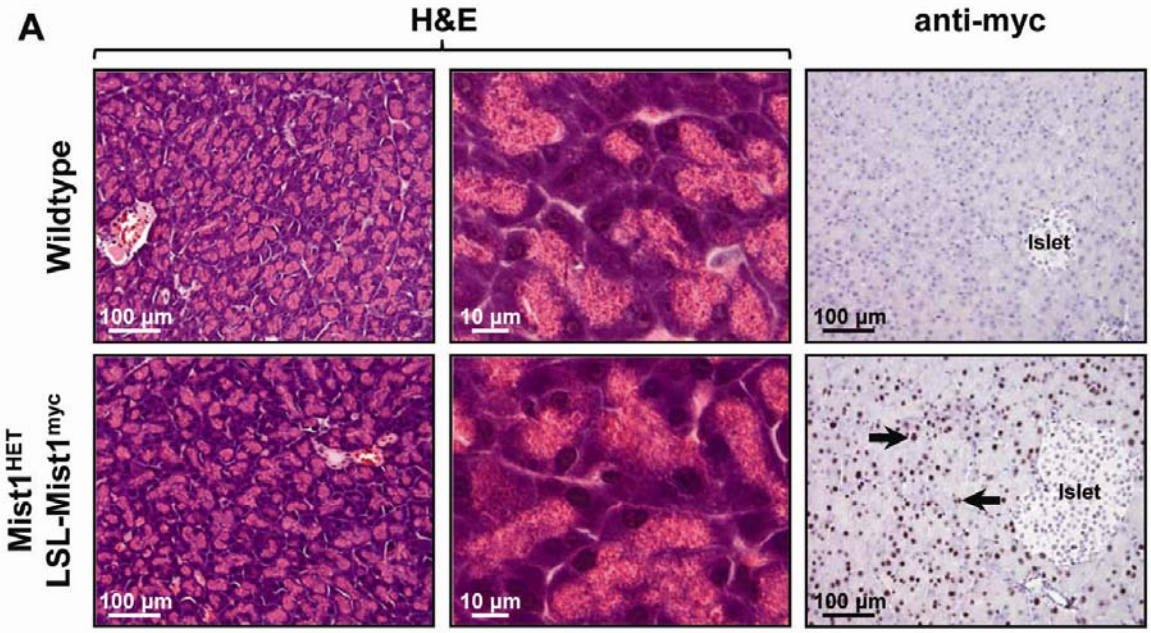
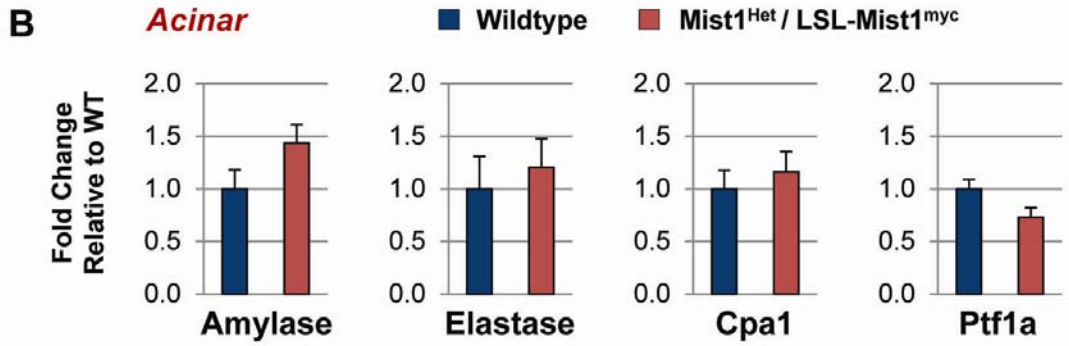
FIGURE S1: *Induced Mist1^{myc} expression has no effect on Mist1^{Het} acinar cells.* **(A)** H&E and anti-myc images of *WT* and *Mist1$^{CreER/+}$ (Mist1^{Het})/LSL-Mist1^{myc}* pancreata 3 months post-TM. arrows - MIST1^{myc} positive acinar cells. **(B)** Analysis of acinar and ductal gene expression profiles by RT-qPCR reveals no significant differences in *WT* and *Mist1^{HET}/LSL-Mist1^{myc}* pancreata expression. **(C)** MIST1 gene targets are not significantly affected by constitutive MIST1^{myc} expression in *Mist1^{Het}* pancreata.

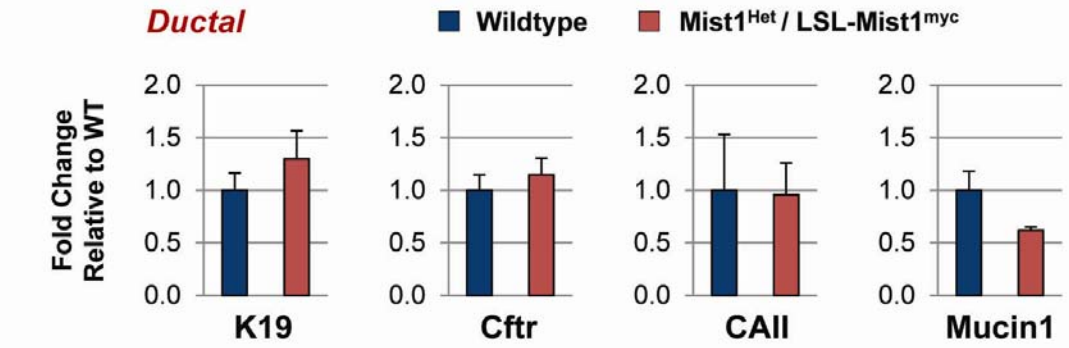
FIGURE S2: *Characterization of MIST1 target genes.* Grouping of 20 MIST1 target genes and their putative functions in acinar cells.

FIGURE S3: *TA- and GC- E-boxes are found associated with the ChIP amplified regions of MIST1 target genes.* Position and sequence of the E-box regulatory elements associated with each ChIP amplicon for the MIST1 target genes.

FIGURE S4: *Zymogen granule localization and diameter are rescued by LSL-Mist1^{myc} expression.* **(A)** Relative positions of individual zymogen granules in the indicated acinar cells. **(B)** Average zymogen granule size in *WT*, *Mist1^{KO}* and 1- and 4-day post-TM *Mist1^{KO}/LSL-Mist1^{myc}* acini.


A
H&E
anti-myc
Wildtype
Mist1HET LSL-Mist1myc
100 µm
10 µm
Islet


B
Acinar
Wildtype
Mist1Het / LSL-Mist1myc
Fold Change Relative to WT
Amylase
Elastase
Cpa1
Ptf1a


Ductal
Wildtype
Mist1Het / LSL-Mist1myc
Fold Change Relative to WT
K19
Cftr
CAII
Mucin1

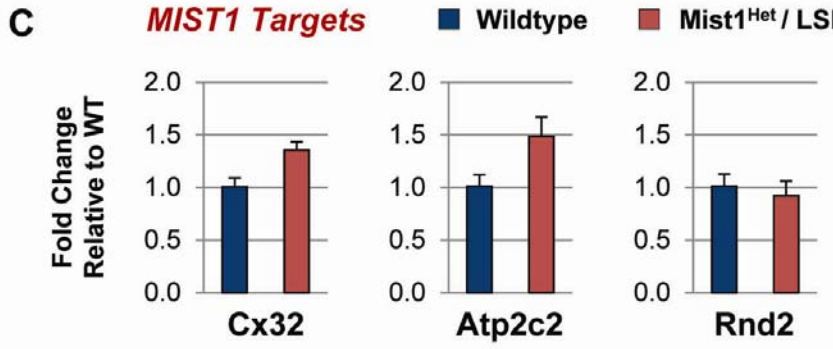

C
MIST1 Targets
Wildtype
Mist1Het / LSL-Mist1myc
Fold Change Relative to WT
Cx32
Atp2c2
Rnd2

FIGURE S1

PUTATIVE FUNCTIONS OF MIST1 TARGET GENES **FIGURE S2**

Secretion	Putative Function	Ref.
Rab3d	Rab GTPase responsible for the formation of large secretory granules	1
Rab27a	Rab GTPase known to regulate vesicle trafficking and granule exocytosis	2, 3
Gjb1 (Cx32)	Gap-junction protein essential for intra-cellular signaling through Ca^{2+} ions	4
Atp2c2	Secretory pathway Ca^{2+}-ATPase localized to the ER in acinar cells	5
Copz2	Subunit of the coatomer protein complex involved in COPI-mediated vesicle transport	6, 7

Stress Prevention/ Response	Putative Function	Ref.
Htra2	Serine protease / chaperone protein involved in mitochondrial homeostasis and cell stress prevention	8-10
Uba5	E1-like ubiquitin activating enzyme that activates Ufm1 ubiquitin-like modifier protein	11, 12
Abcb6	ATP-binding cassette (ABC) transporter involved in porphyrin transport and protects against stress	13-15
Nox4	Subunit of the NADPH oxidase complex upregulated by Nfe2l2 during cell stress events	16, 17
Gstm4	Glutathione S-transferase involved in detoxification of electrophilic compounds	18, 19
Nfe2l2	bZIP transcription factor that activates an antioxidant and cellular detoxification program	20, 21
Aldh1a1	Alcohol dehydrogenase enzyme important for detoxification of oxidative damage	22, 23

Signaling	Putative Function	Ref.
Rnd2	Rho GTPase implicated in the regulation of actin dynamics	24-26
Cldn10	Tight-junction protein expressed in pancreatic acini	27, 28
Ppap2b	Phosphatidic acid phosphatase enzyme important for lipid metabolism and β-catenin signaling	29-32
Ptgr1	Catalyzes the metabolism of leukotriene B4 which plays an important role in pancreatitis inflammation	33-35

Miscellaneous	Putative Function	Ref.
Wdyhv1	N-terminal amidohydrolase comprising a part of the N-end rule pathway of protein degradation	36
Foxp2	Transcription factor known to participate in development of speech and language regions of the brain	37
Slc35d1	Nucleotide sugar transporter that transports both UDP-glucuronic acid and UDP-N-acetylgalactosamine	38
Smarca1	SWI/SNF family chromatin remodeling factor shown to positively regulate transcription	39, 40

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PUTATIVE MIST1 TARGET SITES (1 KB FRAGMENTS FLANKING CHIP SITES) **FIGURE S3**

ChIP Amplicon, **TA E-box**, **GC E-box**

Rab3d

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Htra2

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ca

Rab27a

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Abcb6

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PUTATIVE MIST1 TARGET SITES (1 KB FRAGMENTS FLANKING CHIP SITES) **FIGURE S3**

ChIP Amplicon, **TA E-box**, **GC E-box**

Gjb1 (Cx32)

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Atp2c2

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Copz2

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PUTATIVE MIST1 TARGET SITES (1 KB FRAGMENTS FLANKING CHIP SITES) **FIGURE S3**

ChIP Amplicon, **TA E-box**, **GC E-box**

Gstm4

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Ptgr1

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Cldn10

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PUTATIVE MIST1 TARGET SITES (1 KB FRAGMENTS FLANKING CHIP SITES) **FIGURE S3**

ChIP Amplicon, **TA E-box**, **GC E-box**

Ppap2b

gccttctatgtgtgggcctgtgctggccggtgtcctcatggacattttaccatgtctccatttttaccagtgccatcatgggtcttcctgtcactggctataagtgcattctcatagggca
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Smarca1

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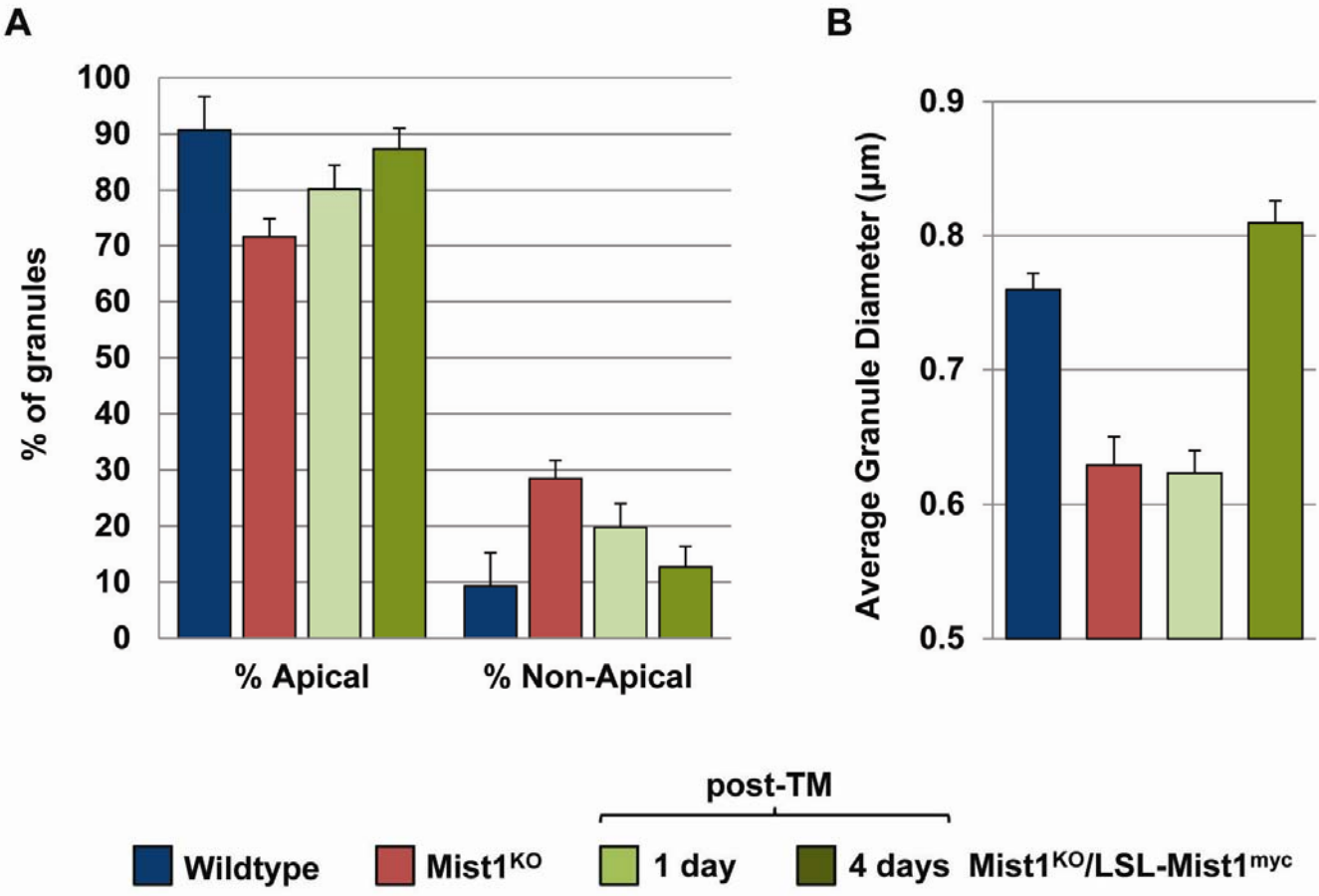
A
100
90
80
70
60
50
40
30
20
10
0
% of granules
% Apical
% Non-Apical
B
0.9
0.8
0.7
0.6
0.5
Average Granule Diameter (µm)
post-TM
Wildtype
Mist1KO
1 day
4 days
Mist1KO/LSL-Mist1myc

FIGURE S4