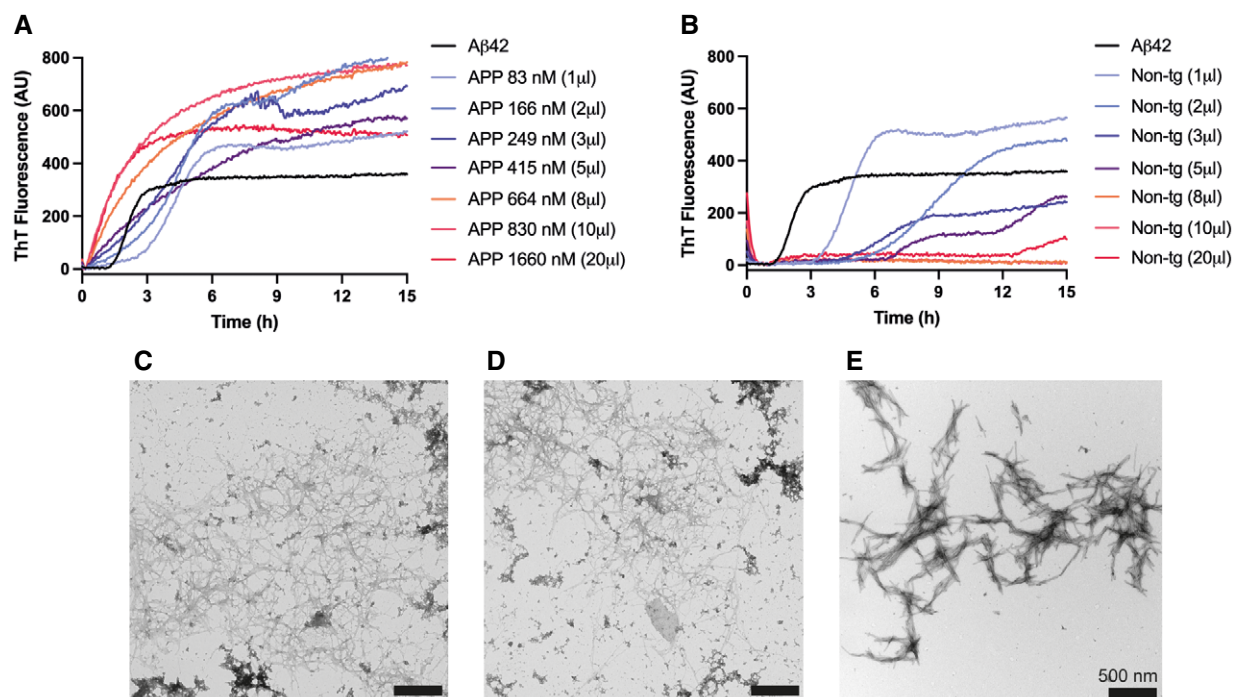


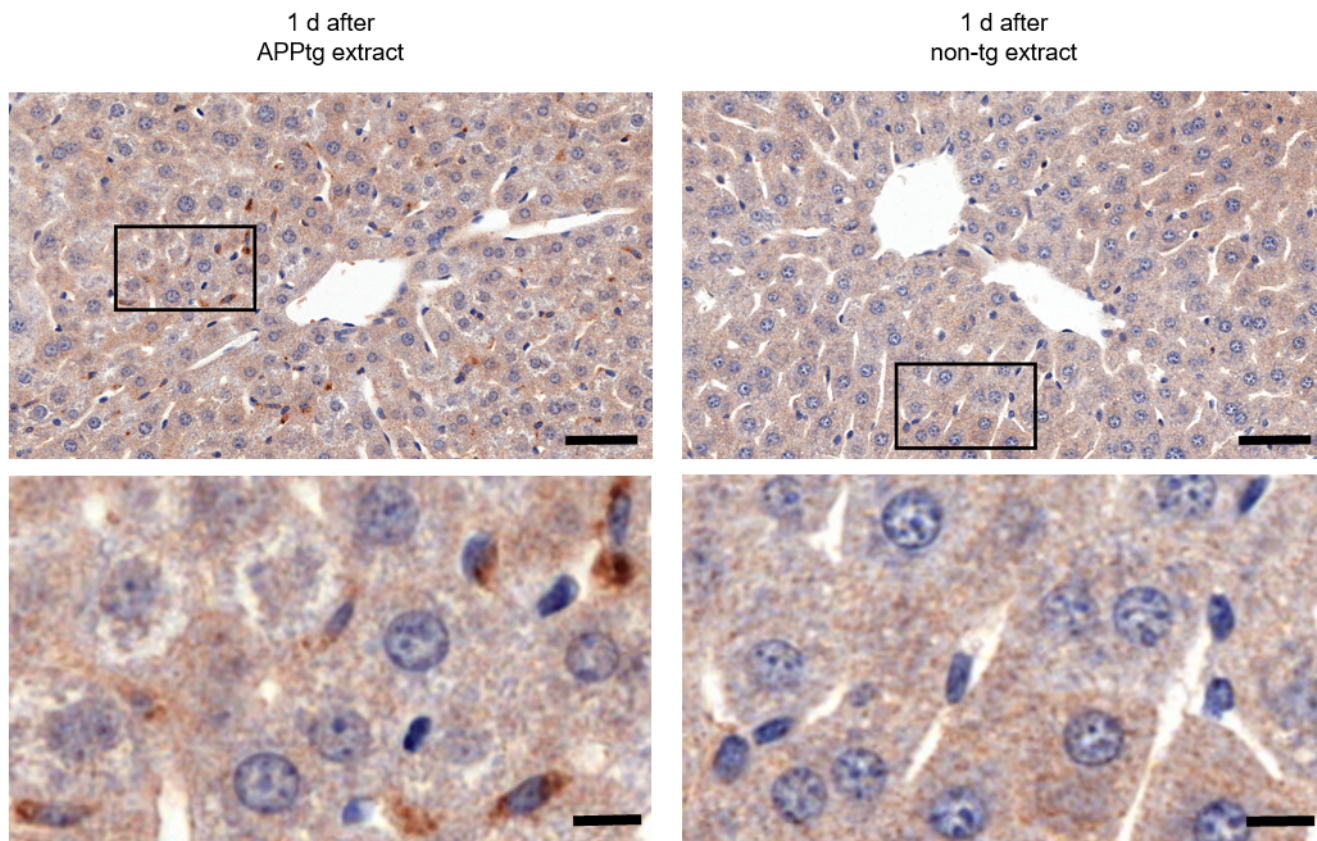
## Expanded View Figures



**Figure EV1. Seeding activity of A $\beta$ 42 fibrils extracted from APptg brain extract.**

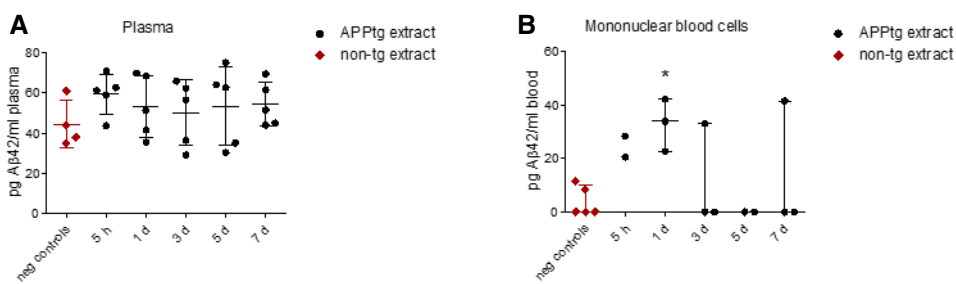
- A ThT fluorescence aggregation kinetics of recombinant A $\beta$ 42 in the presence of extracted fibrils from APptg brain extract at different concentrations from 83 to 1,660 nM, exhibiting a concentration-dependent seeding effect.
- B ThT fluorescence aggregation kinetics in the presence of equal amounts of extract from non-tg brain extract, revealing no seeding activity but a delaying effect on the aggregation kinetics.
- C, D TEM images showing seeded A $\beta$ 42 fibrils at the aggregation kinetic end points using 166 nM seeds (C), and 1,660 nM seeds (D). The fibril morphology is heterogenous.
- E *In vitro* A $\beta$ 42 fibrils aggregated without the presence of seeds. The fibril morphology is more homogenous compared to the seeded A $\beta$ 42 fibrils with brain extract.

Data information: In (A) and (B), the same curve is shown for A $\beta$ 42 aggregated without fibril extract. In (C–E), scale bars correspond to 500 nm. Source data are available online for this figure.



**Figure EV2. Immunopositivity for Aβ in liver cells (macrophages) after intraperitoneal Aβ injection.**

Representative images of liver sections (anti-Aβ staining, clone 4G8) at 1 day after intraperitoneal <sup>13</sup>C-Lys APPtg or non-tg brain extract injection, bottom row insets of delineated areas. Aβ-positivity is detectable in mice injected with APPtg brain extract but not in mice injected with non-tg brain extract. Scale bars correspond to 50 μm (top row) and 10 μm (bottom row), respectively.

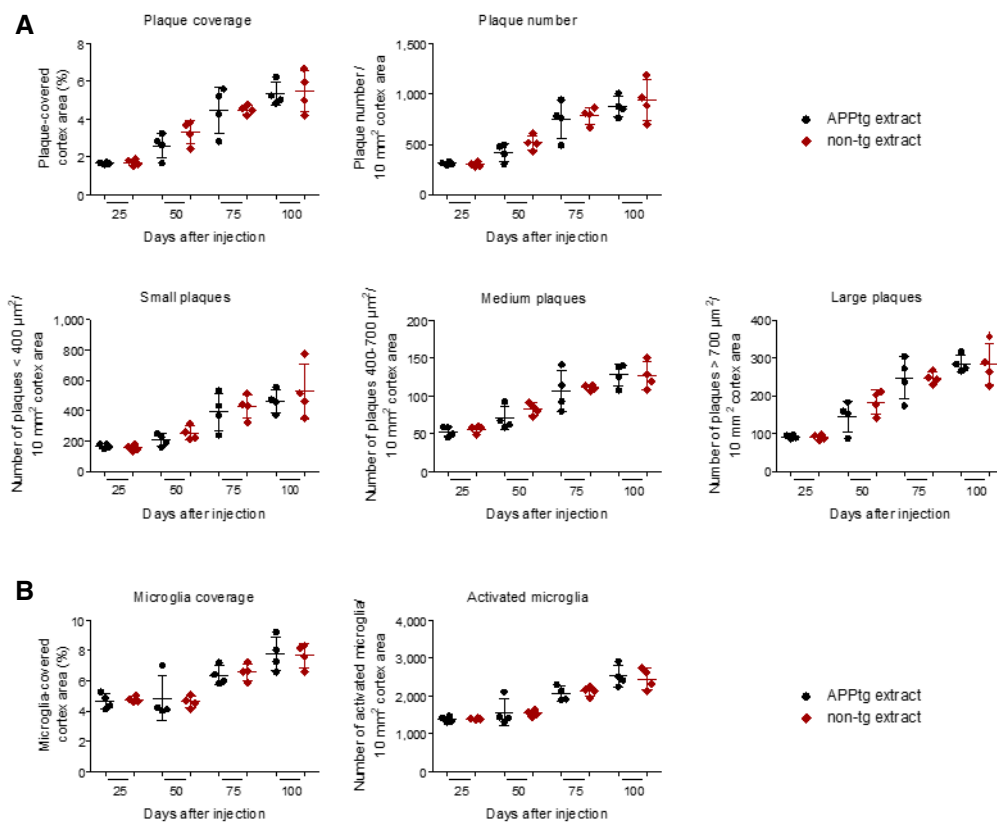


**Figure EV3. Intraperitoneally injected Aβ is not detectable in plasma but in mononuclear blood cells shortly after injection.**

A Temporal and comparative 4G8 immunoassay quantification of Aβ42 in blood plasma after unlabeled APPtg or non-tg brain extract injection (for APPtg extract, *n* = 5 mice per time point after injection; for non-tg extract, mice (*n* = 1 at time points 5 h and 3 days, *n* = 2 at 1 day) were pooled and referred to as negative controls). Data are shown as mean ± SD.

B Temporal and comparative 4G8 immunoassay quantification of Aβ42 in mononuclear blood cells after unlabeled APPtg or non-tg brain extract injection (for APPtg extract, *n* = 2 mice at time points 5 h and 5 days, and *n* = 3 mice at time points 1, 3, and 7 days; for non-tg extract, mice (*n* = 1 per time point) were pooled and referred to as negative controls). Mann-Whitney *U*-test \* *P* = 0.0325, APPtg extract-injected vs. negative controls. Normalization to blood volume. Error bars show median ± interquartile range.

Source data are available online for this figure.

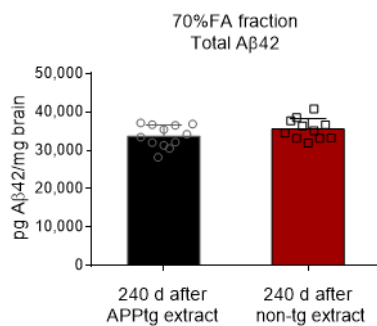


**Figure EV4. Peripheral injection of APPTg brain extract has no influence on the accumulation of A $\beta$  plaques or microglial activation.**

A Analysis of cortical A $\beta$  plaque load, plaque number, and plaque size distribution in anti-A $\beta$  (clone 4G8)-stained brain sections from mice injected with <sup>13</sup>C-Lys APPTg or <sup>13</sup>C-Lys non-tg extract ( $n = 4$  mice per time point and group). Data are presented as mean  $\pm$  SD.

B Analysis of cortical coverage and number of activated microglia in anti-IBA1-stained brain sections from mice injected with <sup>13</sup>C-Lys APPTg or <sup>13</sup>C-Lys non-tg extract ( $n = 4$  mice per time point and group). Error bars are shown as mean  $\pm$  SD.

Source data are available online for this figure.



**Figure EV5. Intraperitoneal injection of APPTg brain extract does not induce exacerbation of  $\beta$ -amyloidosis 240 days after injection.**

Comparative 4G8 immunoassay quantification of A $\beta$ 42 in the insoluble brain fraction after unlabeled APPTg or non-tg brain extract injection ( $n = 12$  mice in the APPTg extract group,  $n = 11$  mice in the non-tg extract group). Normalization to brain weight. Data are presented as mean  $\pm$  SD.

Source data are available online for this figure.