

## Zika virus can cause immune and brain abnormalities in asymptomatic pig offspring

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Zika virus particles (red) shown in African green monkey kidney cells. Credit: NIAID

Zika virus infection in the womb produces altered immune responses and sex-specific brain abnormalities in apparently healthy pig offspring,



according to a study published november 14 in the open-access journal *PLOS Pathogens* by Uladzimir Karniychuk of the University of Saskatchewan, and colleagues. As noted by the authors, the findings could point to new strategies to prevent and alleviate the long-term effects of Zika virus infection.

Zika virus can cause severe abnormalities in fetuses such as brain lesions, and subsequent life-long developmental and cognitive impairment in children. However, the majority of infections in pregnant women are subclinical and are not associated with developmental abnormalities in fetuses and newborns. It is known that disruptions to the in utero environment during fetal development can increase disease risk in adulthood. For this reason, children affected in utero even by mild Zika virus infection can appear deceptively healthy at birth but develop immune dysfunction and brain abnormalities during postnatal development. In the new study, the researchers used the porcine model of subclinical fetal Zika virus infection to determine <u>health outcomes</u> in offspring that did not show apparent signs of the disease.

In apparently healthy offspring without congenital Zika syndrome or other visible birth defects, subclinical fetal infection was associated with abnormal immunological responses, such as excessive interferon alpha (IFN- $\alpha$ ) levels in blood under normal environmental conditions, as well as dramatic IFN- $\alpha$  shutdown during social stress. Whole-genome expression analysis of the prefrontal cortex revealed profound sexspecific transcriptional changes that most likely resulted from subclinical in utero infection. RNA-seq analysis of the Zika virus-infected placenta provided independent support for the sex-specific pattern of in uteroacquired transcriptional responses. Collectively, the results provide strong evidence that two hallmarks of fetal Zika virus infection—altered type I IFN response and molecular brain pathology—can persist after birth in offspring in the absence of congenital Zika syndrome. According to the authors, the study emphasizes that further attempts to



better understand silent pathology and develop interventions in Zika virus-affected offspring should take into account interactions between host factors such as sex and environmental insults such as social stress.

**More information:** Trus I, Udenze D, Cox B, Berube N, Nordquist RE, van der Staay FJ, et al. (2019) Subclinical in utero Zika virus infection is associated with interferon alpha sequelae and sex-specific molecular brain pathology in asymptomatic porcine offspring. *PLoS Pathog* 15(11): e1008038. <u>doi.org/10.1371/journal.ppat.1008038</u>

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