

Table S1. Proportion of *Phb1^{Defα6ΔPC}* and *Phb1^{iMist1ΔPC}* mice that exhibit mitochondrial dysfunction, abnormal Paneth cells, and histological inflammation.

| Age (weeks) | Week after <i>Phb1</i> deletion | % mice with mitochondrial dysfunction* n (%) | | % mice with abnormal Paneth cells# n (%) | | % mice with histological inflammation n (%) | |
|--------------------------------|---------------------------------|---|---------------------------------|---|---------------------------------|--|---------------------------------|
| <i>Phb1^{Defα6ΔPC}</i> | <i>Phb1^{iMist1ΔPC}</i> | <i>Phb1^{Defα6ΔPC}</i> | <i>Phb1^{iMist1ΔPC}</i> | <i>Phb1^{Defα6ΔPC}</i> | <i>Phb1^{iMist1ΔPC}</i> | <i>Phb1^{Defα6ΔPC}</i> | <i>Phb1^{iMist1ΔPC}</i> |
| 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 |
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| <i>β-actin</i> sense | 5'-TATGCCAACACAGTGCTGTCTGG-3' |
| <i>β-actin</i> antisense | 5'-TACTCCTGCTTGCTGATCCACAT-3' |
| <i>Tnfα</i> sense | 5'-AGGCTGCCCCGACTACGT-3' |
| <i>Tnfα</i> antisense | 5'-ACTTTCTCCTGGTATGAGATAGCAAA-3' |
| <i>Il-1β</i> sense | 5'-TCGCTCAGGGTCACAAGAAA-3' |
| <i>Il-1β</i> antisense | 5'-CATCAGAGGCAAGGAGGAAAAC-3' |
| <i>Ifnγ</i> sense | 5'-CAGCAACAGCAAGGCGAAA-3' |
| <i>Ifnγ</i> antisense | 5'-CTGGACCTGTGGGTTGTTGAC-3' |
| <i>Il-10</i> sense | 5'-GGTTGCCAAGCCTTATCGGA-3' |
| <i>Il-10</i> antisense | 5'-ACCTGCTCCACTGCCTTGCT-3' |
| <i>Il-18</i> sense | 5'-ACAACCTTTGGCCGACTTCAC-3' |
| <i>Il-18</i> antisense | 5'-GGGTTCACTGGCACTTTGAT-3' |
| <i>Reg3γ</i> sense | 5'-GCTTCCCCGTATAACCATCA-3' |
| <i>Reg3γ</i> antisense | 5'-CCTTGACCTGAGAAAGGAG-3' |
| <i>Cryptdin 3</i> sense | 5'-CCAGGCTGATCCTATCCAAA-3' |
| <i>Cryptdin 3</i> antisense | 5'-GACACAGCCTGGTCGTCTTC-3' |
| <i>Cryptdin 5</i> sense | 5'-GGCTGCAAAAGAAGAGAACG-3' |
| <i>Cryptdin 5</i> antisense | 5'-CAGCTGCAGCAGAATACGAA-3' |
| <i>Ang4</i> sense | 5'-GAGCCCATGTCCTTTGTTGT-3' |
| <i>Ang4</i> antisense | 5'-GCTTGGCATCATAGTGCTGA-3' |
| <i>Muc2</i> sense | 5'-ACATCACCTGTCCCGACTTC-3' |
| <i>Muc2</i> antisense | 5'-GAGCAAGGGACTCTGGTCTG-3' |
| <i>Muc4</i> sense | 5'-CCAGCAGCAAATCTCAAACA-3' |
| <i>Muc4</i> antisense | 5'-TCGCCAGGAGAGTTTGTCT-3' |
| <i>Hes1</i> sense | 5'-ACACCGGACAAACCAAAGAC-3' |
| <i>Hes1</i> antisense | 5'-ATGCCGGGAGCTATCTTTCT-3' |
| <i>Math1</i> sense | 5'-CAACGACAAGAAGCTGTCCA-3' |
| <i>Math1</i> antisense | 5'-ATTTTTGCAGGAAGCTGTGG-3' |
| <i>Klf4</i> sense | 5'-AAGCCAAAGAGGGGAAGAAG-3' |
| <i>Klf4</i> antisense | 5'-CTGTGTGAGTTCGCAGGTGT-3' |
| <i>Elf3</i> sense | 5'-TTCAACGCCATGTACAGCTC-3' |
| <i>Elf3</i> antisense | 5'-TCCCTTTGGGATCTTGTCTG-3' |
| <i>Sox9</i> sense | 5'-CTGAAGGGCTACGACTGGAC-3' |
| <i>Sox9</i> antisense | 5'-TACTGGTCTGCCAGCTTCCT-3' |
| <i>Lgr5</i> sense | 5'-CCACAGCAACAACATCAGGT-3' |
| <i>Lgr5</i> antisense | 5'-AACAAATTGGATGGGGTTGT-3' |
| <i>ClpP</i> sense | 5'-CATCTGCACGTGGTGTGTTG-3' |
| <i>ClpP</i> antisense | 5'-GGAATTGGGCAGTGAATGGC-3' |
| <i>Hsp60</i> sense | 5'-TCTTCAGGTTGTGGCA-3' |
| <i>Hsp60</i> antisense | 5'-CCCCTCTTCTCAAAC-3' |
| <i>sXbp1</i> sense | 5'-CTGAGTCCGAATCAGGTGCAG-3' |
| <i>sXbp1</i> antisense | 5'-GTCCATGGGAAGATGTTCTGG-3' |
| Total <i>Xbp1</i> sense | 5'-TGGCCGGGTCTGCTGAGTCCG-3' |

| | |
|-----------------------------|----------------------------------|
| Total <i>Xbp1</i> antisense | 5'-GTCCATGGGAAGATGTTCTGG-3' |
| <i>BiP</i> sense | 5'-TTCAGCCAATTATCAGCAAACCTCT-3' |
| <i>BiP</i> antisense | 5'-TTTTCTGATGTATCCTCTTCACCAGT-3' |
| <i>Grp94</i> sense | 5'-AAGAATGAAGGAAAAACAGGACAAAA-3' |
| <i>Grp94</i> antisense | 5'-CAAATGGAGAAGATTCCGCC-3' |
| <i>Polg1</i> sense | 5'-GGAGATGAAGAAGTCGCTGATG-3' |
| <i>Polg1</i> antisense | 5'-CTCCTGCAAATCCCATTCTAGG-3' |
| <i>Polg2</i> sense | 5'-TCCTTGCGTTCTGTCTGTAAG-3' |
| <i>Polg2</i> antisense | 5'-CTTTCTCTGGAGGCTCTTCTTC-3' |
| <i>Tfam</i> sense | 5'-GGAGCTACCAGAAGCAGAAA-3' |
| <i>Tfam</i> antisense | 5'-GACTTGGAGTTAGCTGCTCTT-3' |
| <i>Pgc1</i> sense | 5'-CTAGCCATGGATGGCCTATTT-3' |
| <i>Pgc1</i> antisense | 5'-GTCTCGACACGGAGAGTTAAAG-3' |
| <i>Opa1</i> sense | 5'-CTCCCGACACAAAGGAACTAT-3' |
| <i>Opa1</i> antisense | 5'-AATACTGCGCTCAGCATCTAC-3' |