# Full genomic sequencing of Zika could help unlock virus's secrets

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Credit: Medical Research Council

Scientists have been able to shed more light on how the Zika virus works, by sequencing the full-length genome of the virus from a patient in Brazil and studying how a molecule derived from the genome fights the host antiviral response.

The research, led by the MRC-University of Glasgow Centre for Virus Research, studied a Zika virus isolated from a patient with classic symptoms and shows the full genomic sequence of the virus, including non-coding regions. Importantly, the research also identified a Zika virus-derived molecule that inhibits an important part of the host's immune

system, which may be key to understanding how the virus causes disease.

The study, published today in the journal *PLOS Neglected Tropical Diseases*, was supported by the UK Government and Brazilian partners through the Newton Fund and undertaken in collaboration with a group of international colleges, including in Brazil.

The team compared the genome sequence from this South American Zika virus isolate, which was obtained from a patient in Recife, with other available Zika sequences. They then looked at the non-coding regions of the sequence which are often missing from other sequences, and detected a portion of the viral genome in infected cells called sfRNA. This is also detected in infections by related viruses such as dengue, and the authors described ZIKV sfRNA as having a similar function to those already described as it acts by inhibiting specific parts of the host cell's antiviral response.

They suggest this study highlights the particular importance of studying patient-derived viruses and comparing them to laboratory cultured viruses, which could mutate and therefore not provide as accurate a picture of the current Zika virus epidemic.

Dr Alain Kohl, leader of the Kohl Group at the MRC-University of Glasgow Centre for Virus research, said: "We have used the information from a Brazilian isolate, which we obtained from our colleagues in Brazil and fully characterised it in collaboration with them, to identify a virus-derived molecule that inhibits a very important part of the host antiviral response system.

"It is particularly important to show this with sequence information as close as possible to the patient-derived virus, as virus strains that are adapted in cell culture may start to mutate. This information is important for understanding the pathogenesis of Zika virus infection but may also

be useful for the design of attenuated viruses for vaccine studies in the future."

The authors hope that the full-length sequence of this patient derived Zika virus will support efforts to combatting the virus. They also expect the detection of the immune system inhibiting molecule will be important to further understand the virus and how it interacts with its host.

Dr Claire Donald, the MRC-University of Glasgow Centre for Virus research, said: "This work shows that Zika virus acts in a way that is comparable in some respect to what we know about host immune response antagonism for related viruses such as dengue and West Nile viruses.

"Comparing our isolate with other Zika viruses shows that they are very similar to each other at the genetic level. Therefore it is important for us to understand what factors are involved in the development of disease as well as identifying the key differences between the strains. This may allow us to pinpoint potential outbreaks of concern in the future."

Zika virus is a mosquito-transmitted arbovirus. Although previously poorly investigated, the virus has recently caused large scale outbreaks in French Polynesia in 2013, New Caledonia, the Cook Islands and Easter Island in 2014 and the Americas in May 2015, beginning in Brazil.

The outbreaks have also been characterised by an increased prevalence of neurological syndromes, such as Guillain-Barré syndrome and microcephaly. As of April 2016 the WHO announced that 60 countries had reported transmission in the escalating epidemic, which originated in Bahia, Brazil in 2015 and has so far resulted in over 1.5 million suspected cases.

Dr Jonathan Pearce, head of infections and immunity at the MRC, said: "This study demonstrates the unparalleled importance of cross-border working in the face of a global health threat such as Zika.

"With the help of the Newton Fund, our researchers in the UK were able to get to work with colleagues in Brazil well ahead of the virus being declared a global public health emergency. Together they have gained a much deeper understanding of how the infection develops, and in-depth insights like this is exactly what we need if we are to develop successful approaches to combat the disease."

Universities and Science Minister Jo Johnson said: "This ground breaking research gives us a far greater understanding of the Zika virus and will help protect millions of people in the developing world from the devastating effects of this disease.

"Working closely with Brazilian counterparts, our world leading scientists at the University of Glasgow have demonstrated how the government's £1.5bn investment in the Global Challenges Research Fund brings together the best scientific minds to tackle serious global problems such as the Zika virus."

**More information:** Marion A. L. Picard et al. Sex-Biased Transcriptome of Schistosoma mansoni: Host-Parasite Interaction, Genetic Determinants and Epigenetic Regulators Are Associated with Sexual Differentiation, *PLOS Neglected Tropical Diseases* (2016). DOI: 10.1371/journal.pntd.0004930

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