbances, and memory B cell responses are reported to be impaired, particularly in the context of vaccinations. Hyper activation of B cells during untreated chronic HIV-1 infection is also part of these disturbances and is characterized mainly by increased expression of surface activation markers, increased polyclonal B cell activation, increased cell turnover, increased frequencies of plasma blasts, and manifestation of hyper gammaglobulinemia. The extent of HIV-associated hypergammaglobulinemia and B cell activation is not exclusively linked to HIV specificity, as less than 20% of Ig-secreting B cells have been shown to be specific for gp160 and less than 10% specific for p24. B cell hyper activation and hyper gammaglobulinemia of non-pathogen specificity are frequently observed upon many viral and bacterial infections and in the context of autoimmune diseases. A role for an antigen-dependent mechanism underlying B cell hyper activation during HIV-1 infection could so far not be completely excluded. Indeed, elevated levels of autoantibodies (including specificities for DNA,

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lipids, actin, and myosin) are commonly found in HIV-infected individuals, but poly reactive B cells with irrelevant specificities(e.g., for ovalbumin or haptens) are also found. However, the vast majority of published reports indicate that polyclonal stimulation independent of BCR specificity may lead to B cell hyper activation and hypergammaglobulinemia.

IV. Preparation of B Cell

B cells are produced by immunizing a host with a HIV antigen. The cells that recognize and respond to these antigens are called as B lymphocytes. These B cells produce a unique antibody directed against these HIV antigens. Monoclonal antibodies are mono specific antibodies that are the same because they are made by identical immune cells that are all clones of a unique parent cell, in contrast to polyclonal antibodies which are made from several different immune cells. Monoclonal antibodies have monovalent affinity, in that they bind to the same epitope. Monoclonal antibodies are produced via multiple/identical copies of a certain cell called a hybridoma [10]. To create Hybridoma cells the fusion of 2 cells are needed in order to combine the characteristics of the 2 cells into 1 cell. 1 of the cells is a producing cell antibody which is a B-Lymphocyte used from a laboratory mouse and the other is a tumor cell named myeloma. Tumor cells have the ability to grow indefinitely and at an exceeding rate from normal cell growth. Laboratory produced Hybridoma cells replicate much faster than normal antibody producing cells, and the individual hybridomas produce the specific antibodies for an indefinite period of time. Hybridoma cells manufacture the specific monoclonal antibody that was originally produced by the B-Lymphocyte cell. The hybridoma cells are placed into media that can help them grow and produce the bulk quantities of monoclonal antibodies. There are 2 ways for growing monoclonal antibodies, 1 is to grow them in laboratory flasks meaning In Vitro, and the other is to grow them in the stomach lining of mice.

V. Discussions

CANARY technology is currently used in industrial applications and for other purposes in order to detect the pathogens present in air. This technique has been proved to detect <50 particles in 3 minutes and hence serves as a efficient method to provide warning to public. This method is also more efficient regarding specificity since it involves the concept of B cells. Hence this concept can be innovatively used for medical applications as it satisfies the requirements of response time, sensitivity and specificity. The implementation of this method for HIV detection creates a breakthrough in medical field. However since this sensor involves immobilization of B cells the cost involved is higher. The cost reduction can be achieved by developing efficient methods for B cell production.

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P Hemanthini is studying Biomedical Engineering in PSG College of Technology. She has published a paper entitled "measurement of volume of urinary bladder by implementing localizing region-based active contour segmentation method" in springer. She has undertaken a project work on "EMG Pattern Recognition System for Hand Prosthetic".

K Preetha is studying Biomedical Engineering in PSG College of Technology. She has undertaken a project work on "Development of Portable Sleep Stage Identification System".She is interested in Biosensors.

R Sathya is studying Biomedical Engineering in PSG College of Technology. She is interested in mathematics. She has undertaken a project work on "EMG Pattern Recognition System for Hand Prosthetic".

B Padmapriya is working as Assistant Professor in Department of Biomedical Engineering, PSG College of Technology. She is interested in medical Image Processing .She has published more than ten papers in National and International journals.

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