Supplement figure 1. The combination of carbachol and 8-pCPT-2'-Me-O-cAMP produces a synergic effect on amylase release. Both 250  $\mu$ M 8-Br-cAMP and 250  $\mu$ M 8-pCPT-2'-Me-O-cAMP (CPT-Me-cAMP) weakly increased amylase release by 80 % whereas 10  $\mu$ M carbachol (CCh) increased it by 200 %. The co-stimulation with carbachol and either 8-Br-cAMP or CPT-Me-cAMP potentiated amylase release to 400 %. Data shown are means  $\pm$  SEM (4-6 experiments) of amylase release expressed as percentage of total. \*: p < 0.001 vs Control; †: p < 0.001 vs 8-Br-cAMP or CPT-Me-cAMP and  $\ddagger$ : p < 0.001 vs carbachol.

Supplement figure 2. Active Rap1 does not evoke either Ca<sup>2+</sup> mobilization or cAMP generation in pancreatic acini. Fresh pancreatic acini, β-Gal- (vector control) and Rap1GAP-overexpressing acini were stimulated with secretagogues and then either Ca<sup>45</sup> Ca<sup>2+</sup> mobilization (*A-B*) or cAMP levels (*C*) was measured. CCK, but not VIP or 8-pCPT-2'-Me-*O*-cAMP, released Ca<sup>2+</sup> from acini. The overexpression of Rap1GAP did not affect the CCK-evoked Ca<sup>2+</sup> mobilization or VIP-induced cAMP increase. (*A*) Data shown are means ± SEM (4-5 experiments) of Ca<sup>45</sup> Ca<sup>2+</sup> remaining expressed as percentage of initial.  $\Box$ : Control,  $\blacktriangle$ : 300 pM CCK,  $\blacktriangledown$ : 10 nM VIP and  $\blacksquare$ : 8-pCPT-2'-Me-*O*-cAMP. \*\*: p < 0.01, and \*\*\*: p < 0.001 *vs* Control. (*B*) Data shown are means ± SEM (4 experiments) of Ca<sup>45</sup> Ca<sup>2+</sup> remaining expressing cells without stimulation,  $\blacksquare$ : Rap1GAP-overexpressing cells without stimulation,  $\triangle$ : β-Gal-expressing cells without stimulated by 300 pM CCK, and  $\blacktriangle$ : Rap1GAP-overexpressing cells without stimulation. (*C*) Data shown are means ± SEM (3 experiments) of cAMP levels expressed as pmol/mg protein. \*\*: p < 0.01 *vs* β-Gal-expressing cells without stimulation. (*C*) Data shown are means ± SEM (3 experiments) of cAMP levels expressed as pmol/mg protein. \*\*: p < 0.01 *vs* β-Gal-expressing cells without stimulation. (C) Data shown are means ± SEM (3 experiments) of cAMP levels expressed as pmol/mg protein. \*\*: p < 0.01 *vs* β-Gal-expressing cells without stimulation.





