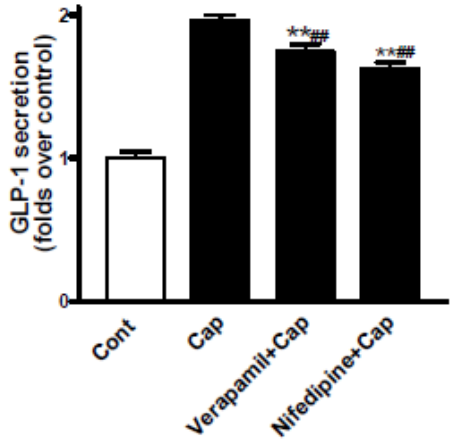
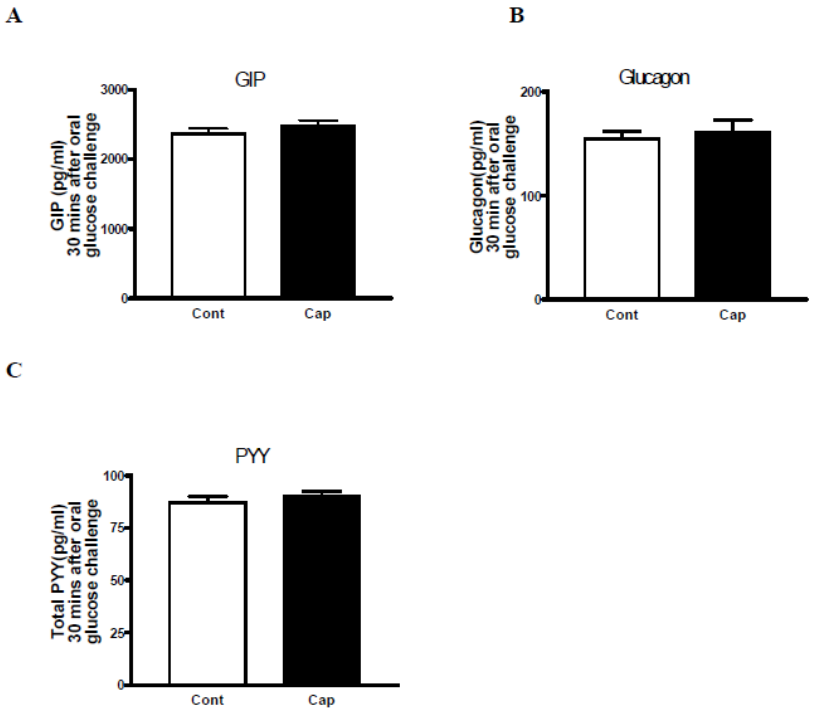
SUPPLEMENTARY DATA

**Supplementary Figure 1.** Voltage-dependent $Ca^{2+}$ channel is partially involved in capsaicin mediated GLP-1 secretion in STC-1 cells. The effects of verapamil (10 μM) and nifedipine (10 μM) on the GLP-1 release in response to capsaicin (1 μM). ***P<0.01* versus capsaicin group (Cap), $^{\#\#}$*P<0.01* versus control group (Cont, n=6).

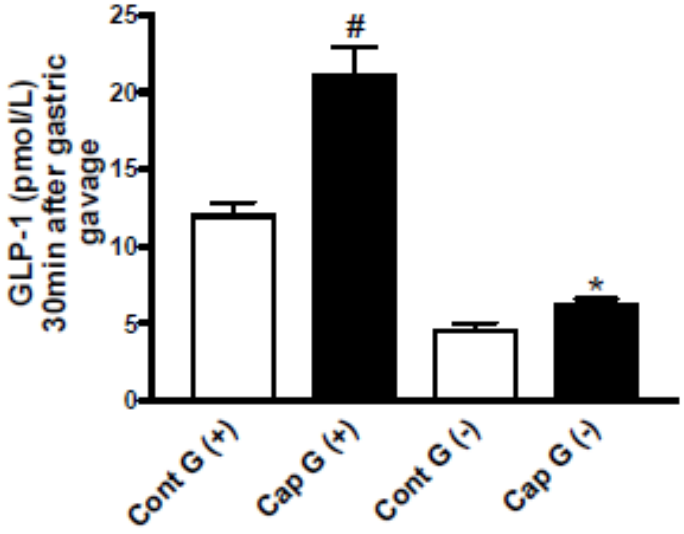



**Supplementary Figure 2.** The circulating levels of GIP, Glucagon and PYY did not increased after acute oral administration of capsaicin. *A, B and C:* Plasma levels of GIP, Glucagon and PYY at 30 minutes after acute oral administration of capsaicin (1 μM) in the presence of glucose (2 g/kg) in C57BL/6J mice (n=6).

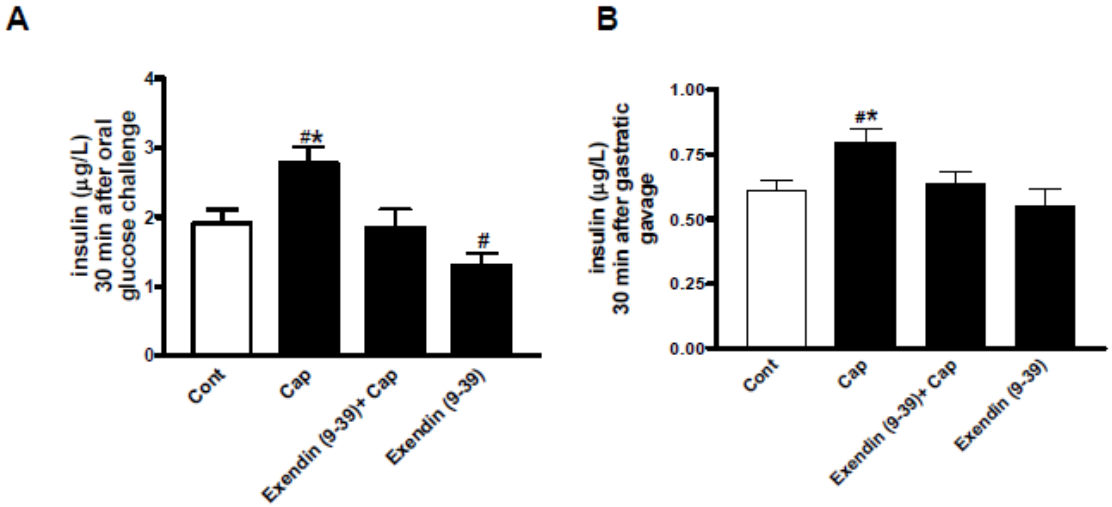


SUPPLEMENTARY DATA

**Supplementary Figure 3.** Acute administration of capsaicin increased the GLP-1 secretion in C57BL/6J mice. Plasma levels of GLP-1 after gastric gavage in the absence or presence of glucose challenge (2 g/kg) combine with or without capsaicin (1 μM). *#P<0.05* versus the presence of glucose challenge control group (Cont $G^+$; n=6); **P<0.05* versus the absence of glucose challenge control group (Cont $G^-$; n=6), data are mean ± SEM and were analyzed by student's unpaired t-test.

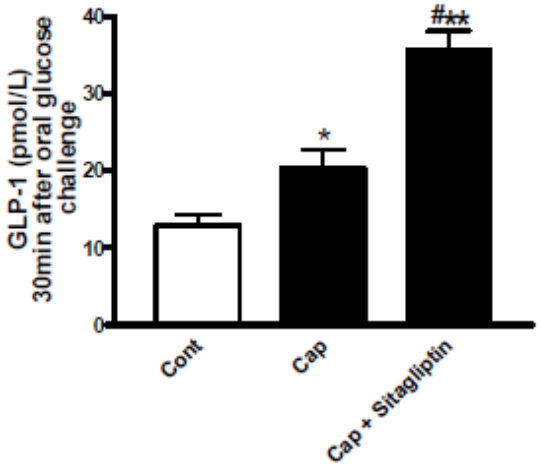



**Supplementary Figure 4.** The insulinotropic effect of capsaicin was blocked by exendin (9-39). A Plasma levels of insulin in C57BL/6J mice after acute oral glucose (2 g/kg) combine with or without capsaicin (1 μM), in pretreatment with or without GLP-1 receptor antagonist, exendin (9-39) (10 μg/mouse, i.p.) (n=6). *#P<0.05* versus control group (n=6), **P<0.05* versus exendin (9-39) plus capsaicin group (n=6). B: Plasma levels of insulin after gastric gavage in the absence of glucose challenge combine with or without capsaicin (1 μM), in pretreatment with or without GLP-1 receptor antagonist, exendin (9-39) in wild type mice (10 μg/mouse, i.p.) (n=6). *#P<0.05* versus control group (n=6), **P<0.05* versus exendin (9-39) plus capsaicin group (n=6). Data are represented as mean ± SEM and were analyzed by Student's unpaired t-test.

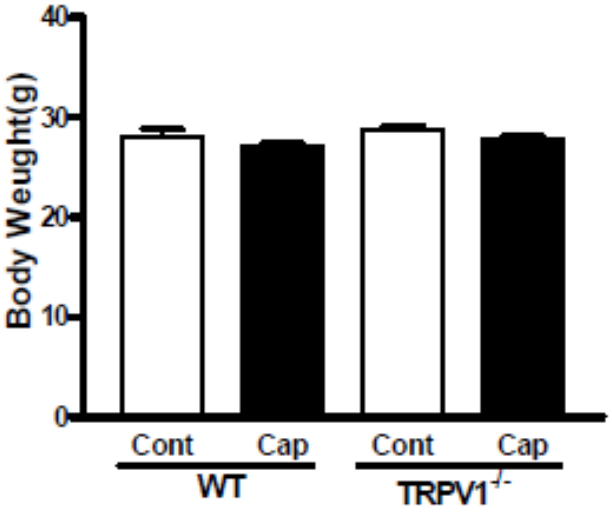


SUPPLEMENTARY DATA

**Supplementary Figure 5.** Sitagliptin maximize the effects of capsaicin in GLP-1 secretion. Plasma levels of GLP-1 in C57BL/6J mice after acute glucose challenge with or without capsaicin, in presence or absence of DPP4 inhibitor, sitagliptin (3mg/kg, oral), ***P<0.01* versus control group, $^{\#}$*P<0.05* versus capsaicin group (n=6), data are represented as mean ± SEM and were analyzed by Student's unpaired t-test.




**Supplementary Figure 6.** The body weights of WT and TRPV1$^{-/-}$ mice after 24 weeks of treatment with or without capsaicin (n=6).



SUPPLEMENTARY DATA

**Supplementary Figure 7.** *A*: The food intake of db/db mice in the first 14 days of treatment with or without capsaicin (0.01%). *B*: The body weights of db/db mice during 14 weeks of treatment with or without capsaicin (n=6). **P<0.05* versus control. *C:* IPITT of the db/db control mice, db/db mice treated with chronic capsaicin, lean littermate, **P<0.05* versus db/db control, ***P<0.01* versus db/db control (n=6). These data are represented as means ± SEM and were analyzed with a Student's unpaired t-test. *D :* The GLP-1 levels after a 30-min glucose challenge in db/db mice treated with or without capsaicin and the lean littermate control, **P<0.05* versus db/db control (n=6).