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Role of P2X7 Receptor in Regulation of P2X4 Receptor Expression on the Plasma Membrane of Microglia

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Abstract

P2X4 receptors (P2X4R) are the family of ATP-gated cation channels and are highly permeable to calcium. We have previously demonstrated that activating P2X4R in spinal microglia plays a key role in the pathogenesis of neuropathic pain. Therefore, P2X4R activity on the plasma membrane of microglia is critical for neuropathic pain. Recent studies have shown that P2X4R in microglial cells are located predominantly within lysosomal compartments. In addition, lysosomal exocytosis resulted in the trafficking of P2X4R to the plasma membrane. However, the mechanism of P2X4R trafficking is still elusive. The present study examined for P2X4R expression on the plasma membrane of microglia activated by lipopolysaccharide (LPS). Using quantitative cell surface biotinylation assay combined with Western blotting, we confirmed that LPS increased the levels of P2X4R protein on the cell surface of microglia. The LPS-induced upregulation of P2X4R protein were dramatically suppressed by pretreatment with the non-selective P2 receptor antagonist suramin and PPADS and with the selective P2X7R antagonists A-740003 and AZ10606120. These P2X7R antagonists also suppressed release of β-hexosaminidase, a lysosomal enzyme, from microglia. Thus, these results suggest that the LPS-induced upregulation of P2X4R to the plasma membrane of microglial cells may be regulated by purinergic signaling via P2X7R.