

Meeting abstract

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US28 in melanoma growth

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The human cytomegalovirus (hCMV) encodes the G protein-coupled receptor (vGPCR) US28. This receptor signals constitutively and interacts with a broad range of chemokines, which are crucial to the pathophysiological significance and immunoregulatory aspects of this receptor. Chemokines and their receptors have been shown to be key determinants of tumor growth and formation of metastases. US28 exerts anti-tumorigenic effects in two melanoma cell lines. Here we show that in contrast to all other previously studied cell lines, US28 is expressed on the cell surface in the melanoma cell lines Sbcl2 and 451Lu. We found that GASP – the G protein-coupled receptor-associated sorting protein – which sorts US28 and many other GPCRs to the lysosomes is absent in melanoma cells. The absence of GASP might affect the tumor-suppressing properties of US28. Melanoma cells produce several chemokines, one of them is the monocyte chemoattractant protein-1 (MCP-1). We found that the MCP-1 level in the supernatants of 451Lu cells increased when US28 wt was expressed. US28 Δ 317, a truncated mutant of US28 which is known to have enhanced signaling capacity compared to US28 wt, increased the MCP-1 concentration up to 20-fold. We speculate that the constitutive signalling of the receptor regulates the MCP-1 production of melanoma cells.