

SUPPLEMENTARY MATERIAL

Loss of chymotrypsin-like protease (CTRL) alters intrapancreatic protease activation but not pancreatitis severity in mice

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Supplementary Figure 1. Genomic sequence of mouse *Ctrl* (NC_000074.6). Exons are highlighted in yellow and the translation start and stop codons are in green. The 5' and 3' splice sites are italicized and underlined. The polyadenylation signal sequence in the 3' region is underlined and emboldened. The position of the primers used for genotyping are underlined and shown in bold typeface. The 43 bp deletion (c.159_201del43) in exon 3 of the *Ctrl-KO* mice is indicated in blue.

Genotyping primers:

mCtrl-F: 5'-GAA GGC ATT AGG GAG AGG TAG ACT GG-3'

mCtrl-R: 5'-GGT TCA GCA TTG GAA GAT CGG TC-3'

PCR product sizes: C57BL/6N 463 bp, *Ctrl-KO* 420 bp

GACCATCTCAACACCATTCCCTTATTTGTCA**ATGCTACTGCTCAGCCTAACCCCTTAGCCTGGTCCCTTGGCTCC**
TCCTGGGGTAAAGTGGGCTGGGAACCGACCTTGGCTGTT**CAGGGGCCAGACAAGGAGCCAGCCTGATGAGAAGGGAA**
CGGACAGTGTAA**GCAAAAGGAAGGAACCTT**CAGGGCTGAGAGTAAGGGAAGAGCCAGGGACCGGTCTCACAAATGAG
GCGGGAGCTT**GAGCCAGACCTAAGGAGGCTCAGGAACATATAAGAGATGTGTATAGACTAACAAAGCCTTCTAGCTG**
CATGGTAGACTGTGCAGGCCTAGAAAAACAGAGGGCAGGGAGATGATAGCAGGAATTAGAGAGAAA**ACTGGCCCAAG**
GTACATTAGGACTAGGTTGGTAGCTGTGAAAGCATGCACAGGACTTGAAGGCTGGTAGGGTGGGGTA**ACCAAGATAG**
CTGTGTATGCCTAAAAGGCACTCAAGGGAAGGCCTTGGAGTAATTCTCTTGGACCTCCTCCTGGATCTACAGCCTGG
GGGCACCTTGA**GAAGGCATTAGGGAGAGGTAGACTGG**GATTGGATTCTCACCAGCCCTATCTATGTT**CAGGCTGTG**
GTGTTCCCTGCCATCACGCCTGCACTGAGCTACAATCAGAGAATTGTCAACGGGGAGAATGCAGTGCCAGGCTCCCTGG
CCCTGGCAGGTGTCTCTCCAGGTAAATGCACCCTATGGGTGGGTTGGGGTCCCTGGGTGCTTTAGGCTATGGGTAACTT
AAGCCCATT**CATGTATCTAACTTTTGACCCTAG**GA**TAACACCGGCTTCCACTTCTGCGGTGGTTCTCTCATCAGTCC**
GAACTGGGTGGT**CACGGCTGCCCACTGCCAAGTCA**CGTGAGTGTATCCCCCTCCCTTGGATGCCCGCTCTGAAACCA
CTTAGCAGCTGCCATTCCATTATCCTTGCAGGCCTGGACGCCACTTTGT**CGTTTTGGGAGAATATGACCGATCTT**
CCAATGCTGAACCTGTGCAGGTCCCTCTCGATCGCAAGGGTAAAGTACTAGCTGTGCATGTAGAAAAGGGAAAATGGACT
GCAGGGCATCCAGGCATGCCCTGACCTACCCGCCTCAGCACAGGCCTGGGCACCTGTGCCACTCCAGCTTTACATG
ACTACTGACTGGCTCCAC**AGGCCATCACACACCCTAACTGGAACGCCAACACCATGAACAATGACCTGACTCTCCTG**
AAGCTTGCCTCGCCAGCCCGGTACACAGCACAAGTCTCACCAGTCTGCCTGGCTTCCACAAACGAGGCACTGCCTTC
GGGGCTCACCTGTGTACCACTGGCTGGGGCCGAATCAGTGGTGTGGG**TAAGA**ACCTGGGTAATGAGGGGAGACCAG
AAGAGCACCATGGGCCAGCCTAACCACTCTCCTGGCCCA**CAGGCAATGTGACACCAGCTCGCCTGCAGCAAGTTGT**
TCTACCCCTGGTCACTGTGAATCAGTGT**CGGCAGTACTGGGGTGCACGCATTACCGATGCCATGATATGTGCAGGTG**
GCTCAGGCGCCTCCTCATGTCAGGTAAAGCACCCTGTCTCCGCACTGTCCAGTGGGACACGTCCCCAAACTGCCATG
CTGACTTCTCCCCTTTTCTTCCCTTT**CAGGGT**GACTCAGGAGGCCCTCTTGTCTGCCAGAAGGGAAACACCTGGGTG
CTTATTGGGATTGTCTCCTGGGGCACTAAGAACTGCAACATA**CAAGCACCGGCCATGTACACTCGGGT**CAGCAAGTT
CAGTACCTGGATCAACCAAGTCATGGCCTACAACTAAACTGTCCACAGATCCGTTCCCCATCTCAATCT**AATAAA**CA
TACTCGTCTCAGTTTCTCTTG

Supplementary Figure 2. Messenger RNA sequence of *Ctrl* from C57BL/6N mice (NM_023182.2) and predicted mRNA sequence of *Ctrl* from *Ctrl-KO* mice. Amino-acid translations are also shown. The translation start and stop codons are indicated in green with underlined, bold typeface. The positions of primers used to amplify *Ctrl* cDNA are underlined and emboldened.

Primers used for cDNA amplification:

Ctrl cDNA F: 5'-GTC ACA ATG CTA CTG CTC AGC-3'

Ctrl cDNA R: 5'-GGA ACG GAT CTG TGG ACA G-3'

PCR product size: C57BL/6N mice, 821 bp

Mouse Ctrl mRNA

GACCATCTCAACACCATTCCCTTATTT**GTCACAATGCTACTGCTCAGC**CTAACCCCTTAGCCTGGTCTCCTTGGCTCC
TCCTGGGGCTGTGGTGTTCCTGCCATCACGCCTGCACTGAGCTACAATCAGAGAATTGTCAACGGGGAGAATGCAGT
GCCAGGCTCCTGGCCCTGGCAGGTGTCTCTCCAGGATAACACCGGCTTCCACTTCTGCGGTGGTTCTCTCATCAGTC
CGAACTGGGTGGTCACGGCTGCCACTGCCAAGTCACGCCTGGACGCCACTTTGTCTGTTTTGGGAGAATATGACCGA
TCTTCCAATGCTGAACCTGTGCAGGTCTCTCGATCGCAAGGGCCATCACACACCCTAACTGGAACGCCAACACCAT
GAACAATGACCTGACTCTCCTGAAGCTTGCCTCGCCAGCCCGGTACACAGCACAAGTCTCACCAGTCTGCCTGGCTT
CCACAAACGAGGCACTGCCTTCGGGGCTCACCTGTGTCACTGGCTGGGGCCGAATCAGTGGTGTGGGCAATGTG
ACACCAGCTCGCCTGCAGCAAGTTGTTCTACCCCTGGTCACTGTGAATCAGTGTGCGGCAGTACTGGGGTGCACGCAT
TACCGATGCCATGATATGTGCAGGTGGCTCAGGCGCCTCCTCATGTGAGGGTACTCAGGAGGCCCTCTTGTCTGCC
AGAAGGGAAACACCTGGGTGCTTATTGGGATTGTCTCCTGGGGCACTAAGAAGTCAACATAACAAGCACCGGCCATG
TACTCTGGGTGAGCAAGTTCAGTACCTGGATCAACCAAGTCATGGCCTACAAC**TAACTGTCCACAGATCCGTTCC**
CCATCTCAATCT**AATAAA**CATACTCGTCTCAGTTTCTCTTG

Translation of mouse Ctrl coding DNA

Blue highlights the secretory signal peptide and yellow indicates the activation peptide.

MLLLSLTSLVLLGSSWGC**GVPAITPALS****YNQR**IVNGENAVPGSWPQVSLQDNTGFHFCGGLISPNWVVTAAHCQ
VTPGRHFVVLGEYDRSSNAEPVQVLSIARAITHPNWNANTMNDLTLKLASPARYTAQVSPVCLASTNEALPSGLT
CVTTGWGRISGVGNVTPARLQVVLPVTVNQCRQYWGARITDAMICAGGSGASSCQDSDGGPLVCQKNTWVLIGI
VSWGTKNCNIQAPAMYTRVSKFSTWINQVMAYNX

Predicted mouse Ctrl mRNA with 43 bp deletion (c.159_201del43)

GACCATCTCAACACCATTCCCTTATTT**GTCACAATGCTACTGCTCAGC**CTAACCCCTTAGCCTGGTCTCCTTGGCTCC
TCCTGGGGCTGTGGTGTTCCTGCCATCACGCCTGCACTGAGCTACAATCAGAGAATTGTCAACGGGGAGAATGCAGT
GCCAGGCTCCTGGCCCTGGCAGGTGTCTCTCCAGGAACTGGGTGGTCACGGCTGCCACTGCCAAGTCACGCCTGG
ACGCCACTTTGTCTGTTTTGGGAGAATATGACCGATCTTCCAATGCTGAACCTGTGCAGGTCTCTCGATCGCAAGGG
CCATCACACACCCTAACTGGAACGCCAACACCATGAACAATGACCTGACTCTCCTGAAGCTTGCCTCGCCAGCCCGG
TACACAGCACAAGTCTCACCAGTCTGCCTGGCTTCCACAAACGAGGCACTGCCTTCGGGGCTCACCTGTGTCAACC
TGGCTGGGGCCGAATCAGTGGTGTGGGCAATGTGACACCAGCTCGCCTGCAGCAAGTTGTTCTACCCCTGGTCACTG
TGAATCAGTGTGCGCAGTACTGGGGTGCACGCATTACCGATGCCATGATATGTGCAGGTGGCTCAGGCGCCTCCTCA
TGTCAGGGTGACTCAGGAGGCCCTCTTGTCTGCCAGAAGGGAAACACCTGGGTGCTTATTGGGATTGTCTCCTGGGG
CACTAAGAAGTCAACATAACAAGCACCGGCCATGTACTCTGGGTGAGCAAGTTCAGTACCTGGATCAACCAAGTCA
TGGCCTACAAC**TAACTGTCCACAGATCCGTTCC**CCATCTCAATCT**AATAAA**CATACTCGTCTCAGTTTCTCTTG

Translation of predicted mouse Ctrl coding DNA with deletion (p.D53EfsX52)

Blue highlights the secretory signal peptide and yellow indicates the activation peptide. The frame-shifted sequence is shown in gray.

MLLLSLTSLVLLGSSWGC**GVPAITPALS****YNQR**IVNGENAVPGSWPQVSLQ**ETGWSRLPTAKSRLD****ATLSFWENMT**
DL**PMLNLCRSSRSQGPSHTLTGTPTPX**

Supplementary Figure 3. Uncropped version of gels shown in Figure 1.

Figure 1 C and E

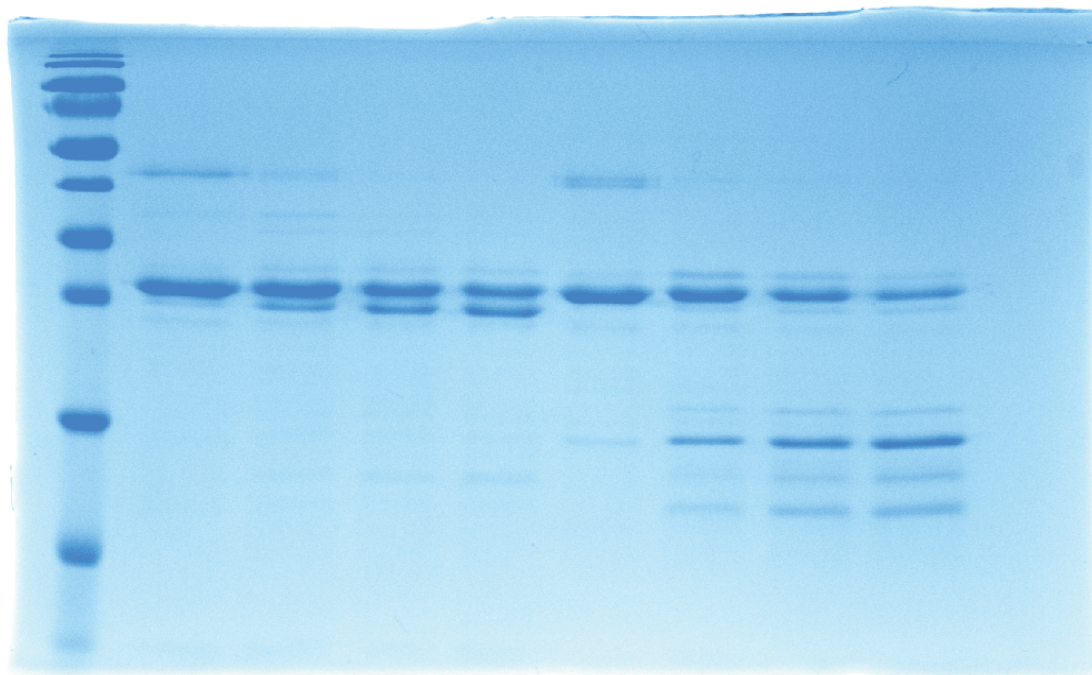
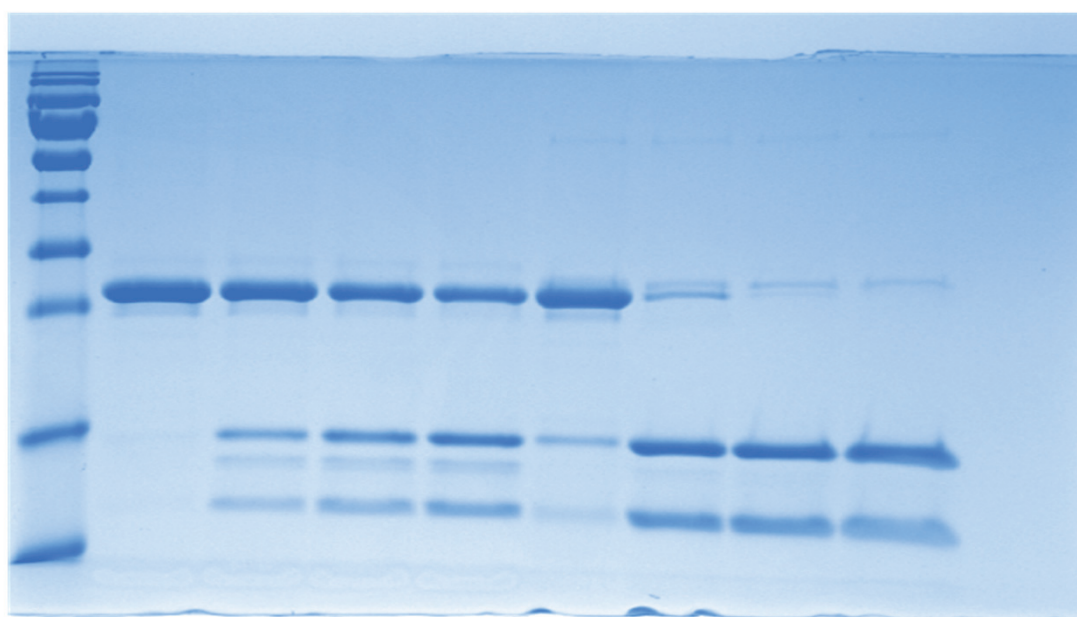
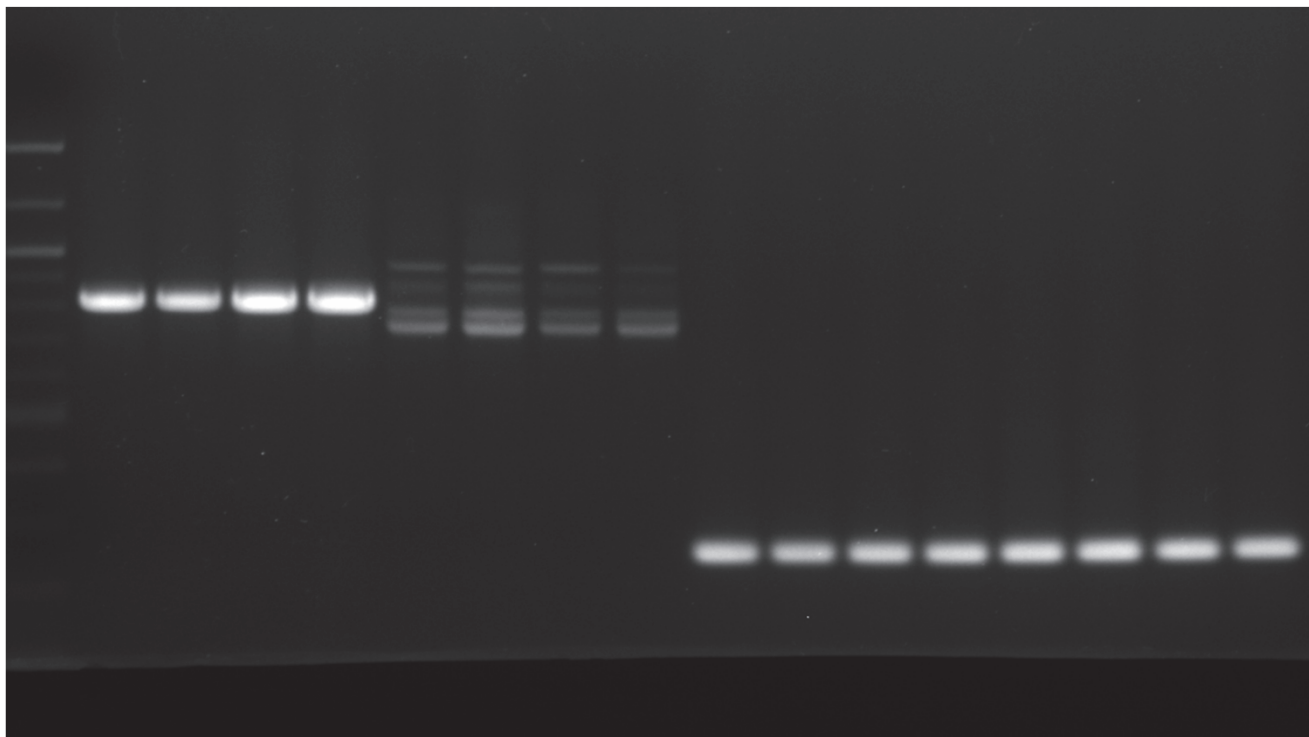


Figure 1 D and F



Supplementary Figure 4. Uncropped version of agarose gel shown in Figure 2C.



Supplementary Figure 5. Uncropped version of western blots shown in Figure 2D.

