Viral infections during pregnancy are major causes of maternal and fetal diseases. Cytomegalovirus (CMV) is a leading cause of prenatal viral infection, occurs in 0.64% of all live births in industrialized countries. Mother-to-child transmission is primarily the result of primary maternal infection, which carriers a risk of transmission of 32.3% (ranging from 14.2% to 52.4%). The rate of transmission from pregnant women with recurrent infection to newborn infants with CMV infection is lower, at approximately 1.4% (1.1%-1.7%). Approximately 11.0% of newborns with congenital CMV infection have detectable manifestations, most commonly central nervous system damage, sensorineural hearing loss, visual impairment and/or neurological dysfunction. It is worth noting that children with CMV-induced sequelae have a wide range of special needs and they often require extensive interventions from health care providers, and, in severe cases, lifelong custodial care.

The innate immune system is triggered by pathogen associated molecular patterns (PAMPs) and represents the first line of defense against invading microorganisms. The primary pattern recognition receptors (PRRs) that are involved in the sensing of viral nucleic acid during replication are RIG-I-like receptors (RLRs) expressed by most cells. RLRs are a family of cytosolic DExD/H-box RNA helicases that sensing various RNA and DNA viruses. To date, three members of the RLR family has been identified: RIG-I (retinoic acid-inducible gene-I), MDA5 (melanoma differentiation-associated gene 5) and LGP2 (laboratory of genetics and physiology 2). Receptors RIG-I and MDA5 sense viral RNA lead to production of type I and type III IFNs and proinflammatory cytokines, whereas LGP2 is postulated as a regulator of RIG-I/MDA5-mediated antiviral responses.

There are no studies regarding the feasible influence of CMV infection on RLRs expression in the placenta and decidua. In the proposed project we hypothesize that RLRs are involved in dsRNA CMV detection and activation of innate antiviral immune response. Several key issues will be investigated including the genes encoding RLRs and protein expression, the role of LGP2 in regulation of RIG-I/MDA5 signaling pathway, the proinflammatory cytokine and chemokine production, and the molecular basis for type I IFN production.

The results of the project will contribute substantially to the understanding of the role of RLRs in placental cell innate immunity activation and will expand the current knowledge of the pathogenetic mechanism of the placental cells-CMV interactions. The findings of the project can also be used as a starting point for further research associated with development of nucleic acid medicine (synthetic RNA analogs), which could induce efficient antiviral response in the placenta and limit transmission of intrauterine infection. The development of knowledge of PRR sensing of pathogen invasion in the placenta and decidua is very important, especially in the light of the lack of effective and efficient vaccine and the limitation of antiviral therapy in pregnant women and newborns. Moreover, our understanding of molecular machinery of RLR-mediated antiviral response will undoubtedly reveal additional uncover factors of *in vivo* regulation in response to virus infection, virus-specific nuances, and help us to determine the novel roles of RLRs in other cellular processes.