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Abstract

Zika Virus Diversity Is Maintained during Transmission from Placenta to Fetal Periphery but Restricted in Fetal Brains †

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Abstract: Since emerging in French Polynesia and Brazil in the 2010s, Zika virus (ZIKV) has been associated with fetal congenital disease. Previous studies have compared ancestral and epidemic ZIKV strains to identify strain differences that may contribute to vertical transmission and fetal disease. However, within-host ZIKV variation during vertical transmission has not been well studied. Here, we used the established anti-interferon-treated Rag1−/− mouse model of ZIKV vertical transmission to compare ZIKV populations in matched placentas, fetal bodies, and fetal brains via RNASeq. ZIKV transmission from the placenta to the fetal periphery involved a loose population bottleneck. There was a restriction in the amount of virus entering the fetus from the placenta but not in ZIKV diversity, as the ZIKV population structures were similar in placentas and fetal bodies. In contrast, ZIKV transmission from the fetal periphery to the brain involved a sharp reduction in ZIKV diversity. All fetal brain ZIKV populations were comprised of either one of two variants as largely homogenous populations. In most cases, the predominant variant present in the fetal brain was also the majority variant present in the placenta. However, in two of ten fetal brains, the predominant ZIKV variants were undetectable in the matched placental ZIKV population, suggesting possible evidence of selection for certain variants during ZIKV transmission to fetal brains. Thus, certain variants may influence ZIKV's ability to enter the fetal brain and cause disease.

Keywords: Zika virus; vertical transmission; viral variants