

Infection with human cytomegalovirus (HCMV) is very common. Primary HCMV infection in healthy individuals is usually asymptomatic, however in immunocompromised patients, for example after transplantation or with AIDS, it may cause severe disease. HCMV is also a cause of congenital disease, because this virus is able to cross from the blood circulation of the mother, through the placenta to the fetus. HCMV congenital disease is associated with infection of the central nervous system and consequently neural developmental disabilities. Symptoms associated with the HCMV congenital disease are for example: hearing loss, eye sight compromise, and learning disabilities.

As is the case for all the herpesviruses the life cycle of HCMV can be divided into lytic phase, when the virus is replicating, and producing new progeny particles and the latent phase, in which virus persists in the cell. In the latent phase in dividing cells, viral genome replicates and persists most probably in a form of circular molecule attached to cellular chromosomes, which prevents loss of the genome during cell division. One of the goals of the project is to check, whether recently discovered latent viral protein IE1x4 participates in binding of the genome to chromosomes. The analysis of IE1x4 protein function can help develop therapies aiming at elimination of the virus, since this protein contributes in different ways to viral persistence.

Thus far HCMV latency was mainly studied in hematopoietic progenitor cells, but recently it was shown that the virus can establish latency also in neuronal progenitors, which is important in the case of HCMV congenital disease. Therefore we would like to compare latent viral genes expressed in hematopoietic and neuronal progenitor cells, in order to understand how the virus manipulates different cell types. We also plan to study at which stage of differentiation, from a stem cell to neuron, HCMV is able to infect these cells, replicate and establish latency. Our studies of the latency and reactivation in the cells of neuronal lineage could therefore aid the understanding of the pathogenesis of congenital HCMV infection and in the future help develop new therapies.

HCMV viral particles were shown to have distinct characteristics with regard to infection of and replication in different cell types, depending on the cell of the origin of the viral particle. Thus we intend to examine the influence of the type of virus producing cell on efficiency of infection of different target cells relevant for congenital infection. These studies will allow us to understand the process of virus spread in the fetus.