**Abstract**

While the specific trigger of Parkinson Disease (PD) in most patients is unknown, considerable evidence suggests that the neuroinflammatory response makes an essential contribution to the neurodegenerative process. Drugs targeting metabotropic glutamate receptors (mGlu receptors), 7 Transmembrane (7TM) spanning/G protein coupled receptors that bind glutamate, are emerging as therapeutic targets for PD and may have anti-inflammatory properties. ADX88178 is novel potent, selective, and brain-penetrant positive allosteric modulator of the mGlu4 which is under evaluation for treatment of PD and other neurological disorders. We used microglia cultured from mouse brain to determine if ADX88178 had direct effects on the inflammatory responses of these cells. We studied both microglia from wild type and *Grm4* knock out mice. We found that activation of mGlu4 with ADX88178attenuated LPS-induced inflammation in primary microglia, leading to a decrease in the expression of TNFα, MHCII, and iNOS, markers of pro-inflammatory responses. These effects were absent in microglia from mice lacking mGlu4. These results demonstrate a cell-autonomous anti-inflammatory effect of ADX88178 mediated mGlu4 activation on microglia, and suggest that this drug or similar activators or potentiators of mGlu4 may have disease-modifying as well as symptomatic effects in PD and other brain disorders with an inflammatory component.