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## Characterization of Calcium-Signalling Mediated by Human GPR55 Expressed in HEK293 Cells

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**Abstract :** The endogenous phospholipid lysophosphatidylinositol (LPI) was recently identified as a novel ligand for the G protein-coupled receptor 55 (GPR55) and an inducer of intracellular Ca2+[Ca2+]i release. This study attempts to characterize Ca2+ signals provoked by LPI in HEK293 cells engineered to stably express human GPR55 and to test cannabinoid ligand activity at GPR55. The study shows that treatment with LPI stimulates a sustained, oscillatory Ca2+ release. The response is characterized by an initial rapid rise, which is mediated by the  $G\alpha q$ -PLC-IP3 pathway, and this is followed by prolonged oscillations that require RhoA activation. Ca2+ oscillations are initiated by intracellular mechanisms and extracellular Ca2+ is only required to replenish Ca2+ lost from the cytoplasm. Analysis of cannabinoid ligand activity at GPR55 revealed no clear effect of the endocannabinoid anandamide, however, rimonabant and the CB1 receptor antagonist AM251 evoked GPR55-mediated [Ca2+]i. Thus, LPI is likely to be a key plasma membrane mediator of signaling events and changes in gene expression through GPR55 activation.

Keywords: lysophosphatidylinositol, calcium, GPR55, cannabinoid

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