Development of a Zika vaccine

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1. Introduction

Currently, there is no approved vaccine against the Zika virus (ZIKV). However, several organizations are actively developing vaccines using various platforms and technologies. While many of these are in the early stages, several are based upon previously approved platforms and designs against dengue and other infectious disease agents. In March 2016, the World Health Organization (WHO) announced a list of organizations describing approaches toward Zika vaccine development. This short editorial describes the overview of ZIKV and vaccine development.

2. Zika virus

ZIKV is a mosquito-borne Flavivirus that was first reported in humans in 1952 [1]. ZIKV has recently reemerged in Brazil and tropical/subtropical nations [2,3]. Presently, this noxious virus is being widely transmitted by Aedes (Stegomyia) mosquitoes [4]. Worse yet, the Brazilian Ministry of Health confirmed the relation between ZIKV and microcephaly, and WHO and the US Centers for Diseases Control and Prevention issued an alert about the association of ZIKV infection with congenital malformations and neurological syndromes [5,6]. There is now evidence that ZIKV may also be transmitted sexually [7]. The rapid spread of ZIKV raises increasing concerns for public health, such as the increased frequency of Guillain–Barré syndrome and congenital neurological anomalies [8].

ZIKV is an 11-kb single-stranded, positive-sense RNA virus from the Flaviviridae family, most closely related to the Spondweni virus [9]. Two major lineages, African and Asian, have been identified through phylogenetic analyses [10,11]. Transmission occurs via mosquito vectors from the Aedes genus in a sylvatic cycle involving nonhuman primates [12], but little is known about the seasonal and spatial dynamics. A substantial proportion of ZIKV infections are subclinical, but patients may also present with clinical symptoms similar to other arbovirus infections, such as dengue virus (DENV) and chikungunya virus [2]. Commonly reported symptoms include rash, fever, arthralgia, and conjunctivitis [13]. Symptoms tend to be mild; however, there is a concern that ZIKV infection may be related to more severe disease pathogenesis.

Each day, more and more information is available regarding the whole genome of ZIKV that may shed light on viral differences between strains. One major reason is diagnosis of ZIKV infection is hampered by serological cross-reactivity with other Flaviviruses, and relies on the detection of ZIKV RNA in blood through ZIKV-specific reverse transcription polymerase chain reaction (RT-PCR) or pan-flavivirus PCR amplification followed by sequencing or viral isolation [14]. For example, DENV is the most prevalent arbovirus in tropical and subtropical countries. However, most cases are acquired from urban transmission by Aedes aegypti mosquitoes. Every year, DENV infections cause more than 50 million cases, 500,000 hospitalizations, and 12,500 deaths worldwide [15]. DENV like ZIKV belongs to the genus Flavivirus and there are four distinct serotypes (DENV-1 to DENV-4), and infection with 1 serotype does not provide long-term, cross-protective immunity [16].

Before 2007, very few human cases of ZIKV infection were reported, but now there is a full-blown epidemic and the beginnings of a ZIKV pandemic [17]. ZIKV from African and Asia lineages cause infection [11]; however, the ‘African strain’ of ZIKV virus is generally non-symptomatic or in some cases causes acute febrile illness that clinically resembled DENV [18]. In contrast, the emerging Asian strain of ZIKV is known to circulate in the same areas and is associated with a suspected ‘congenital syndrome’, while causing asymptomatic or mild febrile infections that can be DENV-like in infected individuals [13]. For both Africa and Asia lineages, little is known about the genetic relationships. The geographic origin of the strains responsible for the recent epidemics most likely is in the French Polynesian islands. There is a need for vaccine countermeasures to control ZIKV spread.

Recently, a clinical trial in which volunteers were infected with the closely related DENV just 6 months after receiving an experimental DENV vaccine or a placebo showed that tetravalent DENV vaccine induces a robust neutralizing antibody response [19]. The candidate DENV vaccine is made from a mixture of four live, attenuated viruses targeted to each of the four serotypes. All 21 volunteers who received the DENV vaccine, TV003, were protected from infection, while all 20 placebo recipients developed infection. The study is important as it shows the proof-of-concept that a
Table 1. Current Zika vaccine landscape.

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**Declaration of interest**

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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**References**

Papers of special note have been highlighted as:
- of interest
- of considerable interest


- One of the earliest papers describing zika virus in Africa.


- Comprehensive review of zika virus infections in Brazil in 2015.


- Descriptions of zika virus and microcephaly in the Americas.


• **Overview of the molecular evolution of zika virus for the last 70 years.**


