

Endocrine/Cardiovascular – GPR 119 Receptor Agonist

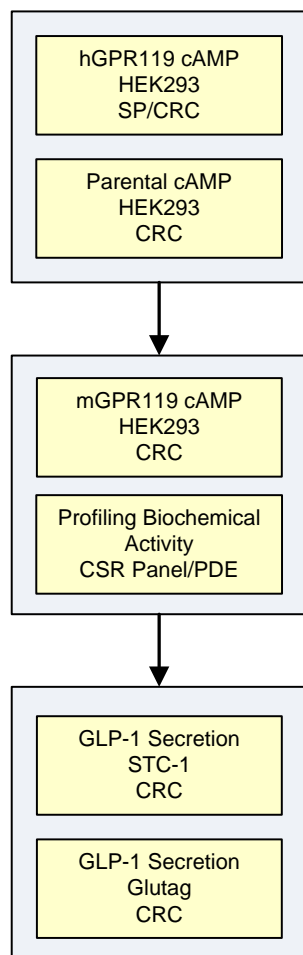
GPR119 belongs to a family of G protein coupled receptors. Activation of GPR119 produces an increase in cAMP levels. GPR119 has a limited tissue distribution, and is expressed only in pancreas and intestine. In pancreas, activation of GPR119 results in a potentiation of glucose-induced insulin secretion. In gastrointestinal tract, activation of the receptor increases secretion of incretin peptides. Thus, GPR119 agonists might exert a dual control of glucose homeostasis.

The GPR119 module tests for compounds that increase intracellular cAMP levels in cells expressing human GPR119 receptor. The active molecules will be further characterized for their specificity, ability to activate the mouse rodent GPR119 receptor and to increase glucagon like peptide 1 (GLP-1) secretion in murine enteroendocrine cells. Compounds of interest selectively activate GPR119 receptors and increase GLP-1 secretion.

- Deorphanization of a G protein-coupled receptor for oleoylethanolamide and its use in the discovery of small-molecule hypophagic agents; Overton HA et al, *Cell Metab.* 3(3):167-75, (2006)
- A role for beta-cell-expressed G protein-coupled receptor 119 in glycemic control by enhancing glucose-dependent insulin release; Chu ZL et al; *Endocrinology*, 148(6):2601-9, (2007)

Flow Scheme & Assay Measures

Endocrine/Cardiovascular: GPR 119 Receptor Agonist



GPR 119 Receptor Agonist

Primary Assays

hGPR119 cAMP agonist HEK293 cells SP (% Efficacy)
hGPR119 cAMP agonist HEK293 cells CRC (EC₅₀)
Parental cAMP agonist HEK293 cells CRC (EC₅₀)

Secondary Assays

mGPR119 cAMP agonist HEK293 cells CRC (EC₅₀)
Profiling Biochemical Activity Kinase Panel (Ki, % Efficacy)
PDE profiling (IC₅₀)

Confirmatory Assays

GLP-1 Secretion STC-1 cells (EC₅₀)
GLP-1 Secretion Glutag cells (EC₅₀)

SP= Single Point

CRC= Concentration Response Curve