$P2Y_2$ receptor is involved in upregulation of phagocytic receptor AXL tyrosine kinase in TLR4-activated microglia

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Microglia are professional phagocytes which play an important role in homeostasis maintenance in the central nervous system. These cells rapidly detect and remove apoptotic cells which expose phosphatidylserine (PtdSer) as the key "eat-me" signal on the cell surface. This process is largely mediated through TAM receptor tyrosine kinases, MER and AXL, and TAM ligands which are soluble bridging proteins binding to PtdSer. We have previously reported that LPS-stimulated microglia promoted dying cell phagocytosis via purinergic $P2Y_2$ receptor signaling. However, the mechanism underlying $P2Y_2$ receptor-mediated phagocytosis remains unknown. In this study, we examined the involvement of $P2Y_2$ receptor in the regulation of TAM receptor MER and AXL expression in LPS-stimulated microglia. In primary rat microglia, LPS stimulation decreased MER and increased AXL mRNA expression, indicating that MER and AXL play distinct roles in microglial phagocytosis depending on physiological and inflammatory conditions. Furthermore, AR-C118925, a selective $P2Y_2$ receptor antagonist, significantly suppressed LPS-induced AXL mRNA expression. These results suggest that $P2Y_2$ receptor may be implicated in dying cell phagocytosis at least through mediating up-regulation of phagocytic receptor AXL tyrosine kinase in TLR4-activated microglia.