Study discovers source of Zika neurodevelopmental defects

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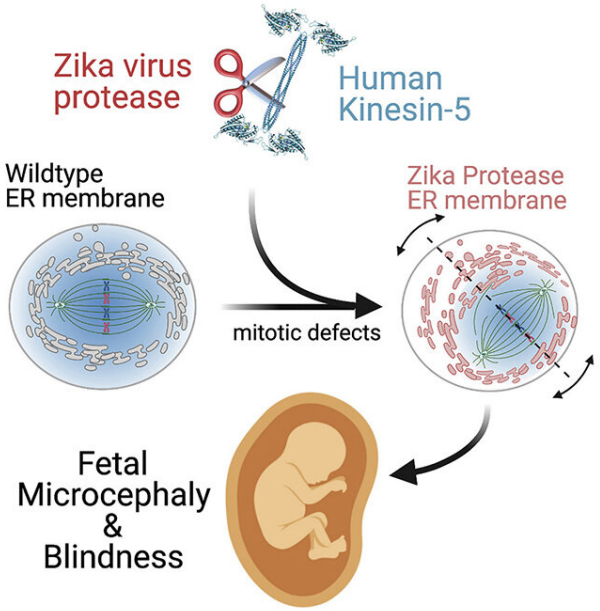

Credit: Louisiana State University

A study led by Edward Wojcik, Ph.D., Associate Professor of Biochemistry & Molecular Biology at LSU Health New Orleans School of Medicine, identified how microcephaly (abnormally small heads) and blindness may develop in Zika-infected fetuses, as well as a new way to potentially prevent these neurodevelopmental defects. The results are published online in *iScience*, available here.

The mechanism by which Zika virus disrupts neuronal development and results in congenital Zika syndrome was unknown. Because of similarities between Zika syndrome and a recognized congenital genetic disease (Kinesin-5) known to cause microcephaly and retinopathies in developing infants, the research team studied both, looking for similarities. They discovered a direct link, the first molecular and cellular evidence supporting a direct connection between the two.

"We had a hunch that the microcephaly and blindness that results from Kinesin-5 genetic disease could be linked to Zika infection, and the hunch paid off," notes Dr. Wojcik. "Our experiments identify a molecular motor as a target for degradation by an encoded Zika virus protein (Zika protease). The molecular motor is Kinesin-5, and it is required for cell division in humans. Our data identify Kinesin-5 as a target for the virus and links the infection to microcephaly."

The researchers observed that Zika protease cuts Kinesin-5 during cell division, disrupting the process and causing a loss of function. They also suggest a way to prevent it.

The Zika protease can degrade only a target protein it can reach. Since the protease is part of the endoplasmic reticulum (ER) membrane, only target proteins that come in direct contact with the ER can be degraded. In this way, the protease acts in a spatially restricted manner in the cell; target proteins are degraded only in certain regions of the cell volume and not in others. So, the research team proposes a drug that would affect only the Zika protease instead of drugs that would affect all target proteins in a cell.

"We predict and hope that potential drugs that inhibit Zika protease may be effective in preventing microcephaly and blindness from developing within Zika-infected fetuses," Dr. Wojcik concludes.

More information: Liqiong Liu et al, Inter-organelle interactions between the ER and mitotic apparatus facilitates Zika protease cleavage of human Kinesin-5 and contributes to distinct mitotic defects., *iScience* (2021). DOI: 10.1016/j.isci.2021.102385

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