



Review

Zika Virus Pathogenesis: A Battle for Immune Evasion

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Abstract: Zika virus (ZIKV) infection and its associated congenital and other neurological disorders, particularly microcephaly and other fetal developmental abnormalities, constitute a World Health Organization (WHO) Zika Virus Research Agenda within the WHO's R&D Blueprint for Action to Prevent Epidemics, and continue to be a Public Health Emergency of International Concern (PHEIC) today. ZIKV pathogenicity is initiated by viral infection and propagation across multiple placental and fetal tissue barriers, and is critically strengthened by subverting host immunity. ZIKV immune evasion involves viral non-structural proteins, genomic and non-coding RNA and microRNA (miRNA) to modulate interferon (IFN) signaling and production, interfering with intracellular signal pathways and autophagy, and promoting cellular environment changes together with secretion of cellular components to escape innate and adaptive immunity and further infect privileged immune organs/tissues such as the placenta and eyes. This review includes a description of recent advances in the understanding of the mechanisms underlying ZIKV immune modulation and evasion that strongly condition viral pathogenesis, which would certainly contribute to the development of anti-ZIKV strategies, drugs, and vaccines.

Keywords: Zika virus (ZIKV); immune evasion; infection; tissue propagation; congenital and neurological disorders

1. Introduction

Between 2011 and 2018, World Health Organization (WHO) identified, alerted and tracked more than 1400 epidemic events in 172 countries due to emerging viruses, such as influenza, Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), Ebola, Yellow Fever, Zika, and others [1]. These epidemic diseases are a prelude of the new global era the world is facing, and hallmark of high-impact, fast-spreading outbreaks that are increasingly difficult to manage, as is occurring nowadays with the new worldwide infection by the emerged SARS Coronavirus 2 (SARS-CoV-2) responsible for the ongoing coronavirus disease 2019 (COVID-19) pandemic [2]. Remarkably, in the last five years, WHO has declared three global health emergencies associated with emerging viruses: SARS-CoV-2 in 2020 [2], Ebola virus (EBOV) in 2014 [3–6] and Zika virus (ZIKV) in 2016 [7]. These threats were the first warnings of the socio-economic impact of emerging viruses, as the world is now experiencing with the SARS-CoV-2 pandemic which has become a global

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