Low density lipoprotein receptor-related protein 1 (LRP1), also known as alpha-2-macroglobulin receptor (A2MR), apolipoprotein E receptor (APOER) or cluster of differentiation 91 (CD91), is a protein forming a receptor found in the plasma membrane of cells involved in receptor-mediated endocytosis. In humans, the LRP1 protein is encoded by the LRP1 gene.

LRP1 is also a key signalling protein and, thus, involved in various biological processes, such as lipoprotein metabolism and cell motility, and diseases, such as neurodegenerative diseases, atherosclerosis, and cancer.

Low-density lipoprotein receptor-related protein-1 (LRP1), a scavenger receptor of apolipoprotein E (apoE), is able to modulate microglia polarization towards anti-inflammatory M2 phenotypes during inflammatory and oxidative insult. In the present study, we investigated the effects of LRP1 activation on WMI and underlying mechanisms of M2 microglial polarization in a rat model of SAH. Two hundred and seventeen male Sprague Dawley rats (weight 280-330 g) were used. SAH was induced by endovascular perforation. LPR1 ligand, apoE-mimic peptide COG1410 was administered intraperitoneally. Microglial depletion kit liposomal clodronate (CLP), LPR1 siRNA or PI3K inhibitor were administered intracerebroventricularly. Post-SAH assessments included neurobehavioral tests, brain water content, immunohistochemistry, Golgi staining, western blot and co-immunoprecipitation. SAH induced WMI shown as the accumulation of amyloid precursor protein and neurofilament heavy polypeptide as well as myelin loss. Microglial depletion by CLP significantly suppressed WMI after SAH. COG1410 reduced brain water content, increased the anti-inflammatory M2 microglial phenotypes, attenuated WMI and improved neurological function after SAH. LRP1 was bound with endogenous apoE and intracellular adaptor protein Shc1. The benefits of COG1410 were reversed by LPR1 siRNA or PI3K inhibitor. LRP1 activation attenuated WMI and improved neurological function by modulating M2 microglial polarization at least in part through Shc1/PI3K/Akt signaling in a rat model of SAH. The apoE-mimic peptide COG1410 may serve as a promising treatment in the management of SAH patients [1)].

1)
Peng J, Pang J, Huang L, Enkhjargal B, Zhang T, Mo J, Wu P, Xu W, Zuo Y, Peng J, Zuo G, Chen L, Tang J, Zhang JH, Jiang Y. LRP1 activation attenuates white matter injury by modulating microglial polarization through Shc1/PI3K/Akt pathway after subarachnoid hemorrhage in rats. Redox Biol. 2019 Jan 23;21:101121. doi: 10.1016/j.redox.2019.101121. [Epub ahead of print] PubMed PMID: 30703614.

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