



## Advancements in electrochemical DNA sensor for detection of human papilloma virus - A review

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### ABSTRACT

Human papillomavirus (HPV) is one of the most common sexually transmitted disease, transmitted through intimate skin contact or mucosal membrane. The HPV virus consists of a double-stranded circular DNA and the role of HPV virus in cervical cancer has been studied extensively. Thus it is critical to develop rapid identification method for early detection of the virus. A portable biosensing device could give rapid and reliable results for the identification and quantitative determination of the virus. The fabrication of electrochemical biosensors is one of the current techniques utilized to achieve this aim. In such electrochemical biosensors, a single-strand DNA is immobilized onto an electrically conducting surface and the changes in electrical parameters due to the hybridization on the electrode surface are measured. This review covers the recent developments in electrochemical DNA biosensors for the detection of HPV virus. Due to the several advantages of electrochemical DNA biosensors, their applications have witnessed an increased interest and research focus nowadays.

### Introduction

One of the most common sexually transmitted infections is the human papillomavirus (HPV) which affects millions of people worldwide. Thus it has gathered huge attention due to increased focus on vaccine development and cancer-screening recommendations for early prevention of the disease [1]. While some common dermatological and sexually transmitted diseases are easily attributed to the presence of the HPV virus, there is still no cure for HPV [2], though a healthy immune system could offer sufficient protection from the virus itself. Around half of the world's population is exposed to the risk of HPV infection at least once in their lifetime [3]. Cervical cancer, from the contamination of high-risk HPV, is the third most prevalent type of cancer in occurrence and fourth in death rate among women worldwide [4,5]. The HPV-16 and HPV-18 are two of the most dangerous cancer-causing HPVs which contain the E6 and E7 oncogenes, are responsible for almost 70% of all cervical cancers. The HPV-16 is basically associated with squamous cell carcinoma, while the HPV-18 is associated with

adenocarcinoma, a less common disease despite being more dreadful than the latter. Both the HPV 16 and HPV 18 are preventable by vaccination [2].

Around 26,900 new cases of HPV-associated cancers are diagnosed each year between 2004 and 2008, with 4100 women deaths from cervical cancer in the United States alone [6]. The National Program of Cancer Registries (NPCR) and the Surveillance, Epidemiology and End Results (SEER) program showed that an average of 33,369 diagnosed HPV-associated cancers are detected annually, including 12,080 males (8.1 per 100,000) and 21,290 females (13.2 per 100,000). The HPV virus is believed to be responsible for 96% of cervical cancers, 93% of anal cancers, 64% of vaginal cancers, 51% of vulvar cancer, 36% of penile cancers and 63% of oropharyngeal carcinomas [7].

The visible epidermal manifestations such as warts or condylomas, occur only in 1% of the infected patients. Therefore, the diagnosis of HPV infection requires specialized equipment to pinpoint the internal lesions at the mucous membranes. The Papanicolaou test is another type of analysis for proven cervical injury cases. In this test, the cervical

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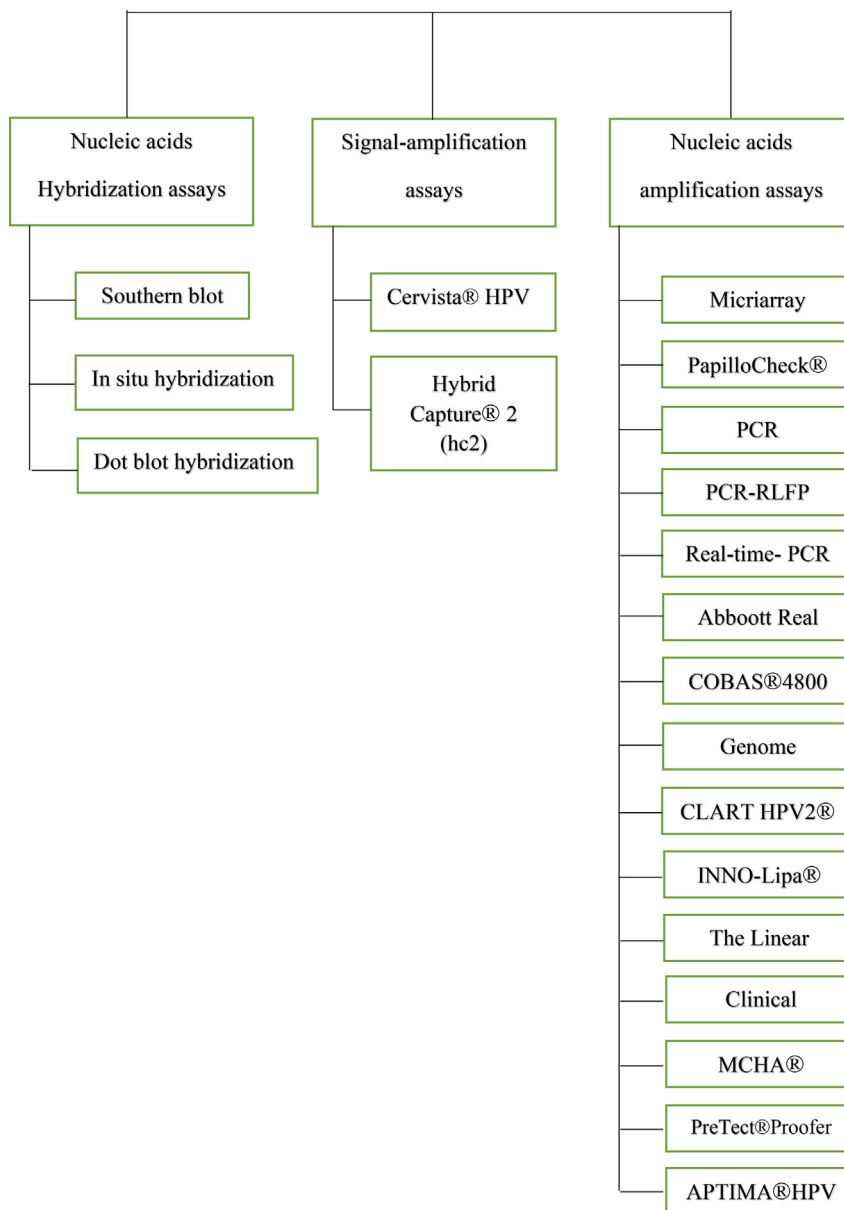
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**Table 1**

Classification of molecular-biology techniques for HPV diagnosis.



cells are collected using swabs, followed by staining with the Papanicolaou staining technique [8,9]. Molecular diagnosis is essential for the accurate differentiation of various HPV strains, which are categorized according to their low, intermediate or high oncogenic risk.

The differentiation of various HPV strains is a challenging task since all HPV strains are closely related. The protein expression ratio analysis could provide some differentiation of the various HPV strains through molecular fingerprinting of the oncogenic potential in histopathological samples [10,11]. The DNA analysis is another essential method of identification of the different types of HPV strains, which is based on the complementarity principle of the DNA strands. For example, the signal amplification of a fragment of target nucleic material can be identified by the polymerase chain reaction (PCR) method and signal amplification of an oligonucleotide hybridization assay [12,13]. At present, HPV diagnosis is based on molecular biological techniques which are categorized into nucleic acid-hybridization assays, signal amplification assays and nucleic-acid amplification (Table 1 and Table 2) [14].

Southern blotting, in situ hybridization, and dot-blot hybridization

used radiolabeled nucleic acid hybridization assays to detect HPV infection in cervical samples. Low sensitivity, large amounts of purified DNA and time-consuming procedures are disadvantages of these techniques. However, generated high-quality information is benefit of using these techniques [14]. Southern blotting, in situ hybridization, and dot-blot hybridization used radiolabeled nucleic acid hybridization assays to detect HPV infection in cervical samples. Low sensitivity, large amounts of purified DNA and time-consuming procedures are disadvantages of these techniques. However, generated high-quality information is benefit of using these techniques [15]. The Hybrid Capture® 2 (hc2) distinguishes between high-risk and low-risk groups, but was not designed for genotyping single HPV [16]. The Cervista® HPV identifies the presence of 14 HR-HPV types and also utilizes a signal-amplification method for the detection of specific nucleic acids. The Cervista® assay demonstrated 100% sensitivity in the detection of CIN III and 98% sensitivity in the detection of CIN II compared to hc2 [17]. Lower false-positive rate, and high sensitivity and specificity to genotyping HPV -16/18 are other properties of this assay [18,19]. However, these techniques involve complex protocols and require specialized

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