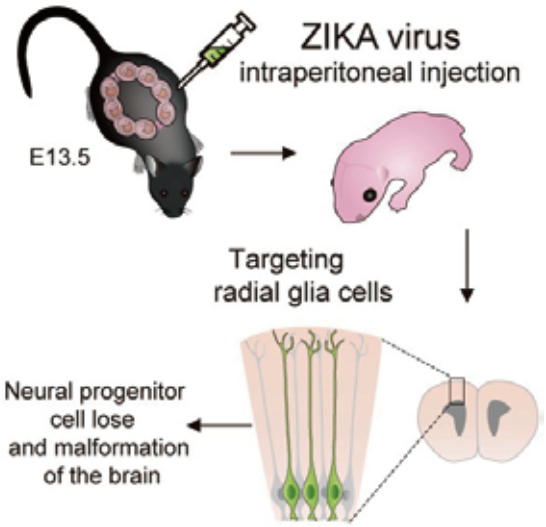
Causal Link between Vertical ZIKV Infection and Malformation of Fetal Brain Established

The recent outbreak of ZIKV infection in the Americas, in particular Brazil, is accompanied by a marked increase in cases of microcephaly of newborns. Considering the potential threat of ZIKV infection to central nervous system development of infants, the World Health Organization declared in February 2016, the danger of ZIKV on pregnancy as a Public Health Emergency of International Concern (PHEIC).

Although accumulating lines of evidence are consistent with observed microcephaly in infected fetuses, there is an urgent need for the development of an animal model to firmly establish the link between vertical ZIKV infection and malformation of the fetal brain.

Recently, a collaborative work by research teams respectively led by Dr. LUO Zhen'ge at Institute of Neuroscience (ION), State Key Laboratory of Neuroscience, Shanghai Institutes for Biological Sciences, Center for Excellence in Brain Science and Intelligence Technology, CAS and Dr. QIN Chengfeng at the State Key Laboratory of Pathogen and Biosecurity, Beijing Institute of Microbiology and Epidemiology, showed that maternally infected ZIKV can cross the mouse placental barrier, leading to a discernable brain developmental defect in offspring mice.



Maternal Zika virus infection affects fetal mouse brain development. (Image provided by Dr. LUO Zhen'ge's lab)

Researchers found that intraperitoneal (i.p.) injection of a contemporary ZIKV strain in pregnant mice led to the infection of radial glia cells (RGs) of dorsal ventricular zone of the fetuses, the primary neural progenitors responsible for cortex development, and caused a marked reduction of these cortex founder cells in the fetuses. Interestingly, the infected fetal mice exhibited a reduced cavity of lateral ventricles and a discernable decrease in surface areas of the cortex. They also investigated mechanisms underlying ZIKV effects on brain development and found that ZIKV infection caused dysregulation of several microcephaly-associated genes, as well as gene expression networks involved in regulating innate immune responses, cell proliferation and cell death.

This study thus supports the conclusion that vertically transmitted ZIKV affects fetal brain development and provides a valuable animal model for the evaluation of potential therapeutic or preventative strategies.

This work was published online in *Cell Research* on May 13th with WU Kongyan, ZUO Guolong, LI Xiaofeng as co-first authors and Dr. LUO Zhenge and Dr. QIN Chengfeng as co-corresponding authors.