Table S1. Proportion of *Phb1*$^{Def\alpha6\Delta PC}$ and *Phb1*$^{iMist1\Delta PC}$ mice that exhibit mitochondrial dysfunction, abnormal Paneth cells, and histological inflammation.

| Age (weeks) | Week after *Phb1* deletion | % mice with mitochondrial dysfunction* n (%) | | % mice with abnormal Paneth cells# n (%) | | % mice with histological inflammation n (%) | |
|---|---|---|---|---|---|---|---|
| *Phb1*$^{Def\alpha6\Delta PC}$ | *Phb1*$^{iMist1\Delta PC}$ | *Phb1*$^{Def\alpha6\Delta PC}$ | *Phb1*$^{iMist1\Delta PC}$ | *Phb1*$^{Def\alpha6\Delta PC}$ | *Phb1*$^{iMist1\Delta PC}$ | *Phb1*$^{Def\alpha6\Delta PC}$ | *Phb1*$^{iMist1\Delta PC}$ |
| 8 | 1 | 12/12 (100) | 8/8 (100) | 9/12 (75) | 4/8 (50) | 0/12 (0) | 1/8 (13) |
| 11 | 3 | 8/8 (100) | 9/9 (100) | 8/8 (100) | 9/9 (100) | 3/8 (38) | 1/9 (11) |
| 20 | 12 | 10/10 (100) | 17/17 (100) | 10/10 (100) | 17/17 (100) | 6/10 (60) | 11/17 (65) |

*Defined as increased mtUPR, ultrastructural abnormalities in IECs by TEM

#Defined as altered lysozyme staining, less abundant secretory granules, and AB$^{+}$ staining.

Table S2. Quantitative real-time PCR primer sequences.

| Primer name | Primer sequence |
|---|---|
| *β-actin* sense | 5′-TATGCCAACACAGTGCTGTCTGG-3′ |
| *β-actin* antisense | 5′-TACTCCTGCTTGCTGATCCACAT-3′ |
| *Tnfα* sense | 5′-AGGCTGCCCCGACTACGT-3′ |
| *Tnfα* antisense | 5′-ACTTTCTCCTGGTATGAGATAGCAAA-3′ |
| *Il-1β* sense | 5′-TCGCTCAGGGTCACAAGAAA-3′ |
| *Il-1β* antisense | 5′-CATCAGAGGCAAGGAGGAAAAC-3′ |
| *Ifnγ* sense | 5′-CAGCAACAGCAAGGCGAAA-3′ |
| *Ifnγ* antisense | 5′-CTGGACCTGTGGGTTGTTGAC-3′ |
| *Il-10* sense | 5′-GGTTGCCAAGCCTTATCGGA-3′ |
| *Il-10* antisense | 5′-ACCTGCTCCACTGCCTTGCT-3′ |
| *Il-18* sense | 5′-ACAACTTTGGCCGACTTCAC-3′ |
| *Il-18* antisense | 5′-GGGTTCACTGGCACTTTGAT-3′ |
| *Reg3γ* sense | 5′-GCTTCCCCGTATAACCATCA-3′ |
| *Reg3γ* antisense | 5′-CCTTGCACCTGAGAAAGGAG-3′ |
| *Cryptdin 3* sense | 5′-CCAGGCTGATCCTATCCAAA-3′ |
| *Cryptdin 3* antisense | 5′-GACACAGCCTGGTCGTCTTC-3′ |
| *Cryptdin 5* sense | 5′-GGCTGCAAAAGAAGAGAACG-3′ |
| *Cryptdin 5* antisense | 5′-CAGCTGCAGCAGAATACGAA-3′ |
| *Ang4* sense | 5′-GAGCCCATGTCCTTTGTTGT-3′ |
| *Ang4* antisense | 5′-GCTTGGCATCATAGTGCTGA-3′ |
| *Muc2* sense | 5′-ACATCACCTGTCCCGACTTC-3′ |
| *Muc2* antisense | 5′-GAGCAAGGGACTCTGGTCTG-3′ |
| *Muc4* sense | 5′-CCAGCAGCAAATCTCAAACA-3′ |
| *Muc4* antisense | 5′-TCGCCAGGAGAGTTTGTTCT-3′ |
| *Hes1* sense | 5′-ACACCGGACAAACCAAAGAC-3′ |
| *Hes1* antisense | 5′-ATGCCGGGAGCTATCTTTCT-3′ |
| *Math1* sense | 5′-CAACGACAAGAAGCTGTCCA-3′ |
| *Math1* antisense | 5′-ATTTTTGCAGGAAGCTGTGG-3′ |
| *Klf4* sense | 5′-AAGCCAAAGAGGGGAAGAAG-3′ |
| *Klf4* antisense | 5′-CTGTGTGAGTTCGCAGGTGT-3′ |
| *Elf3* sense | 5′-TTCAACGCCATGTACAGCTC-3′ |
| *Elf3* antisense | 5′-TCCCTTTGGGATCTTGTCTG-3′ |
| *Sox9* sense | 5′-CTGAAGGGCTACGACTGGAC-3′ |
| *Sox9* antisense | 5′-TACTGGTCTGCCAGCTTCCT-3′ |
| *Lgr5* sense | 5′-CCACAGCAACAACATCAGGT-3′ |
| *Lgr5* antisense | 5′-AACAAATTGGATGGGGTTGT-3′ |
| *ClpP* sense | 5′- CATCTGCACGTGGTGTGTTG-3′ |
| *ClpP* antisense | 5′- GGAATTGGGCAGTGAATGGC-3′ |
| *Hsp60* sense | 5′-TCTTCAGGTTGTGGCA-3′ |
| *Hsp60* antisense | 5′-CCCCTCTTCTCCAAAC-3′ |
| *sXbp1* sense | 5′-CTGAGTCCGAATCAGGTGCAG-3′ |
| *sXbp1* antisense | 5′-GTCCATGGGAAGATGTTCTGG-3′ |
| Total *Xbp1* sense | 5′-TGGCCGGGTCTGCTGAGTCCG-3′ |

| | |
|---|---|
| Total *Xbp1* antisense | 5′-GTCCATGGGAAGATGTTCTGG-3′ |
| *BiP* sense | 5′-TTCAGCCAATTATCAGCAAACTCT-3′ |
| *BiP* antisense | 5′-TTTTCTGATGTATCCTCTTCACCAGT-3′ |
| *Grp94* sense | 5′-AAGAATGAAGGAAAAACAGGACAAAA-3′ |
| *Grp94* antisense | 5′-CAAATGGAGAAGATTCCGCC-3′ |
| *Polg1* sense | 5′-GGAGATGAAGAAGTCGCTGATG-3′ |
| *Polg1* antisense | 5′-CTCCTGCAAATCCCATTCTAGG-3′ |
| *Polg2* sense | 5′-TCCTTGCGTTCTGTCTGTAAG-3′ |
| *Polg2* antisense | 5′-CTTTCTCTGGAGGCTCTTCTTC-3′ |
| *Tfam* sense | 5′-GGAGCTACCAGAAGCAGAAA-3′ |
| *Tfam* antisense | 5′-GACTTGGAGTTAGCTGCTCTT-3′ |
| *Pgc1* sense | 5′-CTAGCCATGGATGGCCTATTT-3′ |
| *Pgc1* antisense | 5′-GTCTCGACACGGAGAGTTAAAG-3′ |
| *Opa1* sense | 5′-CTCCCGACACAAAGGAAACTAT-3′ |
| *Opa1* antisense | 5′-AATACTGCGCTCAGCATCTAC-3′ |