

# Abstract

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## Glutamine potently stimulates glucagon-like peptide-1 secretion from GLUTag cells.

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**AIMS/HYPOTHESIS:** Glucagon-like peptide-1 (GLP-1) and peptide YY (PYY) are secreted from enteroendocrine L cells in response to nutrient ingestion. As glutamine is an important metabolic fuel for the gut, the aim of this study was to investigate the effect of glutamine on the GLP-1-secreting cell line, GLUTag.

**METHODS:** GLP-1 release was measured following incubation of GLUTag cells under a range of conditions. Single cells were studied by electrophysiology, calcium imaging and cytosolic ATP measurement using recombinant luciferase.

**RESULTS:** Glutamine was a more potent GLP-1 secretagogue than glucose or other amino acids, increasing GLP-1 release 7.1 $\pm$ 0.7-fold (n=19) at 10 mmol/l, with an estimated median effective concentration of between 0.1 and 1 mmol/l. Glutamine (10 mmol/l) induced a sodium-dependent inward current of 3.2 $\pm$ 1.2 pA per cell (n=9), which triggered membrane depolarisation and an increase in intracellular calcium. Asparagine and alanine produced electrophysiological and calcium changes that were at least as large as those caused by glutamine, but they were less effective GLP-1 secretagogues, suggesting that glutamine also potentiates secretion downstream of the calcium signal. This was confirmed by measuring secretion in the presence of 30 mmol/l KCl + diazoxide, or in alpha-haemolysin-permeabilised cells. Glutamine increased cytosolic ATP, but was less effective than glucose.

**CONCLUSIONS/INTERPRETATION:** Glutamine acts as a trigger and potentiator of GLP-1 release, consistent with its role as the major metabolic fuel for the gut. The results suggest that nutritional agents like glutamine might have beneficial effects in diabetes and obesity.

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