SUPPLEMENTARY DATA

GPR119 agonism increases glucagon secretion during insulin-induced hypoglycemia

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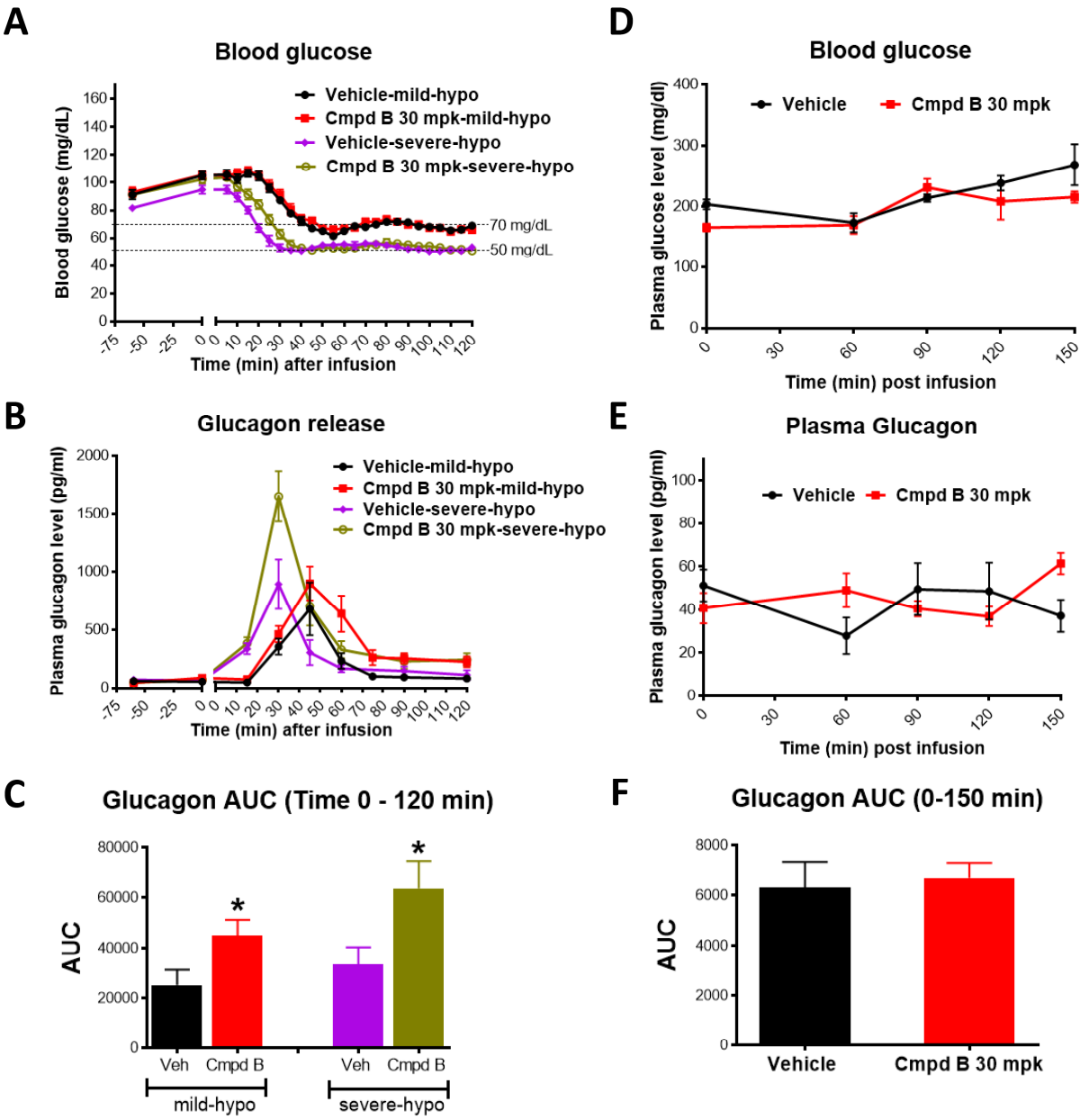
Supplementary Figure 1. Effects of GPR119 agonist on glucagon secretion in normal rats during mild-hypoglycemic (A-C**) and isoglycemic (**D-F**) clamp studies.** Normal Wistar rats were dosed with GPR119 agonist Cmpd B (30 mpk) and subjected to hypoglycemia or isoglycemic clamp studies as described in the Methods. Blood samples were harvested at the indicated time points for measurement of plasma levels of glucose and glucagon. Blood glucose (**A, D**), glucagon (**B, E**), AUC of glucagon (**C, F**) in rats treated with vehicle or Cmpd B. Note Cmpd B only enhanced glucagon release during hypoglycemic conditon (**A-C**), but not under the euglycemic condition (**D-F)**. Data were depicted as mean ± SE from 8-12 rats for each group. * P<0.05 vs. vehicle at the indicated group.



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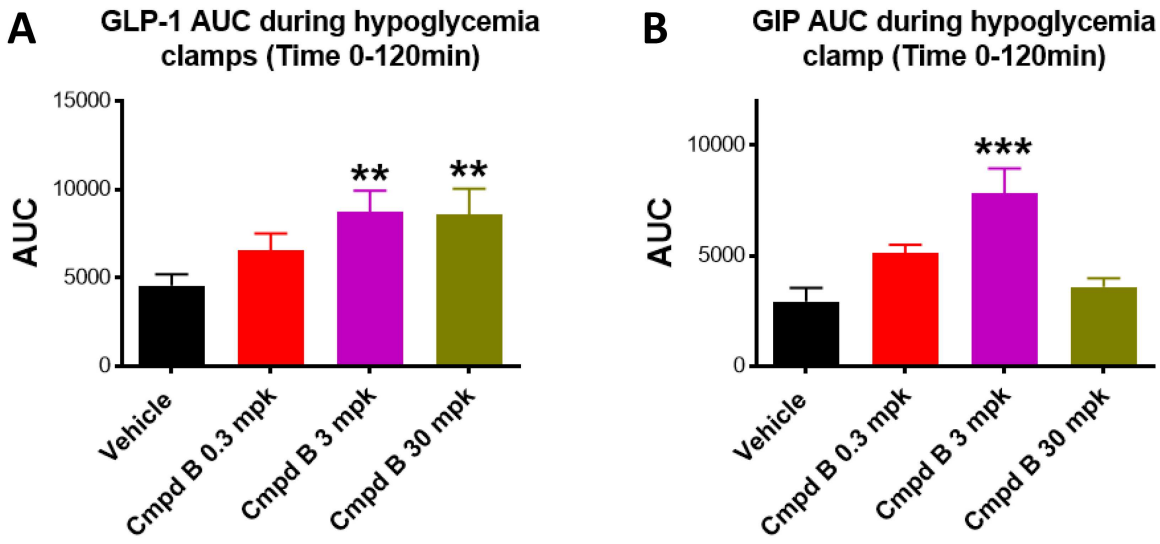
Supplementary Figure 2. Effects of GPR119 agonist on GLP-1 and GIP secretion in normal rats during hypoglycemic clamp study. Normal Wistar rats were dosed with vehicle or GPR119 agonist Cmpd B at the indicated doses and subjected to hypoglycemia clamp studies as described in the Methods. Blood samples were harvested from 0 to 120 minutes after treatment for measurement of plasma levels of GLP-1 or GIP. Data were reported as AUC of GLP-1 or GIP during 2 hours of hypoglycemic clamp. Data were depicted as mean ± SE from 8-10 rats for each group. ** P<0.01, *** P<0.001 vs. vehicle group.



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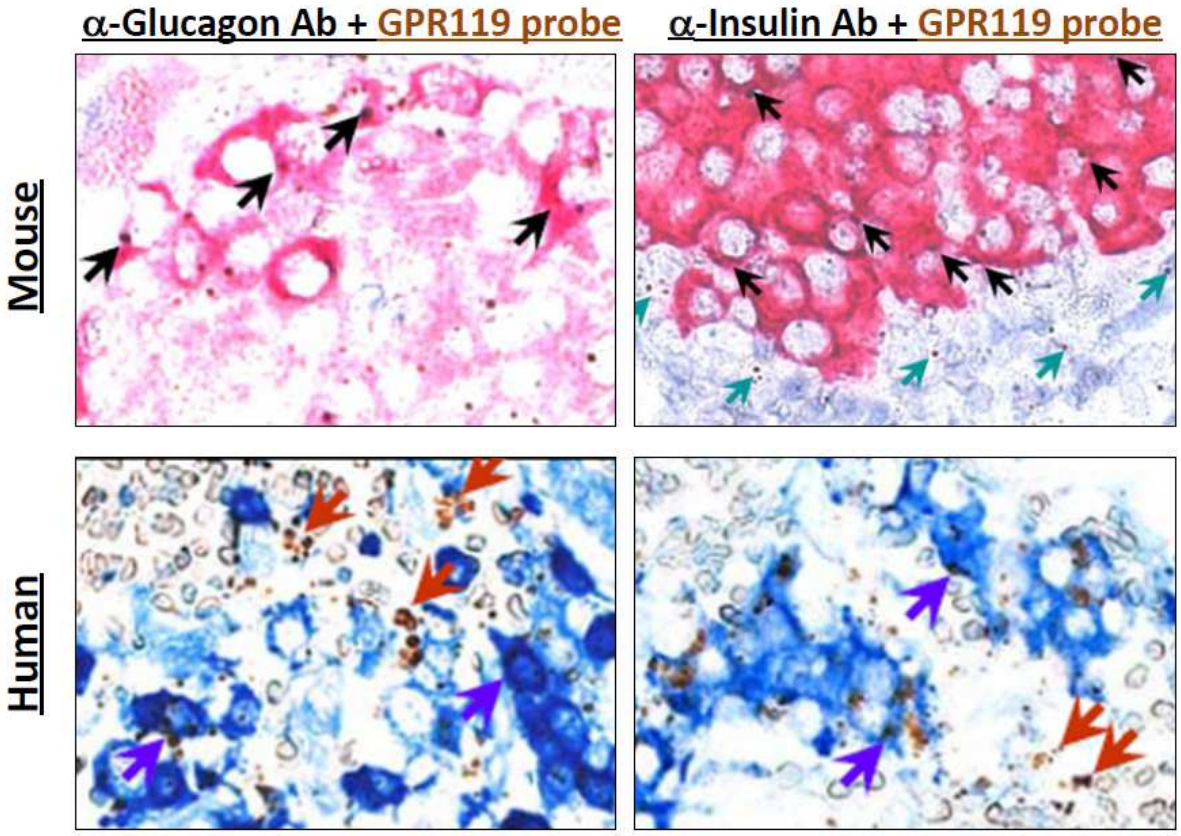
Supplementary Figure 3. Combined *in situ* hybridizaton of GPR119 and co-immunostaining of glucagon or insulin in normal mouse and non-diabetic human pancreas sections. Note that anti-sense probe indicated GPR119 mRNA (brown dots, indicated by arrows) is present in either glucagon^{+} (pink or blue), or insulin^{+} (pink or blue), or glucagon^{-} insulin^{-} cells. Images are representative of multiple assessments of at least 4 individual mouse or human pancreata with similar observations.



SUPPLEMENTARY DATA

Supplementary Figure 4. Combined *in situ* hybridization of GPR119 and co-immunostaining of glucagon or insulin or somatostatin in human pancreas sections from non-diabetic subjects and T1D or T2D patients. Note that anti-sense probe indicated GPR119 mRNA (brown dots) is seen in either insulin$^+$ (pink), glucagon$^+$ (pink) or somatostatin$^+$ (pink) cells. But in particular, GPR119 mRNA is more obviously seen with a higher frequency in glucagon$^+$ cells from diabetic patients (arrows in insert on the right). Images are representative of multiple assessments of non-diabetic (n=2), T1DM (n=4) and T2DM donor (n=1) with similar observations.