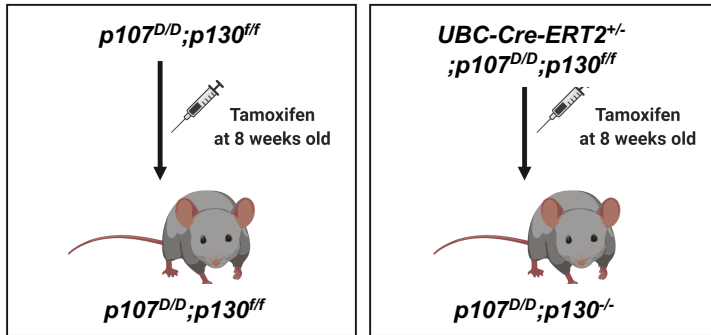
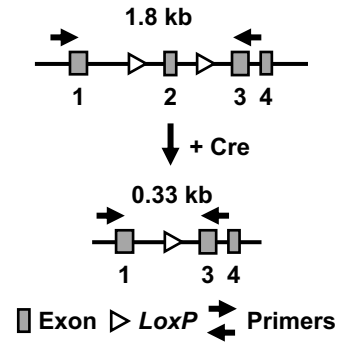
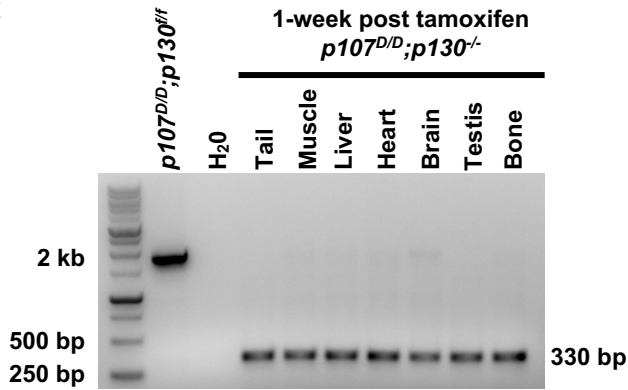
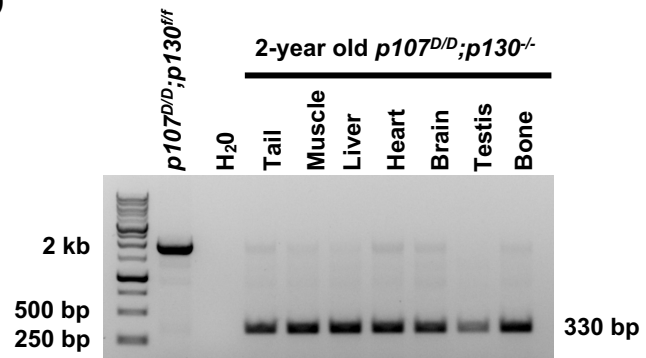


**A****B****C****D**

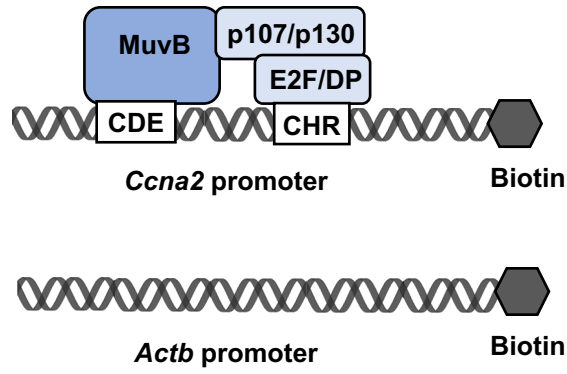
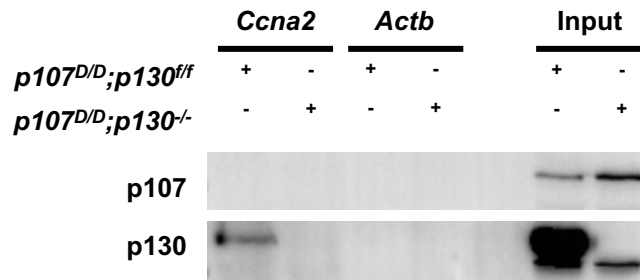
**Supplementary Figure S1. Strategy to create DREAM assembly deficient mice.**

**A:** Tamoxifen treatment of control ( $p107^{D/D};p130^{ff}$ ) and  $UBC-Cre-ERT2^{+/-};p107^{D/D};p130^{ff}$  at 8 weeks of age was used to produce adult control mice that are  $p107^{D/D};p130^{ff}$  and the comparative cohort that are  $p107^{D/D};p130^{-/-}$ .

**B:** PCR genotyping strategy to detect knockout of p130 by conditional deletion of exon 2.

Horizontal black arrows indicate annealing sites for genotyping primers to confirm deletion of exon 2. LoxP sites flank exon 2 and upon Cre activation, exon 2 is excised removing approximately 1.47 kb of genomic sequence.

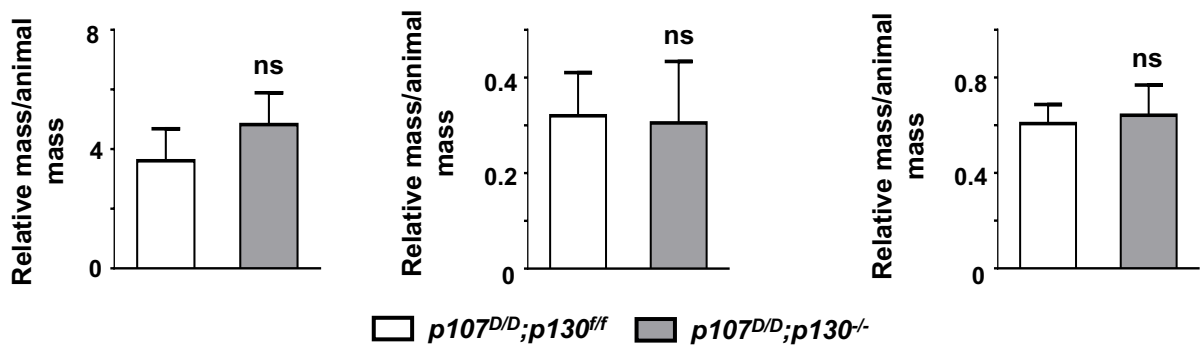
**C-D:** Validation of p130 exon 2 deletion by genotype PCR. Tissues obtained from mice 1-week (**C**) or 2 years (**D**) following tamoxifen treatment. The primer pair shown in **B** was used to detect successful excision of exon 2. PCR was performed on the indicated samples and products were resolved on agarose gels. Wildtype amplicon: 1.8 kb. Deleted allele amplicon: 330 bp.

**A****B**

**Supplementary Figure S2. In vitro DREAM assembly defect in  $p107^{D/D};p130^{-/-}$  mice.**

**A:** Schematic to illustrate biotinylated DNA probes used for affinity capture of protein complexes. In these in vitro assays, stable binding by DREAM requires simultaneous contact with CDE and CHR elements to capture components. Failure to assemble the complex will prevent detection of any components on the *Ccna2* probe. The *Actb* probe is used as a negative control.

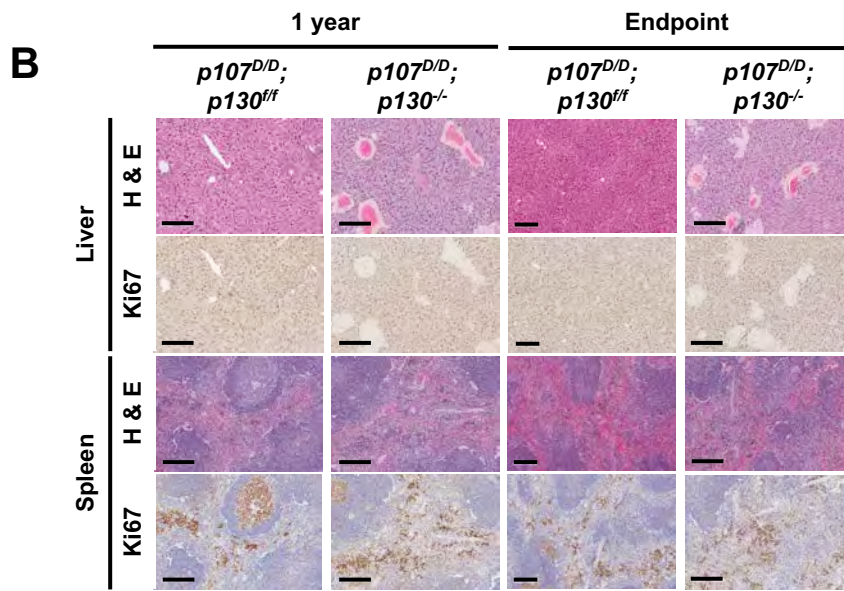
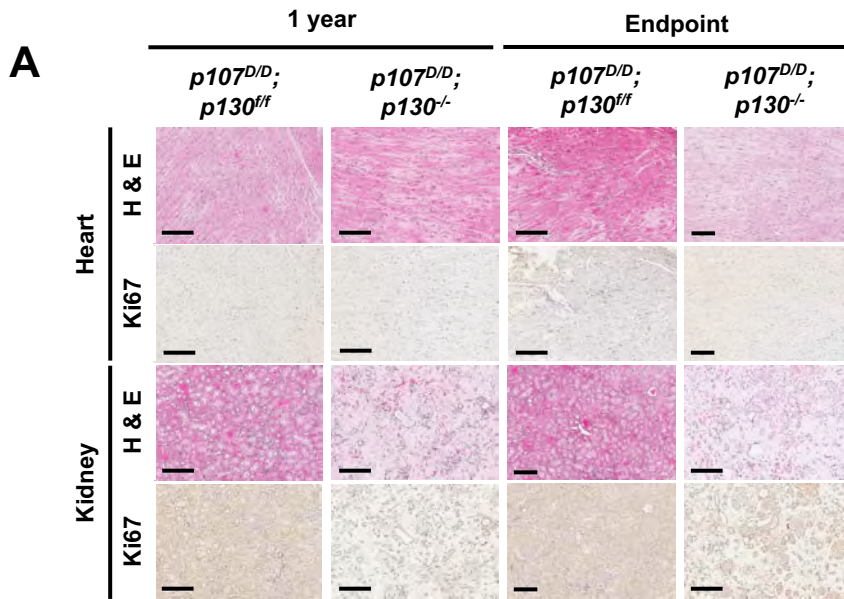
**B:** Control  $p107^{D/D};p130^{ff}$  and  $p107^{D/D};p130^{-/-}$  mice were used to produce liver extracts and proteins were bound to the indicated probes and associated protein complexes were isolated. Probe-bound proteins were separated by SDS-PAGE and western blotted to detect p107<sup>D</sup> or p130 to ascertain if DREAM is assembled in these extracts.

**A****B**

**Supplementary Figure S3. Normal liver, spleen, and kidney mass in  $p107^{D/D};p130^{-/-}$  mice.**

**A:** Whole mount images of the indicated organs are shown, along with their genotypes.

**B:** Comparison of organ mass relative to the animal's body mass is shown for  $p107^{D/D};p130^{ff}$  controls and  $p107^{D/D};p130^{-/-}$  mice.



**Supplementary Figure S4. Similar Ki67 staining in control and *p107<sup>D/D</sup>;p130<sup>-/-</sup>* tissues.**

**A:** Tissue sections were prepared from formalin fixed kidneys and hearts from mice of the indicated genotypes at the indicated ages. Serial sections were stained with H&E and Ki67. Scale bars represent 200  $\mu\text{m}$ .

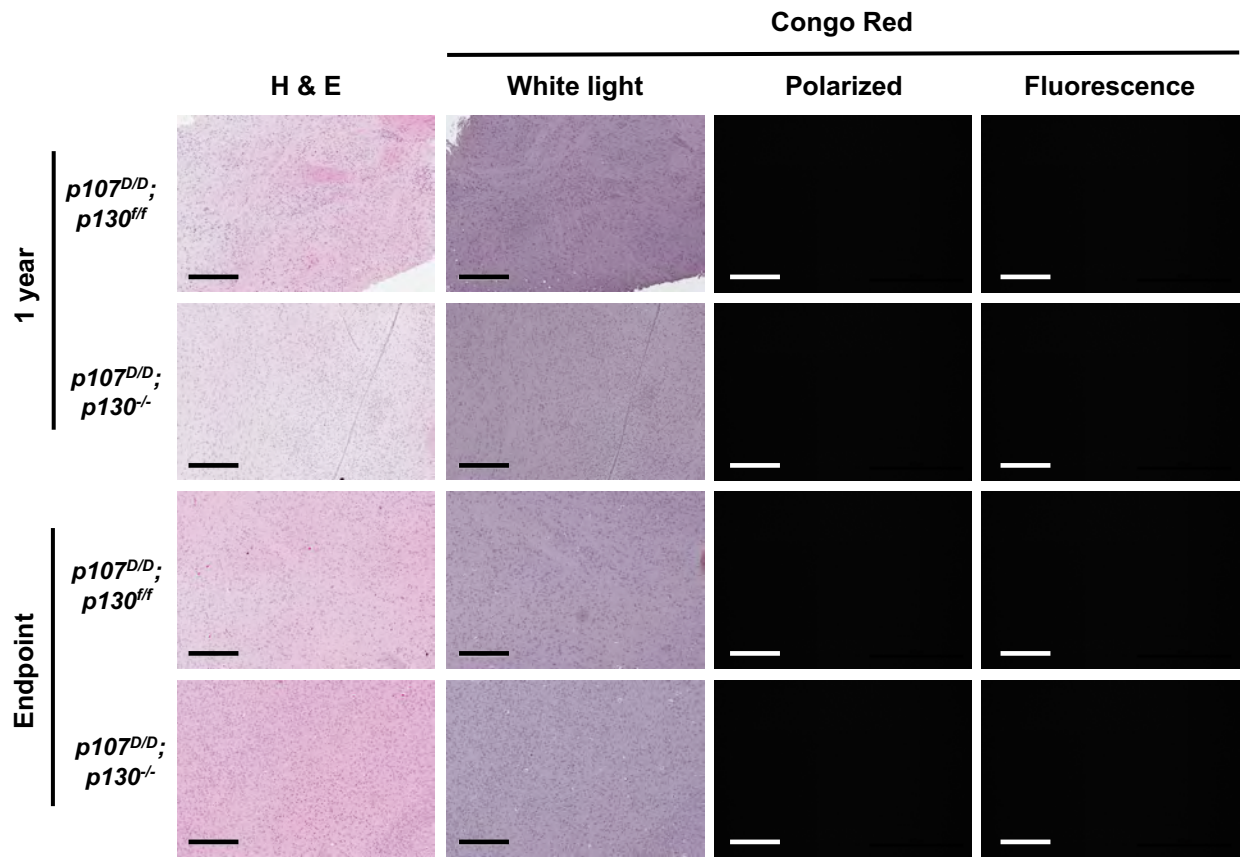
**B:** A similar analysis was performed on spleens and livers. Scale bars represent 200  $\mu\text{m}$ .



<b>Amyloid deposition score</b>	
0	No amyloid
1	Multifocal minimal deposits
2	Mild to moderate amyloid
3	Extensive amyloid expanding stroma
<b>Cellular degeneration score</b>	
0	No necrosis
1	Irregular cellular morphology
1.5	Scattered single cell necrosis/degeneration
2	Multifocal areas of necrosis
3	Multifocal to coalescing areas of necrosis
<b>Inflammation score</b>	
0	No inflammation
1	Scattered inflammatory cells
2	Nodular aggregates of inflammatory cells
3	Sheets of inflammatory cells
<b>Aggregated score = Amyloid deposition score + cellular degeneration score + inflammation score</b>	

**Supplementary Figure S5. Aggregate pathology scores for phenotypes observed in tissue sections.**

Tissues from 1-year and 2-year old endpoint mice from both cohorts were scored for three criteria (amyloid deposition, cellular degeneration, inflammation) on a scale of 0-3 (n=6). Scores were aggregated for each mouse as described.

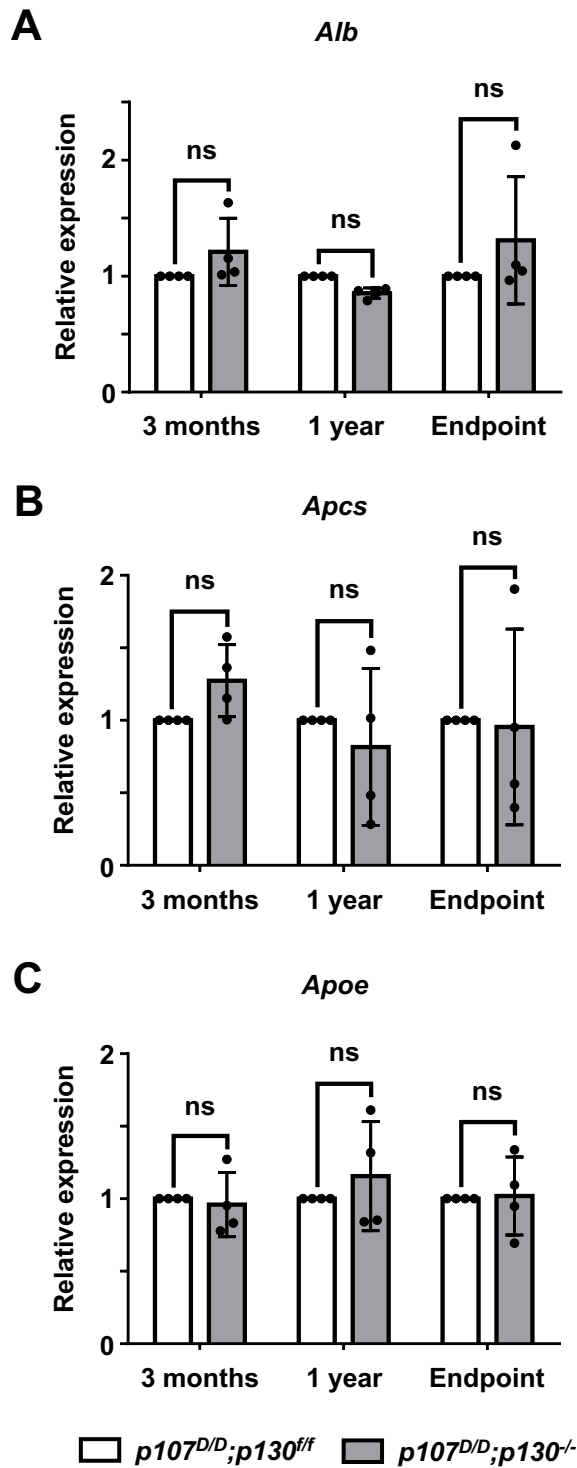


Supplementary Figure 6

**Supplementary Figure S6. H&E histology of control and *p107<sup>D/D</sup>;p130<sup>-/-</sup>* brains.**

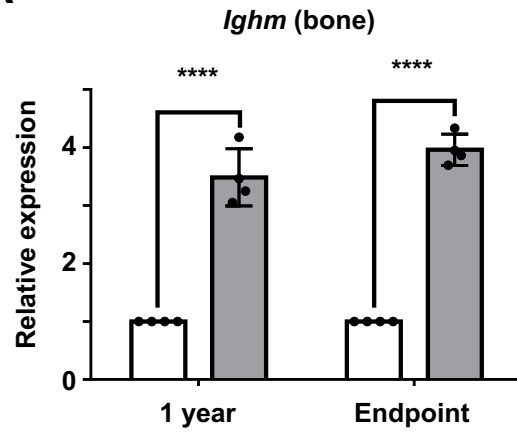
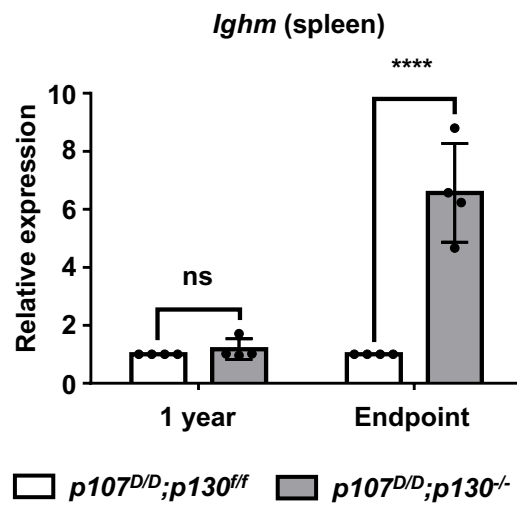
Tissue sections were prepared from FFPE brains and stained with H&E or Congo Red.

Representative sections used for amyloid scoring, cellular degeneration, and inflammation are shown and ages and genotypes are indicated. Scale bars represent 400  $\mu\text{m}$ .



**Supplementary Figure S7. Normal expression of amyloid associated protein coding genes in *p107<sup>D/D</sup>;p130<sup>-/-</sup>* mice.**

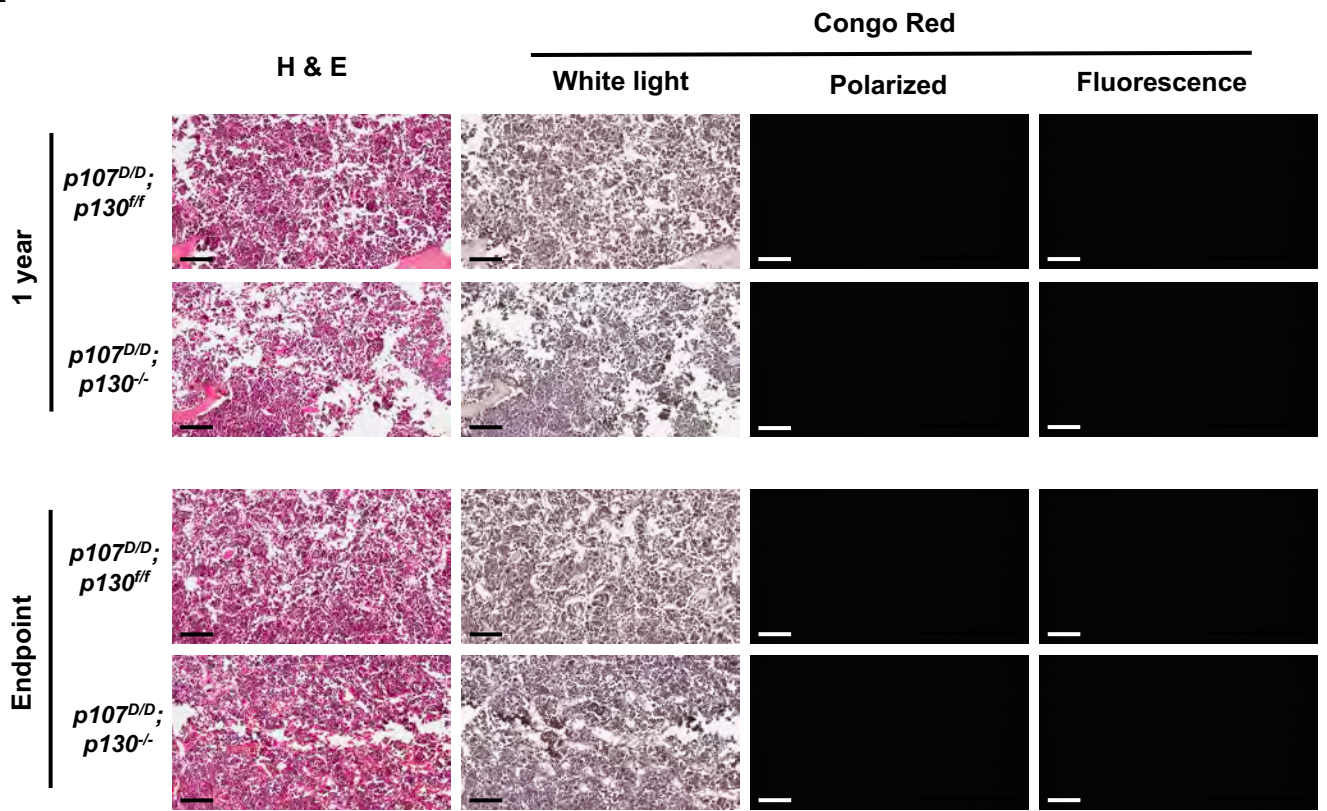
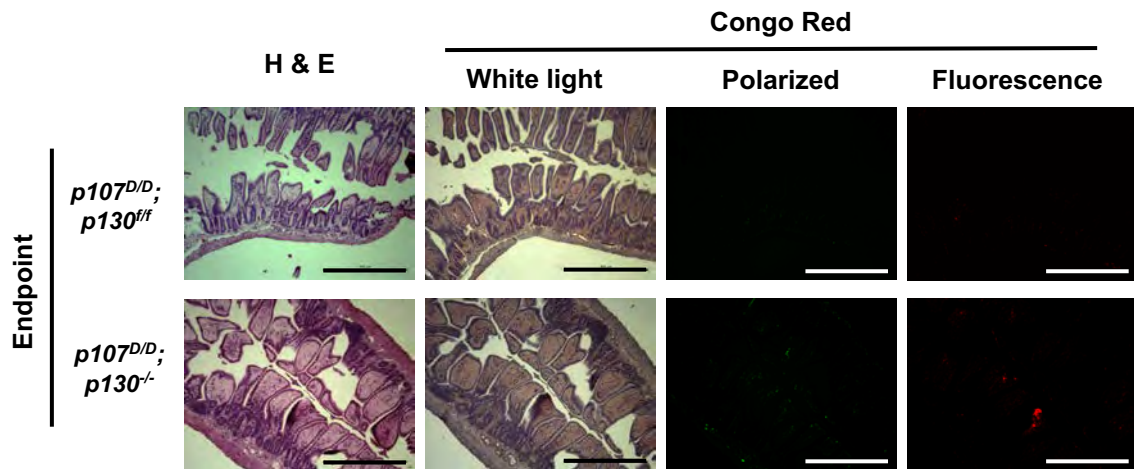
**A-C:** Gene expression in 3-month, 1-year, and 2-year old endpoint *p107<sup>D/D</sup>;p130<sup>fl/fl</sup>* and *p107<sup>D/D</sup>;p130<sup>-/-</sup>* livers was assayed by real time qPCR for *Apcs* (serum amyloid P-component) **(A)**, *ApoE* (apoE) **(B)**, and *Alb* (serum albumin) **(C)** (n=4). Expression values are normalized using *Gapdh* to that of *p107<sup>D/D</sup>;p130<sup>fl/fl</sup>* at each age for each gene. Two-way ANOVA was performed for each gene; ns=not significant.

**A****B**

**Supplementary Figure S8. *Ighm* is overexpressed in  $p107^{D/D};p130^{-/-}$  bone and spleen.**

**A-B:** Expression of *Ighm* in 1-year and 2-year old endpoint  $p107^{D/D};p130^{ff}$  and  $p107^{D/D};p130^{-/-}$  mice was assayed by real time qPCR in bone (**A**) and spleen (**B**) tissue (n=4). Expression values are normalized to *Gapdh* in  $p107^{D/D};p130^{ff}$  samples at each age for each gene. Two-way ANOVA was performed for each and significance levels are indicated (\*\*\*\* denotes  $P < 0.0001$ ; and ns denotes not significant,  $P > 0.05$ ).



**A****B**

**Supplementary Figure S9. Absence of myeloma like amyloid deposits in  $p107^{D/D};p130^{-/-}$  mice.**

**A:** Bone tissues were harvested from 1-year and 2-year old endpoint  $p107^{D/D};p130^{ff}$  and  $p107^{D/D};p130^{-/-}$  mice. Bones were formalin fixed, demineralized, and stained with H & E or Congo Red. Amyloid deposition was investigated by apple green birefringence and red fluorescence. Scale bars represent 100  $\mu\text{m}$ .

**B:** Intestines were harvested from endpoint mice, fixed, and stained with H&E or Congo Red and analyzed microscopically as before. Scale bars represent 500  $\mu\text{m}$ .

**Table 1: Primers used for PCR experiments in this study.**

<b>Primer</b>	<b>Sequence</b>
p130 ( <i>Rbl2</i> ) PCR forward	GTGTTGTAACATTCTCGTGGG
p130 ( <i>Rbl2</i> ) PCR reverse	GTGTTGTAACATTCTCGTGGG
<i>Apoa1</i> qPCR forward	GTGGCTCTGGTCTTCCTGAC
<i>Apoa1</i> qPCR reverse	ACGGTTGAACCCAGAGTGTC
<i>Apoa2</i> qPCR forward	GCCTGTTCACTCAGTACTTTCAG
<i>Apoa2</i> qPCR reverse	CAGACTAGTTCCTGCTGACC
<i>Apoa4</i> qPCR forward	ATGCCAAGGAGGCTGTAGAA
<i>Apoa4</i> qPCR reverse	CAGTTTCCTGGGCTAGATGC
<i>Alb</i> qPCR forward	CATGTTGCAAGGCTGCTGACAAG
<i>Alb</i> qPCR reverse	AGTGACAAGGTTTGGACCCTCAG
<i>Apcs</i> qPCR forward	TGGACCAAGCATGGACAAGCTAC
<i>Apcs</i> qPCR reverse	GGCTTCTGAAAGAAGGCTGGTG
<i>ApoE</i> qPCR forward	GGACTTGTTTCGGAAGGAGCTGAC
<i>ApoE</i> qPCR reverse	TTGCCACTCGAGCTGATCTGTCAC
<i>Ighm</i> qPCR forward	CACCCATCCACCTGGCTGCTCA
<i>Ighm</i> qPCR reverse	AATGGTGCTGGGCAGGAAGT
<i>Gapdh</i> qPCR forward	TGCACCACCAACTGCTTAG
<i>Gapdh</i> qPCR reverse	GGATGCAGGGATGATGTTC
<i>Ccna2</i> probe forward	TGTCGCCTTGAATGACGTCA
<i>Ccna2</i> probe reverse (biotinylated)	ACCCACCCTCCTGCAGATAT
<i>Actb</i> probe forward	AGAGCTACGAGCTGCCTGAC
<i>Actb</i> probe reverse (biotinylated)	AGCACTGTGTTGGCGTACAG
<i>Mybl2</i> -1kb body ChIP-qPCR forward	GCCTGAGCCTAAAGGGCATT
<i>Mybl2</i> -1kb body ChIP-qPCR reverse	TCTGATGGCAAGGGTTGTCTC
<i>Mybl2</i> TSS ChIP-qPCR forward	ACGCACTTGGCGGGAGATAG
<i>Mybl2</i> TSS ChIP-qPCR reverse	CTCAGGCGTCAGCGTGTCT
<i>Apoa1</i> -1kb ChIP-qPCR forward	CCAAGTGCAAAAACCTGGCCA
<i>Apoa1</i> -1kb ChIP-qPCR reverse	GTCTTCCCAGAGTGGTGAGG
<i>Apoa1</i> TSS ChIP-qPCR forward	GGCCAGGCTGAGCTTATCAG
<i>Apoa1</i> TSS ChIP-qPCR reverse	TCCGACAGTCTGGGTGTCCA
<i>Apoa1</i> gene body ChIP-qPCR forward	CAGAAGCTGCAGGAGCTGCAAG
<i>Apoa1</i> gene body ChIP-qPCR reverse	CTAGCTGTGTGCGCAGAGAGTCTA
<i>Apoa2</i> -1kb ChIP-qPCR forward	AGGAATTTCAATTCATGAGACCTATCA
<i>Apoa2</i> -1kb ChIP-qPCR reverse	CACACACACACACACACC
<i>Apoa2</i> TSS ChIP-qPCR forward	GCCATTCTCCGTATCACCTGACGG
<i>Apoa2</i> TSS ChIP-qPCR reverse	CTGCAGTCCTTCCCGTCTACTCT
<i>Apoa2</i> gene body ChIP-qPCR forward	GAGCTTTGGTTAAGAGACAGGCAGAC
<i>Apoa2</i> gene body ChIP-qPCR reverse	CAGAGACTTACTTGGCCTGGC
<i>Apoa4</i> -1kb ChIP-qPCR forward	AGCAAATCAGACTGGGCACA
<i>Apoa4</i> -1kb ChIP-qPCR reverse	GGGCATCCATCATACTGTCCC
<i>Apoa4</i> TSS ChIP-qPCR forward	GCTGTCAGCTTCCACGTTGTCTTAG
<i>Apoa4</i> TSS ChIP-qPCR reverse	TCCCCAGTGTGACTCCACGTTG

<i>Apoa4</i> gene body ChIP-qPCR forward	CGACGCACTGTGGAGCCCATG
<i>Apoa4</i> gene body ChIP-qPCR reverse	GCTCAAGTGGCTTTCCACCTCC
<i>Alb</i> -1kb ChIP-qPCR forward	TGAGGACACAAGATGAGGTCA
<i>Alb</i> -1kb ChIP-qPCR reverse	AGAGAGGAGGAGGAGGAAGAG
<i>Alb</i> TSS ChIP-qPCR forward	CTGAGCCAGACATTCCCAA
<i>Alb</i> TSS ChIP-qPCR reverse	ATTCCAGCAGGTCACCATGG
<i>Alb</i> gene body ChIP-qPCR forward	AGTGAGGTGGAGCATGACAC
<i>Alb</i> gene body ChIP-qPCR reverse	AAGACATCCTTGGCCTCAGC