

Expanded View Figures

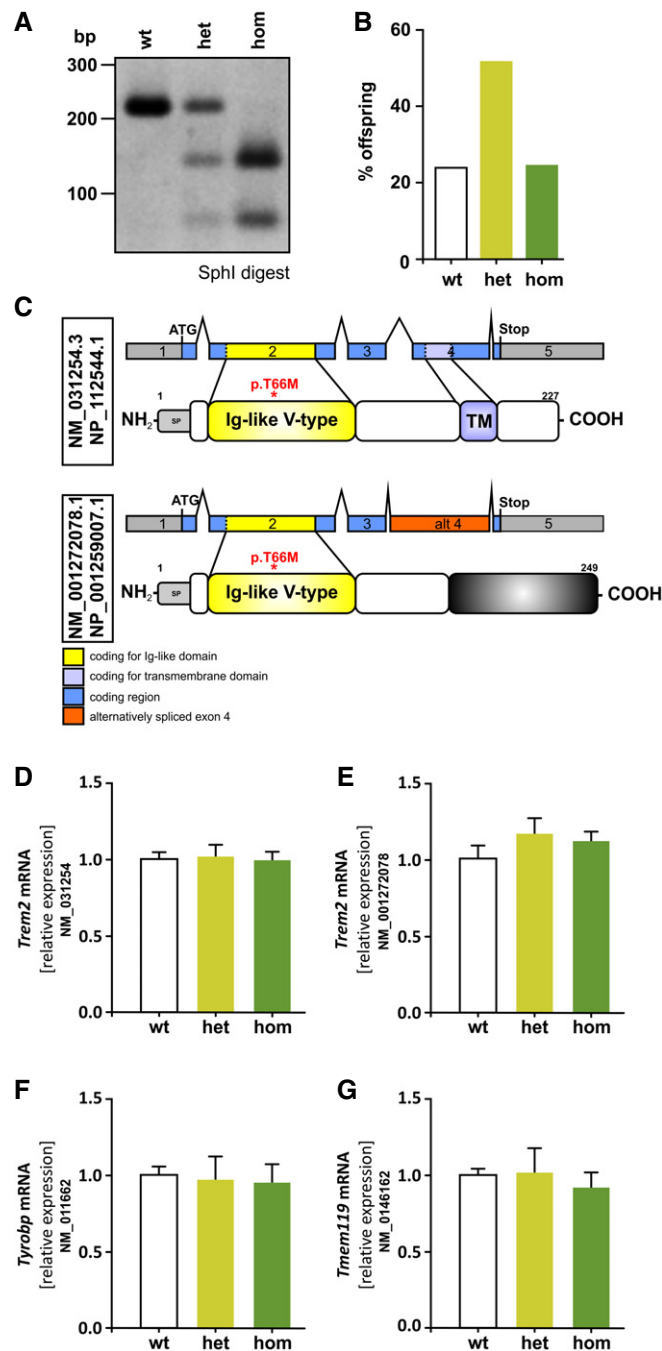


Figure EV1. Characterization of Trem2 p.T66M knock-in mice.

- A Representative of genotyping results using SphI restriction enzyme digest resulting in bands at 215 bp (lane 1: wild-type; wt), 215 bp + 141 bp + 74 bp (lane 2: heterozygous; het), or 141 bp + 74 bp (lane 3: homozygous; hom).
- B Mendelian pattern of inheritance in Trem2 knock-in mice ($n_{wt} = 38$, $n_{het} = 82$, $n_{hom} = 39$).
- C Schematic overview of murine Trem2 transcripts and the respective proteins. Alternative splicing results in a transcript variant encoding soluble Trem2 (NM_001272078.1) lacking its transmembrane domain (NP_001259007.1).
- D–G qRT–PCR analysis of the canonical (D) and alternative (E) Trem2 transcripts as well as the signaling adaptor Tyrobp (F) and a microglia marker Tmem119 (G) shows no significant changes due to introduction of the Trem2 p.T66M mutation in total brain of 6-month-old mice. Data are represented as mean \pm SEM. $n = 4$ mice/genotype.

Source data are available online for this figure.

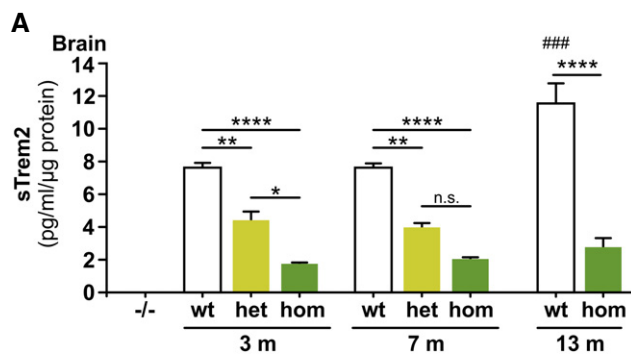


Figure EV2. sTrem2 brain and serum analysis in different age groups of Trem2 p.T66M knock-in mice.

A Brain samples used in Fig 1E split up in three different age groups according to mean age of the group. Data are represented as mean \pm SEM ($n = 4$ /genotype and group). One-way ANOVA, Tukey's *post hoc* test; $*P < 0.05$; $**P < 0.01$; $****P < 0.0001$; $###P < 0.001$; # denotes significant differences between age groups within the wt group.

B Serum samples used in Fig 1F split up in three different age groups according to mean age of the group. Data are represented as mean \pm SEM (3 m: $n_{wt} = 20$, $n_{het} = 8$, $n_{hom} = 16$; 6.5 m: $n_{wt} = 12$, $n_{het} = 13$, $n_{hom} = 15$; 13 m: $n_{wt} = 4$, $n_{hom} = 4$). One-way ANOVA, Tukey's *post hoc* test; $**P < 0.01$; $***P < 0.001$; $****P < 0.0001$.

Source data are available online for this figure.

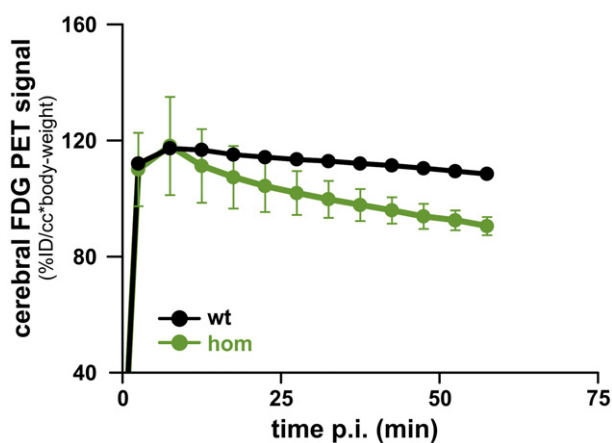
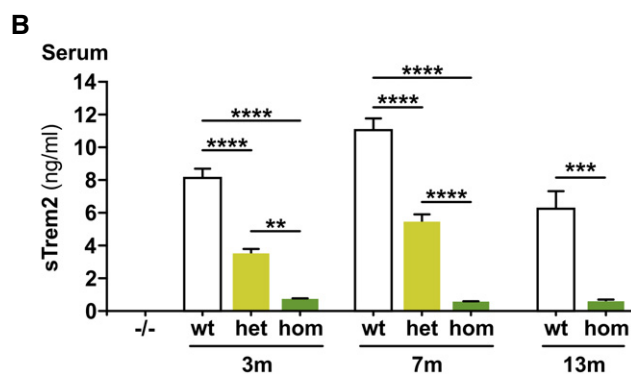


Figure EV3. Dynamic FDG μ PET imaging.

Dynamic FDG μ PET imaging of two homozygous Trem2 p.T66M knock-in mice and one wild-type control revealed no relevant differences in the perfusion phase of μ PET while in the late phase reduced FDG μ PET signal was detected in homozygous (hom) Trem2 p.T66M knock-in mice. Data are represented as mean \pm SEM.

Source data are available online for this figure.