P2RX7

P2X purinoceptor 7 is a protein that in humans is encoded by the P2RX7 gene. The product of this gene belongs to the family of Purinergic receptors for ATP. Multiple alternatively spliced variants which would encode different isoforms have been identified although some fit nonsense-mediated decay criteria.

The activation of P2RX7 plays an important role in endotheliocyte damage and Blood-Brain Barrier disruption. Ferroptosis is a novel pattern of programmed cell death caused by the accumulation of intracellular iron and lipid peroxidation, resulting in ROS production and cell death. Liu et al. explored the mechanism of P2RX7 in reducing hemorrhagic transformation pathogenesis after acute ischemic stroke by regulating endotheliocyte ferroptosis. Male SD rats were performed to establish middle cerebral artery occlusion (MCAO) model injected with 50% high glucose (HG) and HUVECs were subjected to OGD/R treated with high glucose (30 mM) for establishing HT model in vivo and in vitro. P2RX7 inhibitor (BBG), and P2RX7 small interfering RNAs (siRNA) were used to investigate the role of P2RX7 in BBB after MCAO in vivo and OGD/R in vitro, respectively. The neurological deficits, infarct volume, degree of intracranial hemorrhage, the integrity of the BBB, immunoblotting, and immunofluorescence were evaluated at 24 h after MCAO. The study found that the level of P2RX7 was gradually increased after MCAO and/or treated with HG. The results showed that treatment with HG after MCAO can aggravate neurological deficits, infarct volume, oxidative stress, iron accumulation, BBB injury in the HT model, and HG-induced HUVECs damage. The inhibition of P2RX7 reversed the damaging effect of HG, significantly downregulated the expression level of P53, HO-1, and p-ERK1/2, and upregulated the level of SLC7A11 and GPX4, which implicated that P2RX7 inhibition could attenuate oxidative stress and ferroptosis of the endothelium in vivo and in vitro. The data provided evidence that the P2RX7 plays an important role in HG-associated oxidative stress, endothelial damage, and BBB disruption, which regulates HG-induced HT by ERK1/2 and P53 signaling pathways after MCAO [1].

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Liu C, Tian Q, Wang J, He P, Han S, Guo Y, Yang C, Wang G, Wei H, Li M. Blocking P2RX7 Attenuates Ferroptosis in Endothelium and Reduces HG-induced Hemorrhagic Transformation After MCAO by Inhibiting ERK1/2 and P53 Signaling Pathways. Mol Neurobiol. 2022 Oct 25. doi: 10.1007/s12035-022-03092-y. Epub ahead of print. Erratum in: Mol Neurobiol. 2022 Nov 23;: PMID: 36282438.