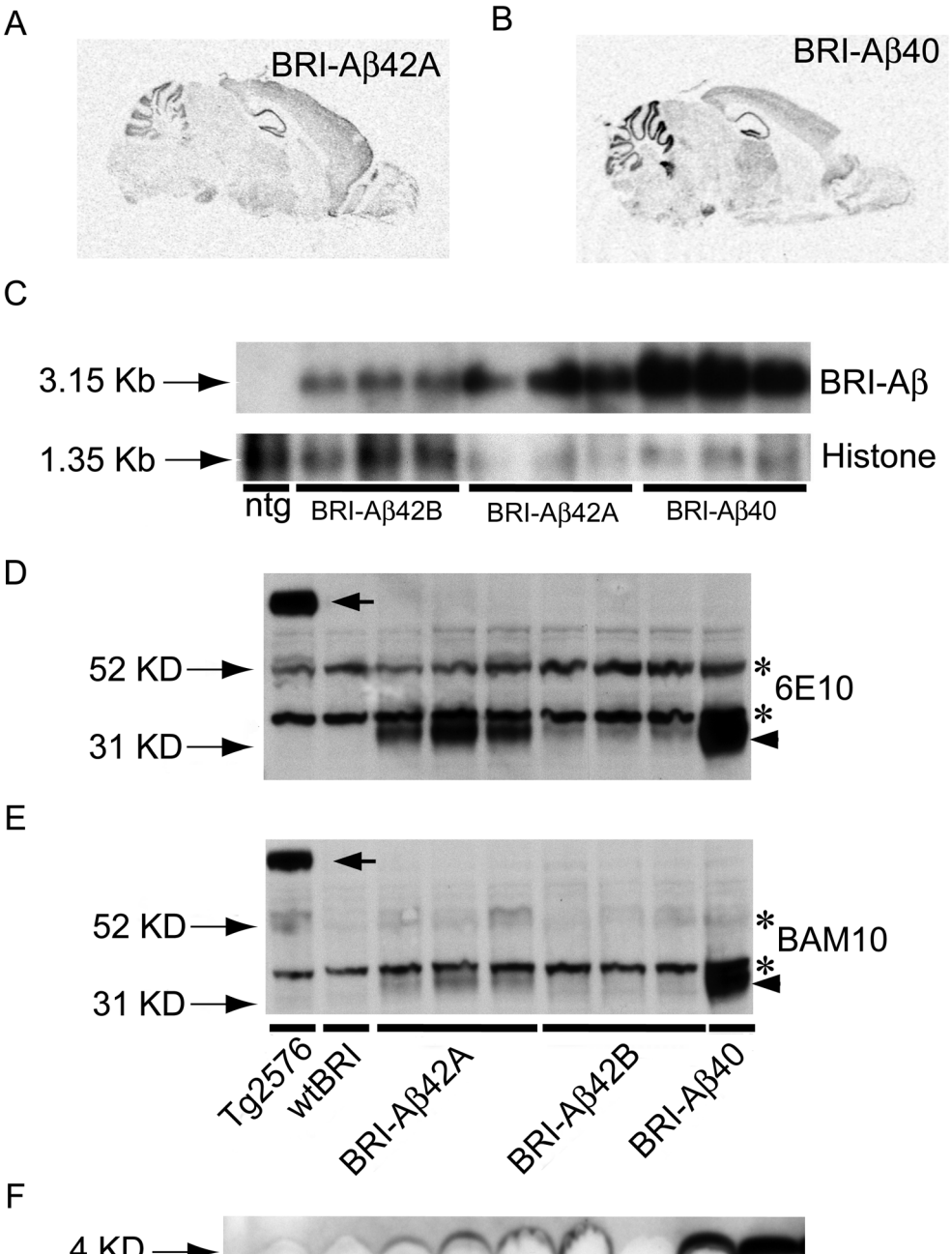
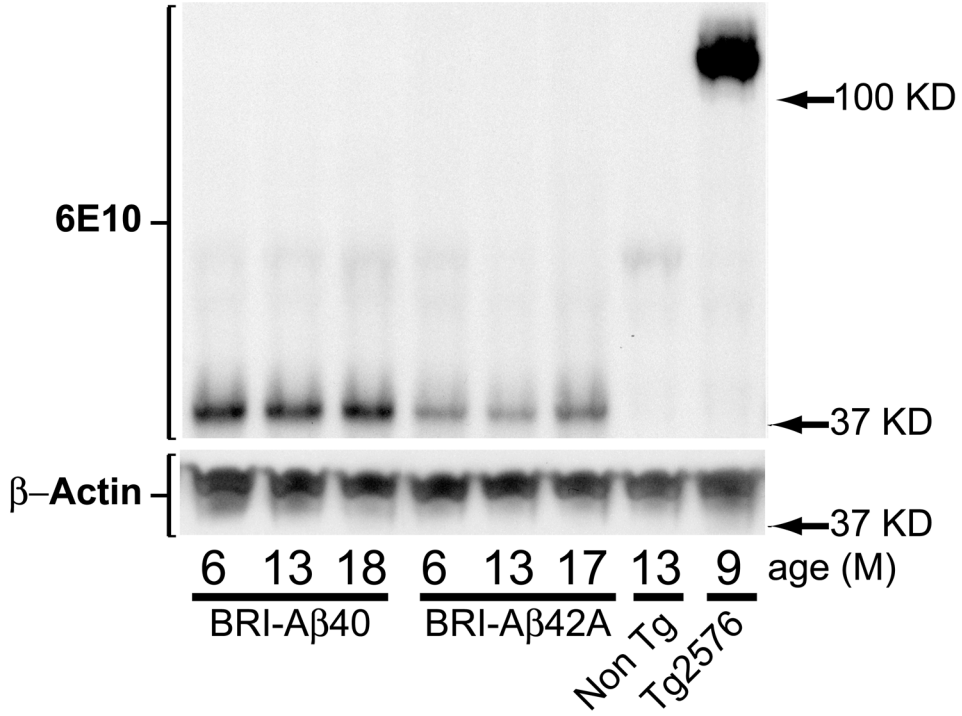
Supplemental Figure 1. Transgene expression and protein levels in BRI-Aβ mice.

Expression patterns were identical in BRI-Aβ42 (A) and BRI-Aβ40 (B) transgenic mice as assessed by *in situ* hybridization. BRI-Aβ mRNA was expressed in a pattern characteristic of the MoPrP promoter, with highest expression in the granular cell layers of the cerebellum and the hippocampus. (C) Northern blots of total RNA indicated that the fusion transgene transcript was expressed at levels approximating endogenous mouse APP mRNA expression (BRI-Aβ42A) or at approximately half the level of endogenous mouse APP expression (BRI-Aβ42B). The BRI-Aβ40 line expressed the transgene at greater levels than the BRI-Aβ42 mice. Northern blots were stripped and reprobed with histone cDNA to assess loading. Human APP protein was detected in Tg2576 (arrow) when Western blots were probed with either (D) 6E10 (anti-Aβ 1-16) or (E) Bam-10 (anti-Aβ1-10), a smaller full-length fusion BRI-Aβ protein (~ 37kDa) was detected in the BRI-Aβ lines (arrow head). Protein levels were highest in BRI-Aβ40 > BRI-Aβ42A > BRI-Aβ42B. Two non-specific bands (*), which were detected by secondary antibody alone, were present at 52kDa and 40kDa. Processed 4kDa Aβ species were detected by immunoprecipitation (IP) western in the BRI-Aβ mice (F). 3160 (anti-Aβ polyclonal antibody) was used to IP the Aβ peptide and 6E10 (anti-Aβ1-16) was used for detection. Tg2576 and Aβ peptide (45fg) samples were used as positive controls and non transgenic extracts as a negative control. Mass spectroscopy was used to definitively identify the 4kDa Aβ isoforms in the BRI-Aβ mice (see Fig.1).


A
BRI-Aβ42A
B
BRI-Aβ40
C
3.15 Kb
BRI-Aβ
1.35 Kb
Histone
ntg
BRI-Aβ42B
BRI-Aβ42A
BRI-Aβ40
D
52 KD
31 KD
6E10
E
52 KD
31 KD
BAM10
Tg2576
wtBRI
BRI-Aβ42A
BRI-Aβ42B
BRI-Aβ40
F
4 KD
Age (M) 6 13 18 6 13 17 13 9
BRI-Aβ40
BRI-Aβ42A
ntg
Tg2576
Aβ peptide

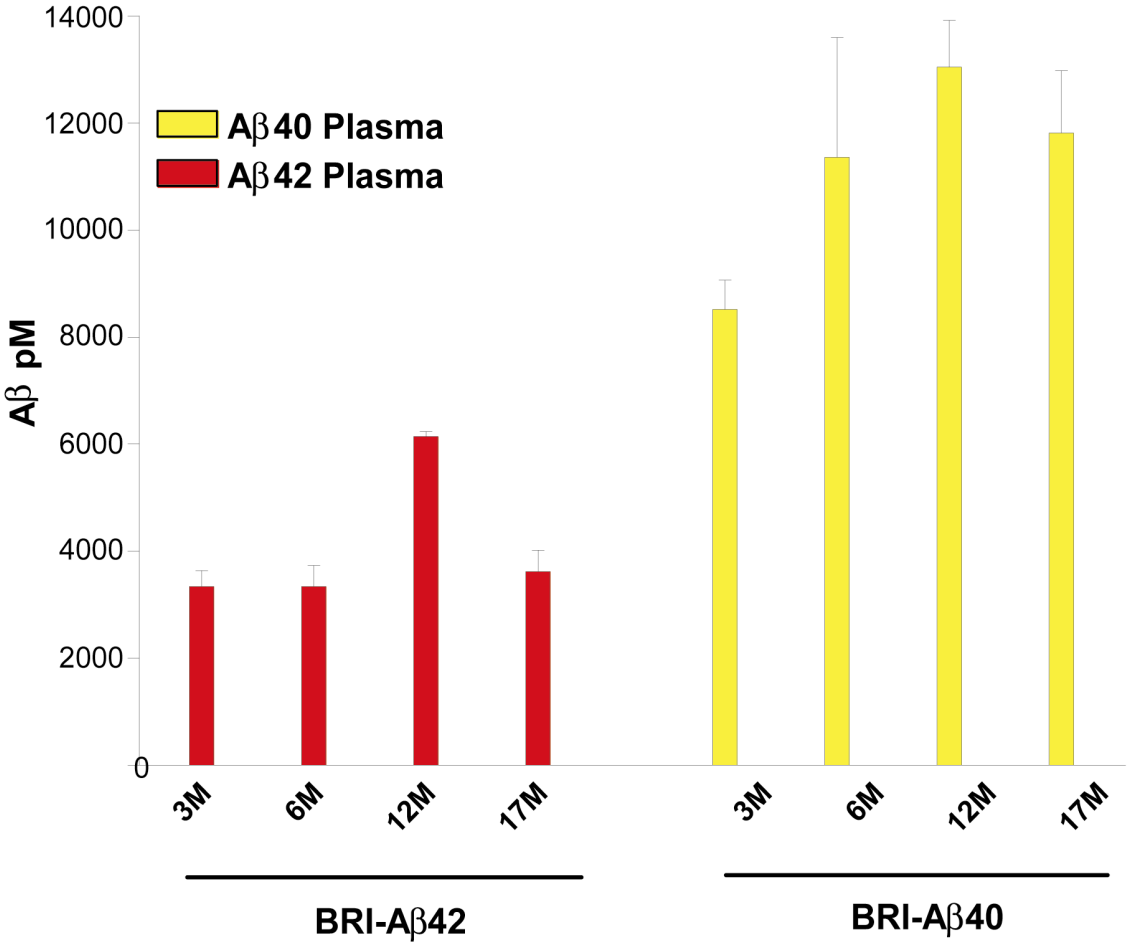
Supplemental Figure 2. Full-length BRI-Aβ protein levels are unaltered by age.

Neither age nor amyloid deposition (in BRI-Aβ42 mice) altered full-length BRI-Aβ transgenic protein levels (37kDa) in the brains of both BRI-Aβ40 and BRI-Aβ42 mice. Blots were probed with 6E10, anti-total Aβ, then stripped and reprobed with anti-β actin to assess loading. Tg2576 and non- transgenic protein extracts were run as positive and negative controls respectively.



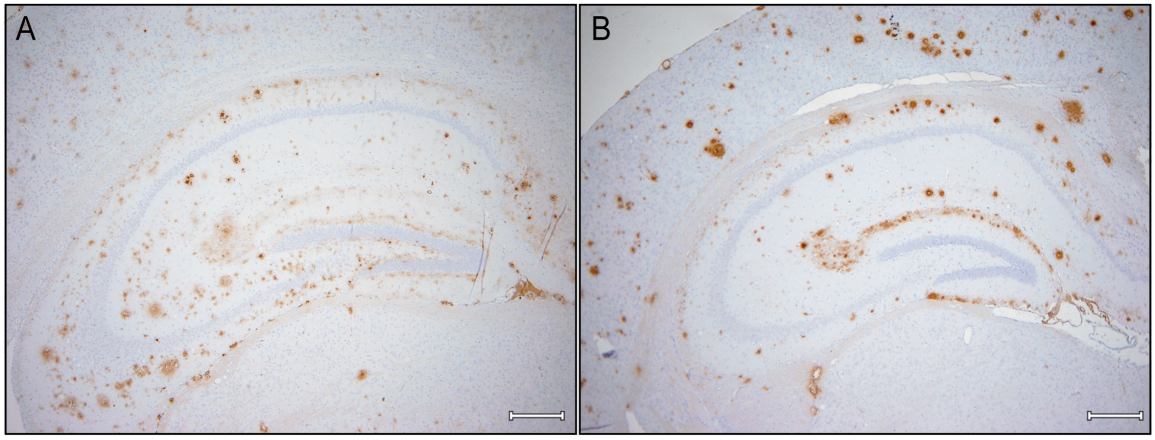
Supplemental Figure 3. Plasma Aβ40 and Aβ42 levels in BRI-Aβ mice.

Both Aβ40 and Aβ42 was readily detected from 3 months onwards in plasma from BRI-Aβ40 and BRI-Aβ42 mice respectively. No Aβ42 was detected in BRI-Aβ40 mice and similarly no Aβ40 was present in plasma from BRI-Aβ42 mice.



Supplemental Figure 4. Similar forebrain Aβ pathology in BRI-Aβ42 and Tg2576 mice

Hippocampal sections from 17 month old BRI-Aβ42 mice (A) and Tg2576 mice expressing mutant APP_{swe} (B) immunostained with an antibody raised against total Aβ. Both the BRI-Aβ42 and Tg2576 mice have extensive amyloid deposition within the hippocampal formation, however, the Aβ plaques tended to be smaller and more numerous in the BRI-Aβ42 mice. Additionally, the BRI-Aβ42 mice had more diffuse Aβ immunoreactivity compared with Tg2576. Scale bar = 300μm.



Supplemental Figure 5. RIPA and plasma Aβ levels in BRI-Aβ42 x Tg2576 transgenic mice.

At 6 months of age, an age prior to forebrain deposition in either Tg2576 or BRI-Aβ42A mice, the levels of RIPA extractable Aβ40 and Aβ42 (A) and plasma Aβ40 and Aβ42 levels (B) in the bigenic BRI-Aβ42/Tg2576 mice were consistent with an additive sum of Aβ levels of their singly transgenic littermates. Both sets of data suggest that there was no increased Aβ or APP production in the bigenic BRI-Aβ42/Tg2576 mice.