In this thesis, the role of two G protein-coupled receptor proteins (GPCRs) encoded by the human cytomegalovirus (HCMV) in signal transduction and oncomodulation is described. The vGPCRs UL28 and UL33 were shown to activate several signal transduction pathways that might be involved in the development of glioblastomas, an HCMV-related pathology.

UL28 induces upregulation of CCR5 expression via the inflammatory G protein-coupled transcriptional regulator (GPR) 30. UL28 is also constitutively activated by ligand-dependent transcription through the beta-o-beta kinase (ROCK) pathway. Both GPRs and p38 play a role in tumor formation. UL33, the UL28 splice variant, may act as an oncomodulatory, opening several cellular signaling pathways. UL33 promotes tumor formation in a xenograft model and is detected in glioblastomas. Hence, UL33 might also play a role in proliferative diseases. Finally, we describe a role of UL33 in epigenetic regulation through hypomethylation of the promoter of the c-myc gene in prostate cancer.

Taken together, our data shed new light on the mechanisms that might be involved in oncomodulatory properties of the vGPCRs UL28 and UL33, and might lead to new strategies in the treatment of glioblastomas and colon cancer.