Regulation of receptor chaperone molecule RTP4 in microglial cells

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Morphine, a μ Opioid receptor (MOPr) agonist, is one of the powerful analgesics, but the development of analgesic tolerance by the chronic use or under some inflammatory diseases such as neuropathy would be a clinical problem. Recently, we have demonstrated that the increase of the receptor transporter protein 4 (RTP4), one of the GPCR chaperone molecules, will facilitate the MOPr-DOPr heteromer formation and thus lead to the analgesic tolerance in neuronal cells. Interestingly, RTP4 is highly expressed in macrophages, so here we focus on the role of RTP4 in the microglial cells, the brain-resident macrophages. In this study, we determined the changes in RTP4 mRNA levels after the treatment of morphine or DAMGO (10 μ M, 24 hrs) in SIM-A9 microglial cell line. In addition, we determined the effects of inflammatory stress by use of lipopolysaccharide (LPS) (1 ng/mL to 1 μg/mL, 24 hrs). As a result, RTP4 mRNA levels in SIM-A9 cells were decreased by morphine or DAMGO, while they were significantly increased by LPS treatment. These results suggest that the regulation of RTP4 expression in microglial cells is differed between under the chronic MOPr stimulation and the inflammatory stress. The role of RTP4 in microglial cells in the development of analgesic tolerance to morphine in these states would be determined in the future.