**a**

**Ensemble Peptide ID: ENSMUSP00000025867**

1 MDDLFPLIFPSEPAQA*SGPYVEIIEQPKQRGMRFRYKCEGRSAGSIPGERSTDTTKTHPT*

*61 IKINGYTGPGTVRISLVTKDPPHRPHPHELVGKDCRDGYYEADLCPDRSIHSFQNLGIQC*

*121 VKKRDLEQAISQRIQTNNNPFHVPIEEQRGDYDLNAVRLCFQVTVRDPAGRPLLLTPVLS*

*181 HPIFDNR*APNTAELKICRVNRNSGSCLGGDEIFLLCDKVQKEDIEVYFTGPGWEARGSFS

*241 QADVHRQVAIVFRTPPYADPSLQAPVRVSMQLRRPSDRELSEPMEFQYLP*DTDDRHRIEE

301 **KRKR**TYETFKSIMKKSPFNGPTEPRPPTRRIAVPTRNSTSVPKPAPQPYTFPASLSTINF

361 DEFSPMLLPSGQISNQALALAPSSAPVLAQTMVPSSAMVPLAQPPAPAPVLTPGPPQSLS

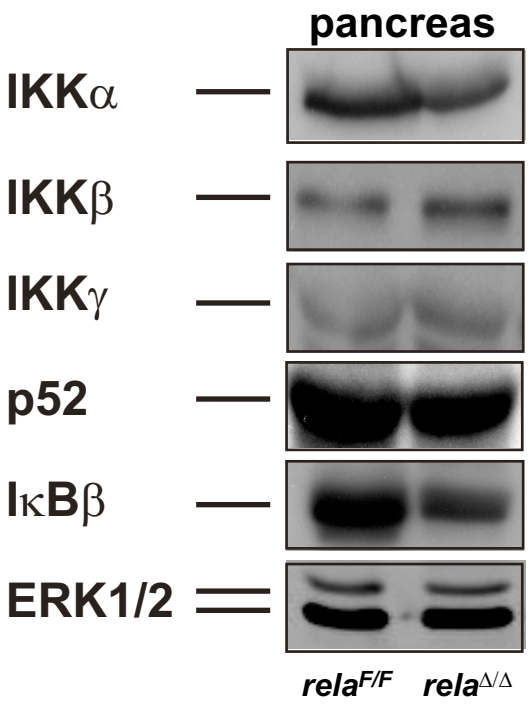
421 APVPKSTQAGEGTLSEALLHLQFDADEDLGALLGNSTDPGVFTDLASVDNSEFQQLLNQG

481 VSMSHSTAEPMLMEYPEAITRLVTGSQRPPDPAPTPLGTSGLPNGLSGDEDFSSIADMDF

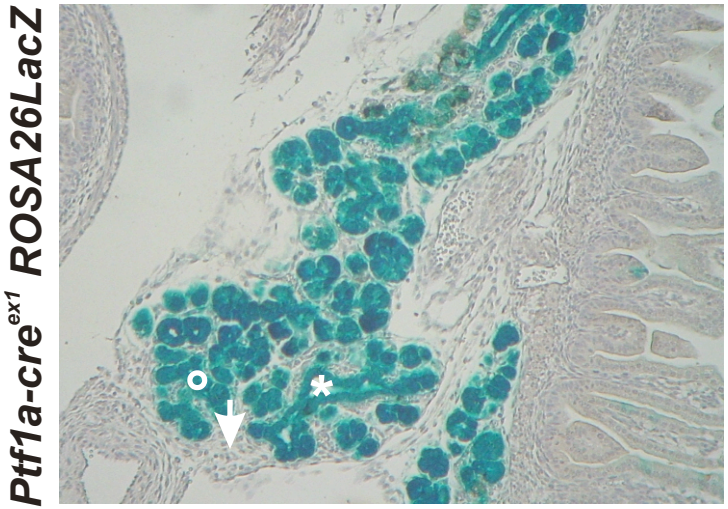
541 SALLSQISS

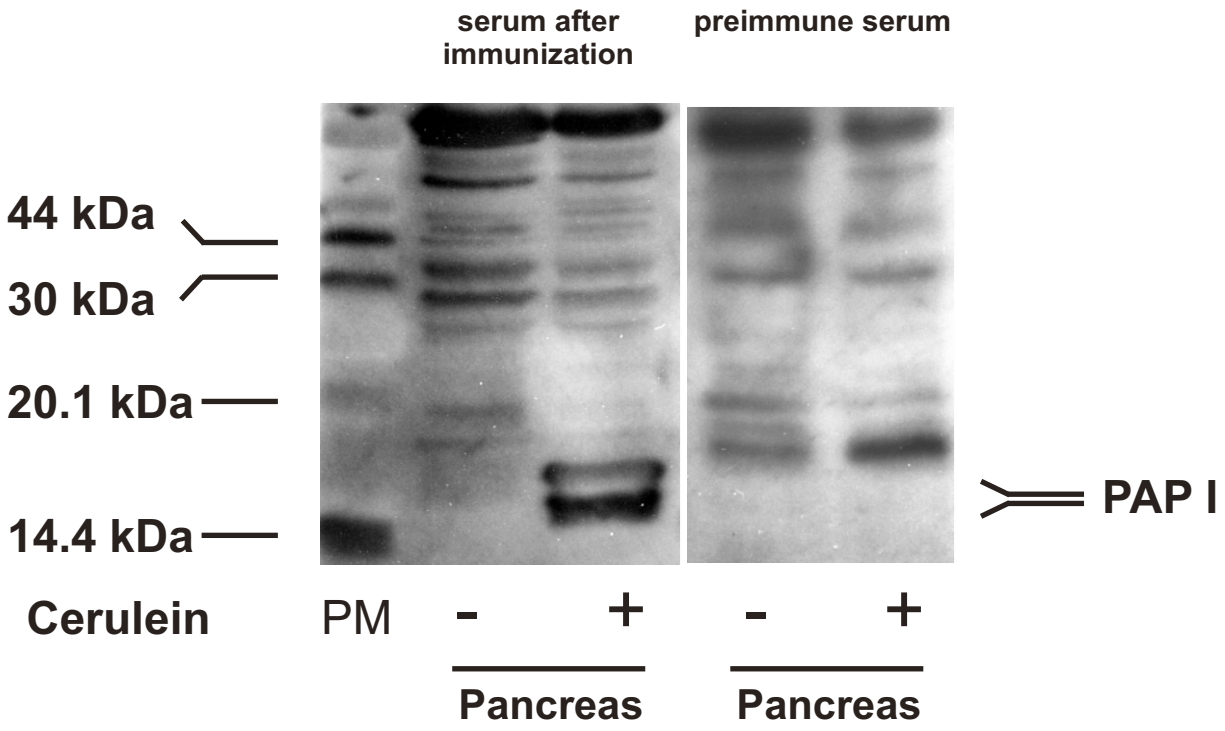
*Italic* : *Rel Homology Domain*
Red : Exon 7 to 10
**Red bold** : **Nuclear localization site**

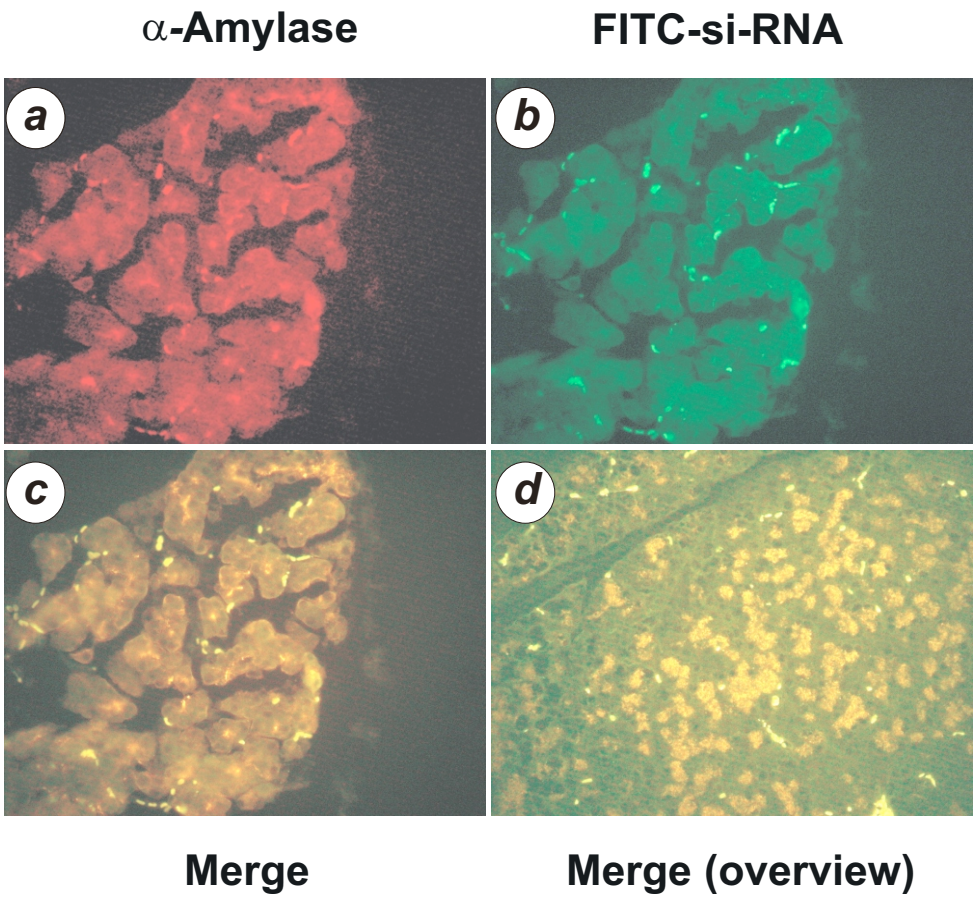
**b**

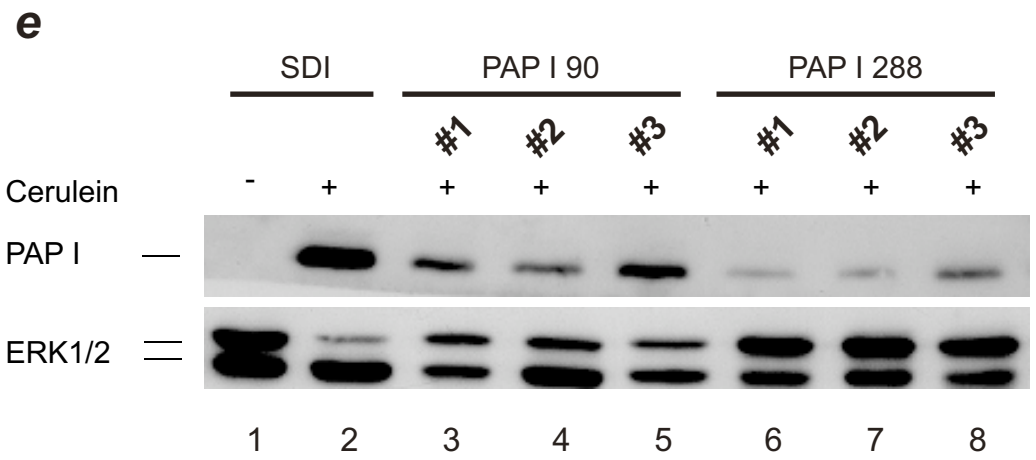


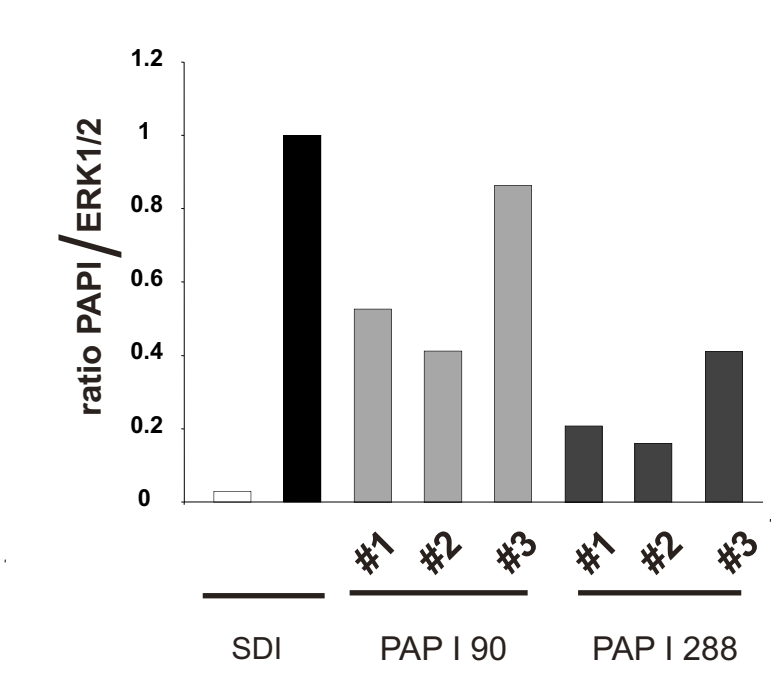

**c**

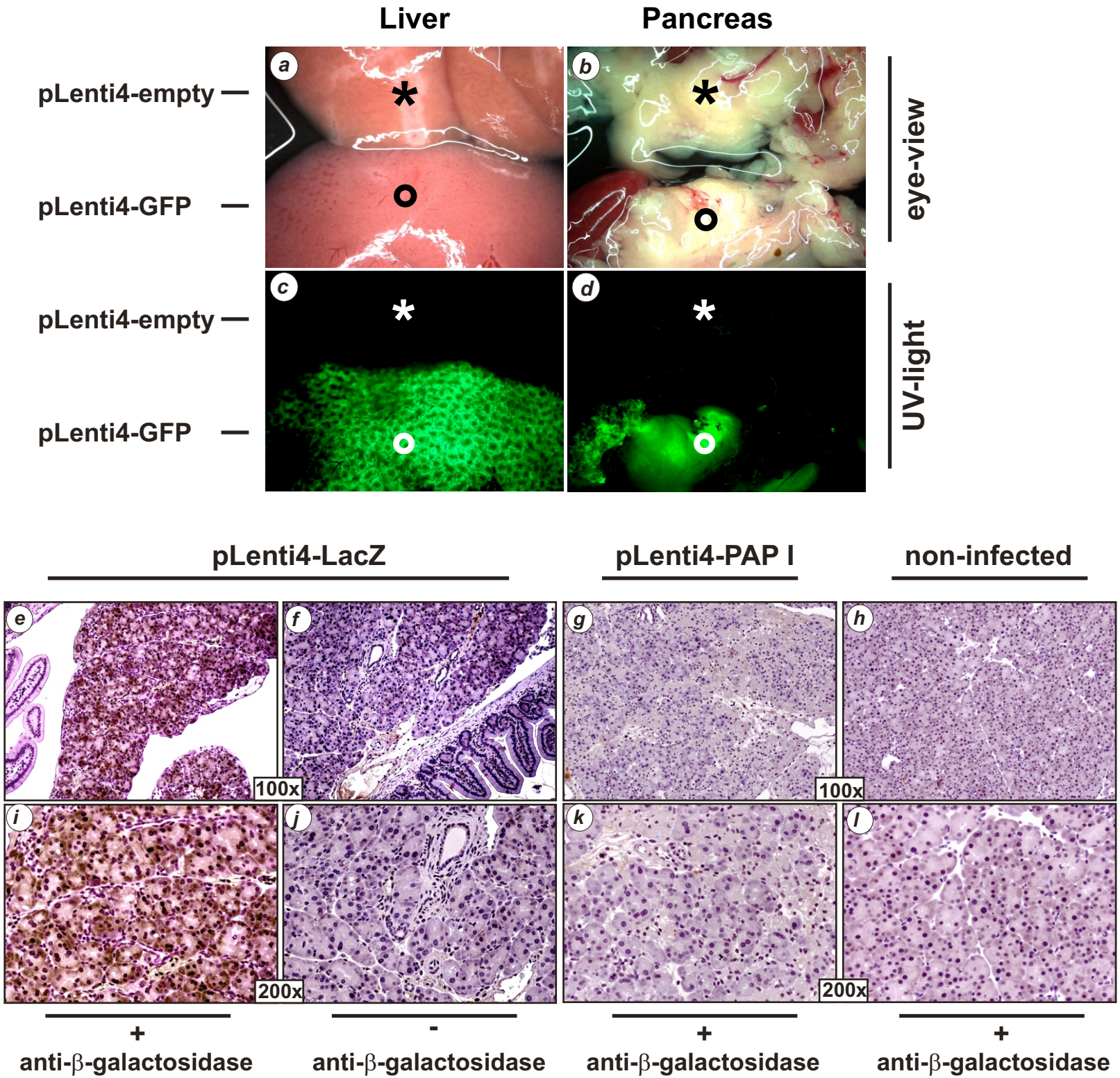



serum after immunization
preimmune serum
44 kDa
30 kDa
20.1 kDa
14.4 kDa
PAP I
Cerulein
PM
-
+
-
+
Pancreas
Pancreas


α-Amylase
FITC-si-RNA
a
b
c
d
Merge
Merge (overview)


e
SDI
PAP I 90
PAP I 288
#1
#2
#3
Cerulein
- + + + + + + +
PAP I
ERK1/2
1 2 3 4 5 6 7 8


f
ratio PAPI/ERK1/2
1.2
1
0.8
0.6
0.4
0.2
0
#1 #2 #3 #1 #2 #3
SDI
PAP I 90
PAP I 288




Supplement 4

**Supplement 1:** (**a**) Illustration of the RelA/p65 protein sequence (Ensemble peptide ID: ENSMUSP 00000025867). The Rel Homology Domain (RHD) is highlighted in italic, while exon 7-10 are illustrated in red. The nuclear localization site (NLS) is in red bold letters. (**b**) Pancreatic protein extracts (40 µg) from *rela*$^{F/F}$ and *rela*$^{\Delta/\Delta}$ were analyzed using antibodies against IKKα, IKKβ, IKKγ, p52, IκBβ, and ERK1/2 (as a loading control). (**c**) To assess Cre activity, *Ptf1a-cre* $^{ex1}$ mice were crossed to Gt (ROSA) 26Sortm1Sor (R26R) mice, which carry a modified *lacZ* gene driven by the cell-type independent ROSA26 promoter (62). Cre excises a stop cassette upstream of *lacZ* and thereby activates expression of β-galactosidase. The *Ptf1a-cre* $^{ex1}$ mice exhibited LacZ expression and revealed Cre activity in nearly all acinar (circle) and ductal cells (asterik), but not in interstitial parts (arrow).

**Supplement 2:** Specificity of PAP I antibody was tested by using pancreatic protein lysates from mice treated either with saline or cerulein. Serum after and before immunization was tested in western blot analysis. While serum from immunized rabbits detects a band at around 16 kDa, serum from non-immunized rabbits did not. The upper band might represent the unprocessed and uncleaved PAP I protein.

**Supplement 3: (*a-d*)** FITC-labeled siRNA were used to evaluate efficacy of transfection in the pancreas after i.p. injection according to the schedule. Immunofluorescence of α-Amylase detects acinar cells showing that part of the pancreas are targeted by the marked siRNA (merge, overview). (***e-f***) Pancreatic homogenates from pretreated mice (SDI, PAP I 90, PAP I 288) were subjected to western blot analysis. Membranes were probed with PAP I and ERK1/2 antibodies. The densities of the observed bands were analysed with Quantity One® 1-D Analysis

Software from Bio-Rad. Density of PAP I band was related to ERK 1 and ERK2 and expressed as x-fold induction over positive control.

**Supplement 4: (*a-d*)** pLenti4-GFP were used to infect *rela*$^{F/F}$ mice and followed according to the schedule in Figure 7. Control mice were treated with an empty pLenti4 virus. Seven days post infectionem mice were sacrificed and organs (liver, pancreas) were removed. For direct comparison liver and pancreas from pLenti4-GFP and empty pLenti4 treated mice were observed under normal light (a, b) and UV-light (c, d) to detect specific transduction of GFP. Organs from pLenti4-GFP treated mice were marked with circle (**o**), while mice undergoing injections with an empty virus were highlighted by an asterisk (*). (***e-h***) Paraffin-embedded sections of pLenti4-LacZ or pLenti4-PAP I pretreated mice were incubated with (e, g, i, k) or without (f, j) an anti-β-galactosidase antibody. Uninfected pancreas was used as control (h, l). Cytoplasmic signals were detectable in e and i (100 x and 200 x), while no signal was visible on control slides without the first antibody (f, j and 50 x , 100 x). Pancreas from pLenti4-PAP I or unifected mice displayed no signals (g, h, k, l).