Cytomegalovirus (CMV) is the most common congenital infection, causing permanent neurodevelopmental disability in >1 per 1000 live births world-wide. CMV vaccine development has focused on simulating natural immunity in uninfected women of child-bearing age, to prevent primary maternal infection during pregnancy and transmission to the fetus. However, rates of congenital CMV infection among children born to women who have natural immunity to CMV infection prior to conception are actually higher than those born to women who were CMV-naïve. Emerging evidence indicates that these “non-primary” congenital CMV infections result from reinfection of the pregnant woman with different CMV strains, which are typically transmitted by young children due to their prolonged, high-level viral shedding in saliva and urine. This talk will explore the importance of viral strain differences and transmission dynamics as risk factors for maternal CMV (re)infection, and explore novel vaccine strategies to prevent congenital CMV infection.”