ZIKA VIRUS AND THE CHAMBER OF SECRETS: UNRAVELLING VIRUS-HOST IMMUNE RESPONSE INTERACTIONS.

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Zika virus (ZIKV, Flaviviridae) has proven to be a rapidly emerging mosquito- borne virus in recent years. Previously considered to be an insignificant pathogen, recent outbreaks have been characterized by the increased prevalence of neurological conditions, such as Guillain-Barré syndrome and microcephaly, which have placed substantial strain on local healthcare providers and heightened public concern. As a result of its rapid spread and altered clinical outcome, the World Health Organisation declared it a public health emergency of international concern in early 2016. ZIKV is divided into three recognised genotypes; East African (MR766 prototype cluster), West African (Nigerian cluster), and Asian strains. Sequencing of strains from the outbreak in the Americas indicates that they are related to isolates associated with the French Polynesian outbreak in 2013 which are part of the Asian lineage. Most Brazilian and other American ZIKV isolates are genetically very similar to each other with a high degree of conservation at both the nucleotide and amino acid levels. Furthermore, comparative analysis of viral genomes does not highlight any genetic explanation for the increased incidence of neurological syndromes associated with certain strains. Therefore, it is important to understand the factors that result in the generation of severe clinical outcomes. One determinant which may play a considerable role is the strategy employed by ZIKV to obstruct the host's antiviral immune responses in order to establish a productive infection. It has been shown that, as seen with other flaviviruses, ZIKV infection decreases the induction of type-I interferon which impairs downstream production of interferon-stimulated genes. The virus uses a multi-facetted approach through the action of different viral proteins and subgenomic flavivirus RNA (sfRNA) interfering at specific stages of the pathway to subdue host interferon production and enhance virus replication. Our work compares the action of isolates from different ZIKV lineages which provides key insights into understanding the way the virus impairs the host cell's defense system and how this impacts on disease pathogenesis. Understanding these processes may provide a starting point for the development of targeted antiviral therapies.