

# Infectious Disease



## Chronic Viral Infection: The Kaur Lab

Cytomegalovirus (CMV) infection is ubiquitous in humans. If infection occurs during pregnancy, especially during the first trimester, it can be passed to the fetus in utero and lead to potentially serious complications. These include CNS problems like mental retardation and microcephaly, similar to those symptoms caused by Zika infection. Mothers that are already CMV seropositive have a decreased risk of infecting their children in utero, meaning that vaccines would be useful in combatting congenital CMV infection and its complications. The lab of Amitinder “Miti” Kaur uses a unique non-human primate model to study congenital CMV infection with the ultimate goal of developing a viable vaccine. The Lab is also interested in immune response differences of progressive vs. non-progressive hosts of SIV, with an eye towards identifying the possible mechanisms for HIV pathogenesis in humans.

## Congenital CMV Infection

Seronegative women who become infected with CMV during their pregnancy have a 30% chance of passing that infection to their fetus. If this occurs during the first trimester, there is a probability of serious complications – which could be avoided by vaccinating seronegative mothers. Natural immune responses to CMV are often non-neutralizing, meaning that any vaccine strategy would need to move beyond natural immunity to be truly effective. The Kaur Lab is working with a unique rhesus macaque model to study congenital CMV transmission, with the hopes of furthering vaccine research.

The Lab’s use of this monkey model offers unique advantages. This is the only model that closely recapitulates disease transmission and virus replication cycle of human CMV. For comparison, the other animal model widely used to test vaccine candidates is the guinea pig.

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## Congenital CMV Infection (cont.)

The macaque model demonstrated that observable transmission across the placenta is possible when CMV negative mothers are infected in the first trimester. This is the first time that this has been observed in a non-human primate animal model. Additionally, when mothers are immunocompromised through CD4+ T-cell depletion prior to infection, there are spontaneous abortions that correlate with high viremia. The lab also proved that transmission can be blocked with high levels of purified anti-CMV IgG, further demonstrating its viability as an asset for vaccine development and testing.

## HIV: Progression vs. Non-Progression

Rhesus macaques develop an AIDS-like illness when infected with SIV, the simian equivalent and close relative of HIV. However, they are not the natural host of this virus. Sooty mangabeys, which are the natural host of SIV, do not develop an AIDS-like illness. Interestingly, while rhesus macaques have sustained chronic immune activation, sooty mangabeys do not.

The Kaur Lab has discovered that this difference in immune regulation and activation during SIV infection may partly hinge on Natural Killer T-cells (NKTs), a component of the innate immune system. Sooty mangabey NKTs lack CD4 receptors on their surface, meaning that unlike the NKTs of rhesus macaques, they cannot be productively infected. The lab is investigating the role of these NKTs in the two model systems in bridging the innate and adaptive immune responses, and how they serve to regulate the T-cell response to SIV infection.

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