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Electrochemical biosensors for influenza virus a detection: The potential of adaptation of these devices to POC systems

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ABSTRACT

Influenza virus A still causes serious pandemics every year which result in high mortality. Though there are promising developments involving newly emerged diagnostic tests for the detection of this virus, the "perfect" test has not been developed yet. In this review, we focus on the electrochemical biosensors for influenza virus A detection. Firstly, brief information about structure, species and pandemics of influenza virus A has been presented. After elucidating the invasion of host cells with this virus, conventional detection methods have been discussed. Then, definition of electrochemical biosensors was made and the existing electrochemical influenza virus A biosensors have been critically evaluated. Lastly, the prospects of electrochemical influenza virus A biosensor in POC technology have been discussed.

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1. Introduction

Influenza which causes serious pandemic resulting in high morbidity and mortality each year, is an acute respiratory virus which belongs to the family *Orthomyxoviridae* [1]. According to the antigenic differences in the matrix (M) protein and the nucleoprotein (NP), the virus can be categorized in three groups as the influenza virus A, influenza virus B, and influenza virus C. Among them, influenza virus A is the most contagious one which causes high mortality to the population [2]. Considering the structure of influenza virus A, it could be stated that it is a negative single stranded RNA virus which contains eight segments. Each RNA segment encodes at least one protein and the M1 matrix protein encapsulates the segmented genome. The single- stranded negative RNA that the segmented genome is consisted of, is decorated with the nucleoprotein and the trimeric polymerase complex which includes PB1, PB2 and PA proteins. Hemagglutinin (HA) and neuraminidase (NA) are the two of these encoded glycoproteins which interact with cellular molecules (Fig. 1). Since these glycoproteins locate on the virus surface, they also act as antigens. Also there is a M2 proton channel protein that provides the proton transport across the viral membrane. These RNA-protein structures are surrounded by a lipo-protein envelope where M1 stays inside while M2, HA and NA present on the outer surface of the viral particle [2–4] (Fig. 1).

Based on these surface proteins, influenza virus A can be separated into its subtypes. Up to now, seventeen HA and ten NA subtypes have been identified [3].

HA is a type II integral membrane glycoprotein that plays very important role in the replication of influenza virus A in the unin-

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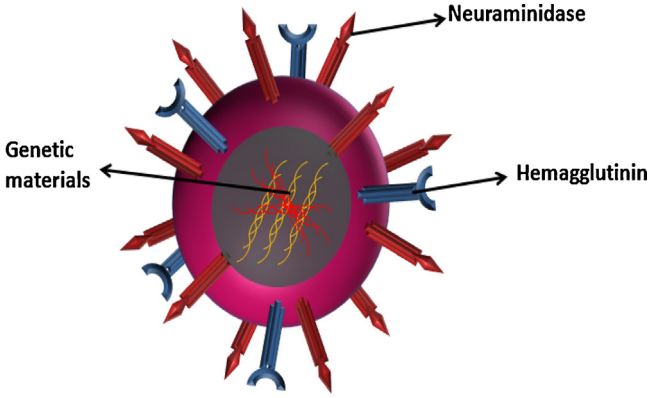

Fig. 1. The general illustration of the structure of influenza virus A.

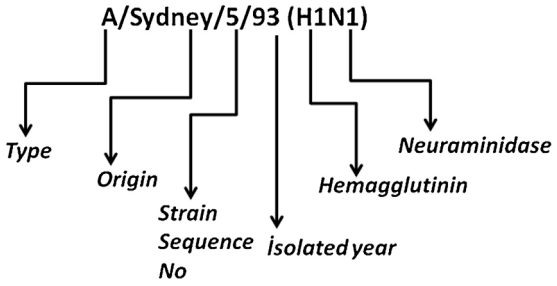

Fig. 2. An example of the unabbreviated form of influenza virus.

fected cells. Host proteases cleave the first membrane glycoprotein HA, into two disulfide-linked chains, HA1 and HA2. In this way, the membrane fusion peptide located at the amino terminus of the HA2 subunit becomes exposed which is important for the viral infectivity [5].

On the other hand, NA molecule can be described as a type II integral membrane glycoprotein that contains a box-shaped catalytic head. It also has a stalk at the center with a hydrophobic transmembrane-spanning region and as a tail, NA contains a cytoplasmic tail [5]. NA cleaves α-ketosidic linkage between the sialic (N-acetylneuraminic) acid and an adjacent sugar residue [6] which in this way frees the influenza virus A for the infection of the host cells [4].

2. Infectivity of the virus

Aquatic birds can be defined as the source of influenza virus A in the nature, which means they carry this virus into their bodies without showing any symptoms. On the contrary, when influenza virus A is transferred to poultry, lower mammals and humans, flue type respiratory diseases have emerged. H1, H2 and H3, which are the virus subtype of HA, and the subtypes of NA as N1 and N2 can all be transmitted to humans and are responsible for the annual flu [7]. The schematic representation of influenza pandemic is presented at Fig. 2.

Considering the death rates in infected poultry, the avian H5 and H7 subtypes can be accepted as low and highly pathogenic viruses respectively. It is obvious that low pathogenic avian influenza viruses A cause milder respiratory disease while highly pathogenic avian influenza viruses A lead to more serious consequences, sometimes with 100% mortality among poultry within 48 h [8,9]. In 2004, a form of H5N1 pandemic, resulted with great mortality among birds. The transmission of this virus from birds to humans and to other mammals has also been occurred. Luckily, because of the limited binding of H5N1 to human-type receptors, effective human-to-human transmission that could cause huge amounts of deaths did not happen [10–12]. However, the development of this human pathogenic H5N1 strain and transmission of this strain from human to human is still possible. For this to happen, four mutations in the HA protein structure would be enough [9]. Another example about

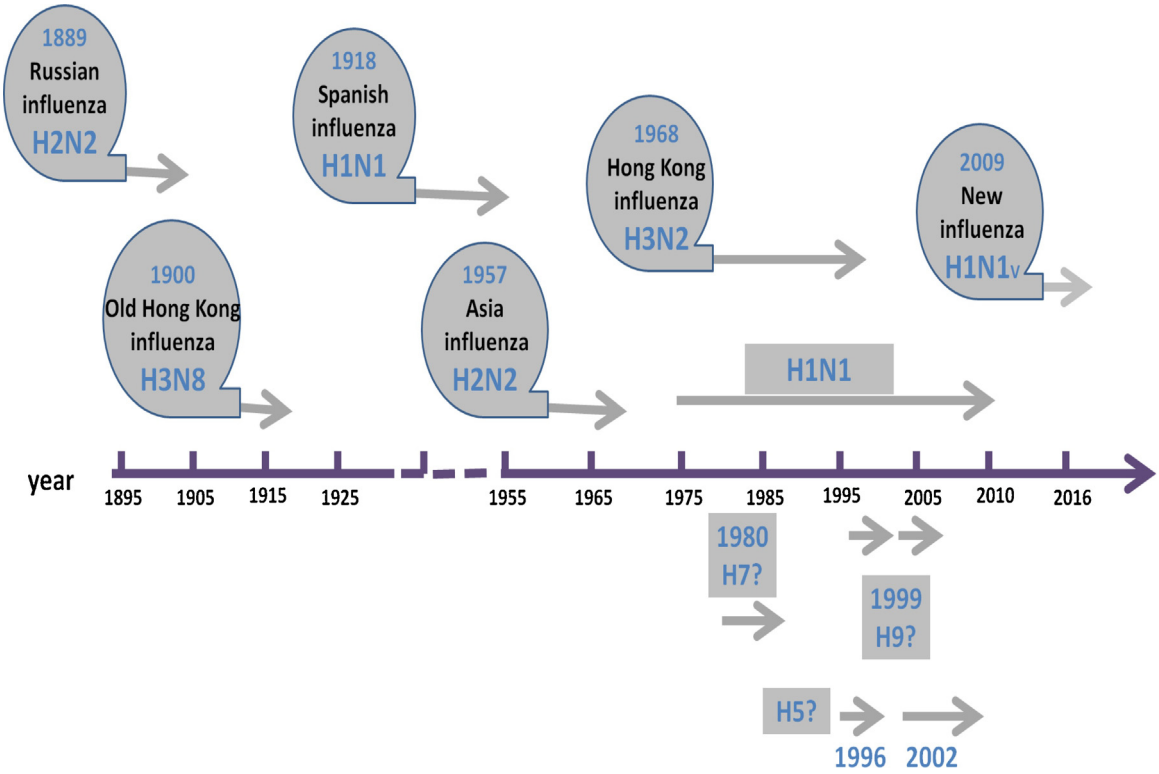

Fig. 3. Influenza A pandemics according to year and type (? means that unidentified type of NA).