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Prototype and Nicaraguan strains of Zika virus infect primary human placental cells expressing Axl, Tyro3 and TIM1 receptors at the uterine-placental interface modulated by individual donors

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The Zika epidemic that began in Brazil and has spread throughout the Americas has been reported as definitively linked to severe birth defects: Microcephaly, miscarriage and stillbirth. Detection of ZIKV RNA in the placenta and fetus and frequent intrauterine growth restriction suggests infection of the placenta leading to pathology. Our studies in primary cells from 14 placentas reveal that prototype and recently iso¬lated Nicaraguan ZIKV 2016 strains infect cells that express Axl, Tyro3 and TIM1 tyrosine kinase receptors, which modulate innate immune responses and mediate infection by ZIKV and the closely related dengue virus (DENV) infection in skin. Infected placental cells, including fetal-derived amniotic epithelial cells (AmEpC), trophoblast progenitor cells (TBPC), placental fibroblasts (HPF), umbilical vein endothelial cells (HUVEC) and differentiating cytotrophoblasts (CTBs) showed cytopathic effects, expressed ZIKV envelope and non¬-structural NS3 proteins and titers of infectious progeny depended on cell type, receptors expressed, individual donors and gestational age. Indicative of infection route, the decidua (decidual cells, invasive CTBs), chorionic villi (HPF, Hofbauer cells, blood vessels) and amniochorionic membranes (AmEpC, TBPC) expressed the receptors. Nonetheless, differential expression was found in 26 biopsy specimens, in particular TIM1 was detected throughout pregnancy but Axl was absent in late gestation. In summary, the results suggest that ZIKV could infect the pregnant uterus and spread to the placenta, fetus and amniochorionic membranes. The models of placental infection we have developed can be used to understand molecular mechanisms of ZIKV infection and assess the therapeutic potential of antibodies and small molecule inhibitors to block infection in the placental-fetal unit.

Biography

Lenore Pereira is a Molecular Virologist for over 30 years and Professor in the Department of Cell and Tissue Biology at the University of California San Francisco. She has focused the last 16 years on the biology of human *Cytomegalovirus* replication and pathogenesis at the uterine-placental interface. She has published over 120 papers and invited reviews. Recently, her group in collaborative studies with Dr. Eva Harris at the University of California Berkeley identified ZIKV target cells and immune mechanisms that protect the placenta.

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