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Researchers infect a 'brain in a dish' in search for Zika antivirals

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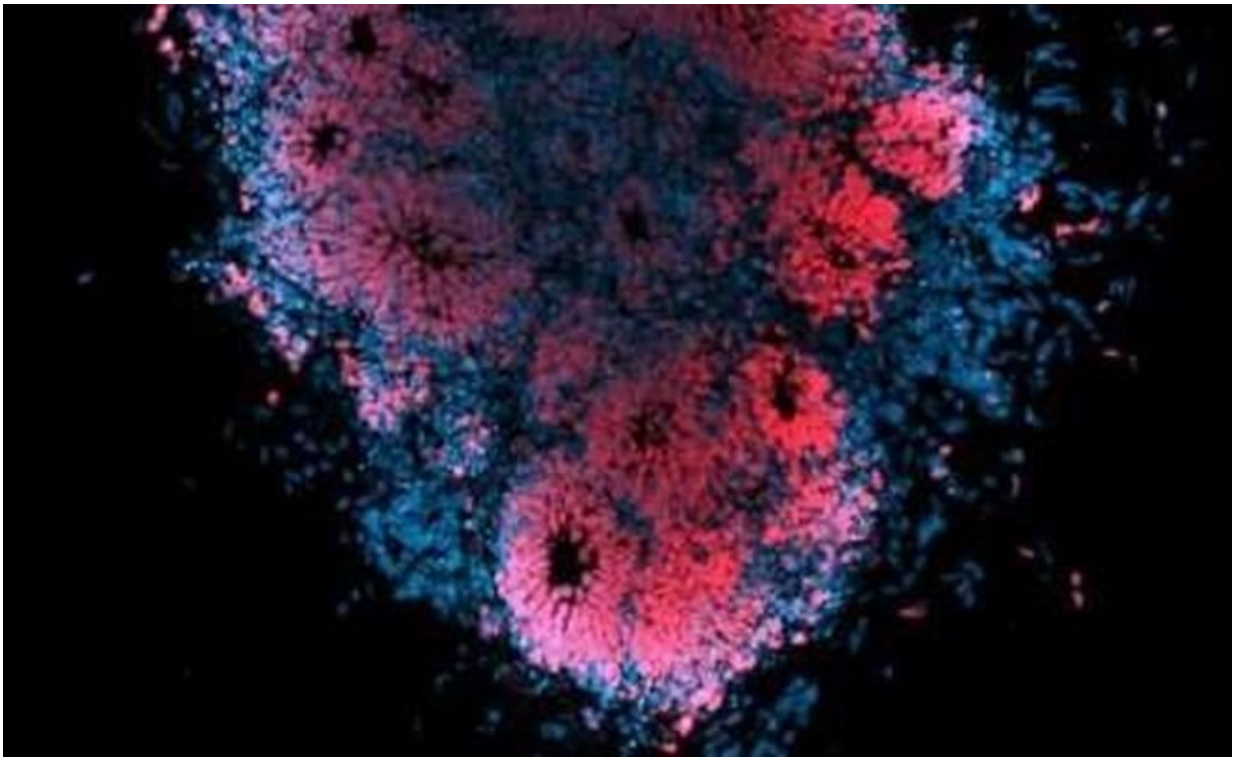

Microscopic image of human brain organoid infected with Zika virus. Credit: Dr Julio Aguado (AIBN, UQ)

A University of Queensland-led project has used a "brain in a dish" to study the effects of the Zika virus, taking research a step closer towards developing drugs to combat the infection.

The mosquito-borne Zika virus is found in 89 countries and can penetrate the placenta of a pregnant mother to infect her baby, causing severe brain abnormalities.

Dr. Andrii Slonchak and Dr. Alexander Khromykh from UQ's School of Chemistry and Molecular Biosciences found a crucial element to Zika infection, viral noncoding RNA (sfRNA), helps it evade antiviral responses and cause cell-death in developing brains. Their research is published in *Science Advances*.

"It's a little like something out of a science fiction movie—we're growing an artificial and microscopic human brain in a petri dish and testing the effect of the virus on its cells," Dr. Slonchak said.

"Stem cells self-organize into organ-like structures, or organoids, and in this case they have the structure and tissue architecture of the developing human brain.

"Our study shows the role of viral noncoding RNA in transplacental infection in pregnant mice and in cell death in human brain organoids.

"This finding gives us a whole new look at how the virus works its way into the developing brain and knowledge we can use to develop more effective antiviral drugs."

Dr. Khromykh said while the number of recorded cases of Zika may seem low, at round 1.3 million in total globally, its impact warrants urgent attention.

"Zika can cause significant abnormalities in babies, so there's a race to understand how it works and how to stop it," Dr. Khromykh said.

"Abnormalities can include optic nerve damage, smaller than expected

head sizes, problems in the area of the brain that connects the two hemispheres and wasting of tissue in critical brain regions.

"No cases of Zika-related birth defects have been reported in Australia, but given the unpredictable nature of viral outbreaks and the endemic nature of Zika in the Oceanic region, it very well might strike and we should be prepared for it."

The next step for researchers is to further understand how a specific viral protein, NS5, interacts with sfRNA at the molecular level and how this interaction helps the virus to escape antiviral response.

"This information will help researchers develop antiviral drugs to block this interaction and combat Zika," Dr. Khromykh said.

This study was a collaborative effort between researchers at UQ's School of Chemistry and Molecular Biosciences and Australian Institute for Bioengineering and Nanotechnology (AIBN) and the QIMR Berghofer Medical Research Institute.

More information: Andrii Slonchak et al, Zika virus noncoding RNA cooperates with the viral protein NS5 to inhibit STAT1 phosphorylation and facilitate viral pathogenesis, *Science Advances* (2022). DOI: 10.1126/sciadv.add8095

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