| | Parameter | | | | | | | | | | | |
|-----------------------------|-----------|--------|--------|--------|---------|-------|------------|---------|------------|----------|--------|---------------|
| | ALP | ALT | AST | CPK | Albumin | BUN | Creatinine | Glucose | Phosphorus | Chloride | Sodium | Triglycerides |
| | (U/L) | (U/L) | (U/L) | (U/L) | (g/L) | (μM) | (μM) | (mM) | (mM) | (mM) | (mM) | (mM) |
| +/+ average | 86.5 | 21.5 | 56.5 | 145.38 | 3.14 | 17.88 | 0.138 | 252 | 7.0875 | 102.125 | 19.13 | 150.6 |
| -/- average | 92.5 | 25.1 | 66.9 | 207.25 | 3.04 | 18.25 | 0.125 | 245 | 7.0125 | 102.875 | 18.65 | 163.1 |
| Average pairwise change (%) | -6.9% | -16.9% | -18.4% | -42.6% | 3.2% | -2.1% | 9.1% | 2.9% | 1.1% | -0.7% | -0.25% | 13.35% |
| p-value | 0.560 | 0.107 | 0.442 | 0.512 | 0.200 | 0.825 | 0.351 | 0.723 | 0.825 | 0.265 | 0.351 | 0.082 |

Supplemental Table S1. Changes in clinical chemistry in adult *Anp32b*^{-/-} **mice.** Indicated parameters demonstrated statistically significant changes between adult paired +/+ and -/- mice (n=8). Statistical p-value determined by paired Student t-test. *ALP*, Alkaline Phosphatase; *ALT*, Alanine Aminotransferase; *AST*, Aspartate Aminotransferase; *CPK*, Creatine Phosphokinase; *BUN*, Blood Urea Nitrogen.

A/ Balb/c-congenic *Anp32b*^{-/-} acquisition against time

| <u> </u> | | | | |
|----------|-----|-------------------------------------|-----|-----------------------|
| | Anp | Proportion of Anp32b ^{-/-} | | |
| Litters | +/+ | +/- | -/- | Anp32b⁻ ^{/-} |
| 1 to 10 | 11 | 32 | 10 | 18.8% |
| 11 to 20 | 20 | 27 | 8 | 14.5% |
| 21 to 30 | 19 | 32 | 11 | 17.7% |
| 31 to 40 | 19 | 27 | 7 | 13.2% |
| 41 to 50 | 17 | 36 | 8 | 13.1% |
| 51 to 60 | 16 | 27 | 6 | 12.2% |

B/ Balb/c-congenic *Anp32b*^{-/-} acquisition against dam age

| | Anp3 | Proportion of Anp32b ^{-/-} | | |
|------------|------|-------------------------------------|-----|-----------------------|
| age of dam | | | | Anp32b ^{-/-} |
| (weeks) | +/+ | +/- | -/- | |
| <15 | 33 | 45 | 16 | 17.0% |
| 15-21 | 19 | 51 | 16 | 18.6% |
| 22-28 | 40 | 55 | 12 | 11.2% |
| 29+ | 10 | 30 | 6 | 13.0% |

Supplemental Table S2. Failed hypothesis tests for variable $Anp32b^{-/-}$ acquisition in the six-generation Balb/c congenic background.

| | Mouse 1 | Mouse 2 | Mouse 3 | Mouse 4 |
|-----------------------------|---------|---------|---------|---------|
| Retained non-linked somatic | 20 | 4 | 12 | 6 |
| SNPs | | | | |
| Total non-linked somatic | 1270 | 1270 | 1270 | 1270 |
| SNPs analysed | | | | |
| p (retained B6) | 0.0157 | 0.0032 | 0.0094 | 0.0047 |
| p (congenic Balbc) | 0.9843 | 0.9968 | 0.9906 | 0.9953 |

B/

| SNP | Chromosome | Retained on | Calculated |
|------------|------------|-------------|--|
| | | Mouse # | Probability |
| rs3707642 | 1 | 1 | $0.0157 \times 0.9968 \times 0.9906 \times 0.9953 =$ |
| | | | 0.0154 |
| rs3710548 | 3 | 2, 4 | $0.9843 \times 0.0032 \times 0.9906 \times 0.0047 =$ |
| | | | 1.46 x 10 ⁻⁵ |
| rs6190775 | 11 | 1,2,4 | $0.0157 \times 0.0032 \times 0.9906 \times 0.0047 =$ |
| | | | 2.32 x 10 ⁻⁷ ** |
| rs13482738 | 15 | 1,3 | $0.0157 \times 0.9968 \times 0.0094 \times 0.9953 =$ |
| | | | 1.48×10^{-4} |
| rs3686467 | 19 | 1,3 | $0.0157 \times 0.9968 \times 0.0094 \times 0.9953 =$ |
| | | | 1.48×10^{-4} |

Supplemental Table S3. Calculation of probability of retention of non-linked somatic SNPs. A. Calculation of C57BL/6J SNPs retention rates in mice of the sixgeneration Balb/c-congenic colony. B. Representative calculation of SNP retention probability from the five somatic chromosomes that were identified as carrying some C57BL/6J SNPs. X-chromosome had no C57BL/6 SNP retention but was excluded from analysis based on complex segregation. **, Very high statistical significance is determined using Bonferroni adjustment of p<0.001, i.e. 0.001/1270 = 7.87 x 10⁻⁷

| Chromosome 11 nucleotide location | Gene | Substitution | SNP Identifier | Present in Sanger Database | Present in Leo et al. colony | Location in Gene | Predicted effect |
|-----------------------------------|-------|--------------|-------------------|-------------------------------|------------------------------|------------------|-------------------------------|
| 5867697 | Aebp1 | C to T | N/A | No | Yes | Coding sequence | Missense mutation S394F |
| 7063524 | Adcy1 | G to C | rs212110788 | Yes | No | 5' UTR | unknown |

Supplemental Table S4. Deviations from reported Balb/c polymorphisms against reference C57BL/6 sequence in region surrounding rs6190775. N/A, not available; 5'UTR, 5' untranslated region