

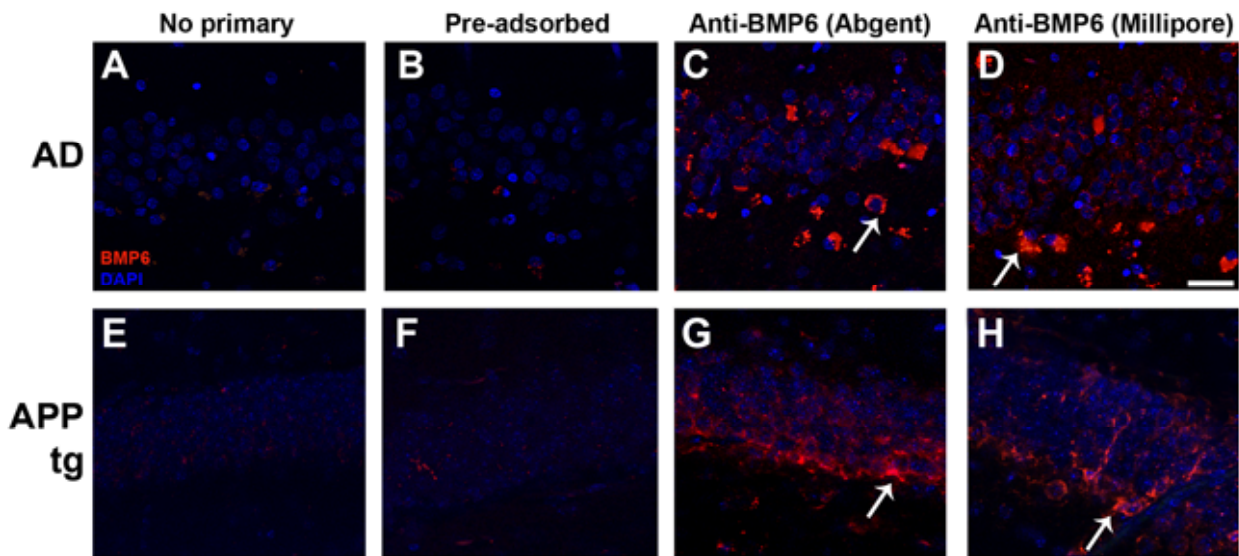
Supplemental Fig. 1. Validation studies to examine the specificity of the BMP6 antibodies for immunohistochemistry. Panels A-D depict immunolabeling of hippocampal sections from a representative AD case, and panels E-H show immunolabeling of sections from the brain of a representative APP tg mouse. Sections were incubated with no primary antibody (A, E), or with polyclonal antibody pre-incubated with a specific blocking peptide (B, F), or with polyclonal (Abgent, C, G) or monoclonal (Millipore, D, H) antibodies against BMP6. All images are from the dentate gyrus, and sections were co-stained with DAPI (blue) to label cell nuclei. Scale bar = 30 μ m for all images. (A, B) Immunolabeling of AD hippocampal sections with no primary antibody (A), or with primary polyclonal BMP6 antibody pre-adsorbed with blocking peptide (B) showed only background immunoreactive signal. (C, D) Immunolabeling of AD hippocampal sections with polyclonal (C) or monoclonal (D) BMP6 antibodies showed similar patterns of BMP6 immunoreactivity (arrows) in the dentate gyrus. (E, F) Immunolabeling of APP tg mouse brain sections with no primary antibody (E), or with primary polyclonal BMP6 antibody pre-adsorbed with blocking peptide (F) showed only background immunoreactive signal. (G, H) Immunolabeling of APP tg mouse brain sections with polyclonal (G) or monoclonal (H) BMP6 antibodies showed similar patterns of BMP6 immunoreactivity (arrows) in the dentate gyrus.

Supplemental Fig. 2. Immunohistochemical analysis of BMP6 levels in the cortex of AD brains and APP tg mice. Panels A and B show representative sections from the brains of human non-demented (ND) control and AD cases, and panels D and E show representative sections from the brains of non-tg and APP tg mice. Sections were immunolabeled with a monoclonal antibody against BMP6 (Millipore) detected with Tyramide Red. All images are from layer V of the

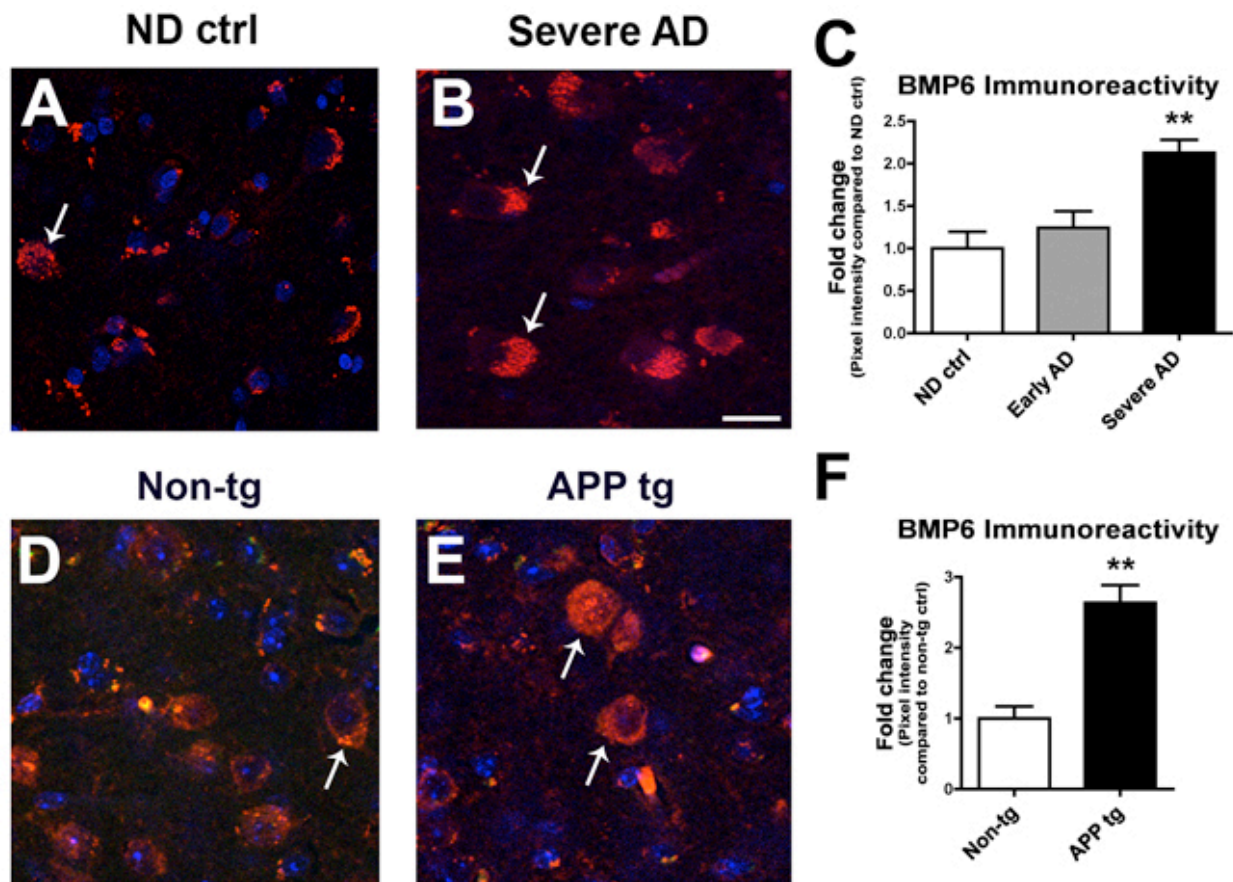
cortex, and sections were co-stained with DAPI (blue) to label cell nuclei. Scale bar = 10 μ m for all images. (A-C) BMP6 immunoreactivity (arrows, A, B) was increased in the cortex of AD cases compared to non-demented controls (N=5 non-demented control cases, N=7 early AD and N=7 severe AD cases analyzed, $**p < 0.01$ compared to non-demented controls by one-way ANOVA with post-hoc Dunnett's test). (D-F) BMP6 immunoreactivity (arrows, D, E) was increased in the cortex of APP tg mice compared to non-tg controls (N=4 animals per group, $**p < 0.01$ compared to non-tg controls by unpaired two-tailed Student's t-test).

Supplemental Fig. 3. Double-immunohistochemical analysis of BMP6 immunoreactivity and a marker of neurogenesis in the hippocampus of human AD cases and APP tg mice. Panels A-C show a representative section from the brain of a human AD case, and panels D-F show a representative section from the brain of an APP tg mouse. Sections were immunolabeled with a monoclonal antibody against BMP6 (Millipore) detected with Tyramide Red and co-labeled with a polyclonal antibody against DCX (SantaCruz) detected with a FITC-tagged secondary antibody. All images are from the hippocampal dentate gyrus, and sections were co-stained with DAPI (blue) to label cell nuclei. Scale bar = 30 μ m for all images. (A-C) In the hippocampus of an AD patient, BMP6 immunoreactivity (arrows) was detected within and surrounding cells that were DCX-positive (arrows). (D-F) In the hippocampus of an APP tg mouse, BMP6 immunoreactivity (arrows) was detected within and surrounding cells that were DCX-positive (arrows).

Supplemental Figure 1.



Supplemental Figure 2.



Supplemental Figure 3.

