**Supplementary Figure**

(A–B) qPCR analysis of interferon-stimulated genes (*Ifi27l2a, Ifi44, Ifit1, Isg15, Rsad2, Siglec1*) in brains of *Rnaset2-/-* mice normalized to *Rnaset2+/+* and a reference gene at three (A), six, 17, and 28 weeks of age (B). The panel demonstrates a consistent and broad ISG upregulation, indicative of a robust interferon signature in *Rnaset2-/-* brains (A-B). Data are shown as scatter dot plots with mean ± SEM. One-way ANOVA with Tukey’s multiple comparison test; ✱ = p < 0.05, ✱✱ = p < 0.01, ✱✱✱ = p < 0.001, ✱✱✱✱ = p < 0.0001, ns = not significant. *n=*2 per groupfor three weeks; *n=4* per group for six, 17 and 28 weeks (except for *Siglec1* at 17 weeks, *n=3*). *Ifi27l2a*: *interferon alpha-inducible protein 27-like 2A (human ortholog: IFI27)*; *Ifi44: interferon-induced protein 44*; *Ifit1:**interferon-induced protein with tetratricopeptide repeats 1*; *Isg15:* *interferon-stimulated gene 15*; *Rsad2: radical S-adenosyl methionine domain containing 2*; *Siglec1*: *sialic acid binding Ig-like lectin 1.*

(C–F) Western blot analysis of apoptotic markers at three weeks. BAX protein expression was comparable between genotypes, with one *Rnaset2-/-*animal showing a minor increase (C). Cleaved CASPASE 3 (cl. CASP3) was undetectable in both genotypes. Caspase 3 control cell extracts (#9663, Cell Signaling Technology) were included as a positive control (D). No differences were observed in full-length PARP (E) or cleaved PARP (F). β-ACTIN or GAPDH served as loading controls. WT1-2: *Rnaset2+/+*, KO1-2: *Rnaset2-/-*.BAX*:* Bcl-2-associated X protein; cl. CASP3: cleaved caspase-3; PARP: poly(ADP-ribose) polymerase 1; cl. PARP: cleaved poly(ADP-ribose) polymerase 1.