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Meeting abstract

The role of GASP in the post-endocytic sorting and signaling of virally encoded chemokine receptor US28

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Human cytomegalovirus, which infects up to 80% of the general population, causes severe complications in immunocompromised patients and is thought to be linked to vascular diseases, such as atherosclerosis and restenosis. This β-herpesvirus encodes a G protein-coupled receptor (GPCR), namely US28, which does not only show homology to endogenous chemokine receptors but also binds endogenous CC chemokines and fractalkine. Here, we set out to elucidate the mechanisms by which the viral receptor US28 is endocytosed and targeted to these intracellular lysosomal compartments. The recently identified protein GASP (GPCR-associated sorting protein) specifically targets GPCRs to the lysosomal pathway. By addressing the post-endocytic trafficking properties of the viral receptor and its possible interaction with GASP we hope to gain important insights in the function and pathology of these viral proteins. Additionally, the sorting of individual receptors between recycling and degradative fates is a fundamental mechanism that controls the signaling capacity of GPCRs. Therefore, we investigated the role of GASP in the regulation of the postendocytic sorting and signaling of US28. As a result, we were able to show that GASP-1, but not GASP-2, is involved in the post-endocytic sorting of US28. In wild type and GASP-2 knockout mouse embryonic fibroblasts, the receptor showed a vesicular distribution. When GASP-1 was knocked down, US28 was localized to the cell surface. Thus, our findings suggest that GASP-1 plays an important role in the regulation of the post-endocytic sorting and signaling of the virally encoded chemokine receptor US28.