Role of the GPR55 receptor in microglial cell function

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Microglial cells could be considered to be the macrophages of the central nervous system. Upon activation, these cells release pro-inflammatory signals including nitric oxide (NO) which normally plays an immune protective role, but excessive activity might be damaging as seen in stroke, Alzheimer’s disease and neuropathic pain. The orphan G protein-coupled receptor GPR55 (Ross, 2009) is thought to be involved in pain signalling and it has been shown to produce anti-inflammatory effects in microglia. The aim of this study, therefore, was to examine the potential involvement of GPR55 receptors in the control of NO formation in the BV-2 mouse microglial cell line.

Generation of NO was assessed by measuring accumulation of the stable end product nitrite in BV-2 culture supernatants by the Griess assay using an optical density endpoint (540 nm) determined spectrophotometrically. Cell viability was assessed using the Neutral Red assay. Data were analysed using ANOVA and post-hoc Dunnett’s tests. Results represent the means of 3 separate experiments, each performed in duplicate.

BV-2 cells showed time- and concentration-dependent increases in NO in the presence of bacterial lipopolysaccharide (LPS). Minocyclin, a selective microglial inhibitor, reduced LPS-stimulated NO formation in a concentration-dependent manner although higher concentrations also reduced cell viability.

A selective GPR55 receptor antagonist (from GSK Pharmaceuticals), CP55940 (cannabinoid CB1/CB2 receptor agonist and putative GPR55 antagonist), AM251 (CB1 antagonist and putative GPR55 antagonist) and the phytocannabinoid cannabidiol (also a putative GPR55 antagonist) all at 10 µM, produced significant (P<0.05) inhibitions of LPS (100 ng)-stimulated NO production. The GPR55 receptor agonists. VSN19 and O1602 were without effect, as was the endogenous GPR55 activator lysophosphatidylinositol (LPI). A number of other cannabinoid receptor agonists and antagonists were also without effect on LPS-stimulated NO formation.

The data presented demonstrate that a number of structurally different GPR55 receptor antagonists reduced LPS-stimulated NO formation. On the other hand, GPR55 agonists were without effect, possibly suggesting that some part of the LPS effect is mediated by GPR55 activation. Whether this involves mediation by an endogenous GPR55 agonist (e.g. LPI) or a more direct effect of the drugs on NO formation remains to be investigated.


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