

## Scientists develop improved model for study of Zika virus

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An international research team has developed a new animal model used to study the pathogenesis of the Zika virus. Scientists were able to induce the disease in mice in a way that is similar to human pathology. The new model reflects the most dangerous manifestation of the Zika virus: infection of the fetus from a pregnant woman, which leads to developmental problems. This was achieved due to a new, more pathogenic virus strain, as well as a specially bred group of mice with a human-like immune response. The new model paves the way for more detailed study of the Zika virus, which should result in a more effective fight against it. The research is published in *Cell Host & Microbe*.

The Zika virus is widespread across Asia, Africa and Latin America. It can be transferred sexually or by mosquitoes. Although the virus can cause fever, sometimes accompanied by inflammation and joint pain, in most cases, the symptoms are very mild and pass by themselves. Nevertheless, pregnant women remain vulnerable to the virus, as it can affect the fetus and cause microcephaly or other developmental problems.

To combat this issue, scientists are actively exploring the development of a virus-induced disease in animal models, for example, in mice. However, healthy mice are resistant to human-like infection symptoms. Therefore, mice with mute immune response genes are usually used to study the virus. Such models are not very effective, as they cannot accurately reflect what happens when a human is infected.



A research group from the University of Washington in St. Louis and ITMO University has solved this problem by making mice more vulnerable to the disease and the virus itself more infectious for mice. "One of the key targets for the Zika virus is the transcription factor STAT-2, which triggers an antiviral immune response. Ordinary mice are resistant to the virus since their version of this factor does not bind with viruses. Our colleagues succeeded in replacing the mouse STAT-2 with a human one. What is more, they adapted the virus for mice. As a result, we got a relatively healthy mouse in which the disease developed as it does in humans. And like humans, it is able to transmit the virus to its offspring through the placenta," says Professor Maxim Artyomov from the University of Washington in St. Louis.

The research was based on a large-scale analysis of the gene activity in the stem cells of the brain. In a developing brain, these cells are most susceptible to the destructive effect of the virus. Different cells react to the virus differently, but most have internal mechanisms to fight the infection. The more effectively the virus can bypass these protection mechanisms, the more pathogenic it is. To understand what happens to brain stem cells infected with the Zika virus, scientists used a new method of single-cell RNA-sequencing. This method provides a massive amount of data, allowing one to track the individual gene activity in each cell.

"This data helped us monitor the cell response to the infection. This is what our research is about. We compared the changes in the <u>cells</u> caused by two strains of the Zika virus: natural and mouse-adapted. It turned out that the activity of genes for the production of interferon, the main modulator of the <u>immune response</u>, was the same for both strains. However, the activity of the genes for response to interferon was significantly weaker with the new strain. We later found that this was due to protein translation disruption," notes Konstantin Zaitsev, researcher at the Computer Technologies Laboratory of ITMO



## University.

According to the scientists, experiments have confirmed that the new model provides adequate reflection of the key features of a virus infection in humans. It will, therefore, help researchers all around the world to learn more about the nature of the Zika <u>virus</u> and find new ways to fight it.

**More information:** Matthew J. Gorman et al. An Immunocompetent Mouse Model of Zika Virus Infection, *Cell Host & Microbe* (2018). DOI: 10.1016/j.chom.2018.04.003

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