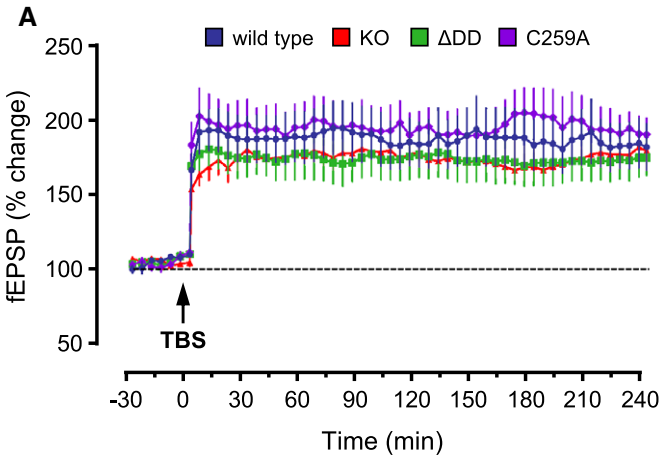
Expanded View Figures



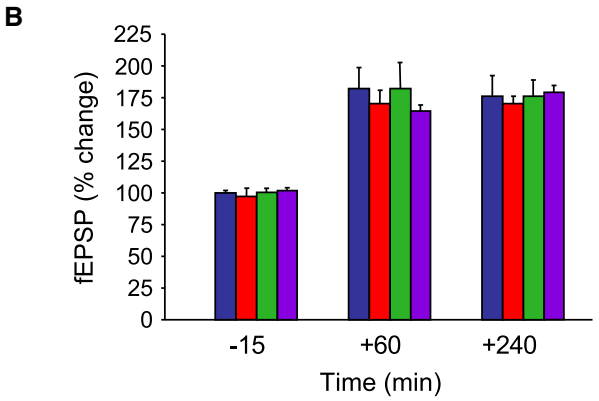


Figure EV1. Normal TBS-LTP in p75^{NTR} mutant mice.

A Percentage of change in field excitatory post-synaptic potential (fEPSP) recorded after theta-burst stimulation (TBS) in Schaffer collaterals of hippocampal slices from WT and p75NTR mutant mice.

B Quantification of fEPSP (% change) in different genotypes at 3 time points. There was no significant difference between them (n = 7 slices from N = 3 mice per condition). Data are shown as average ± SEM.

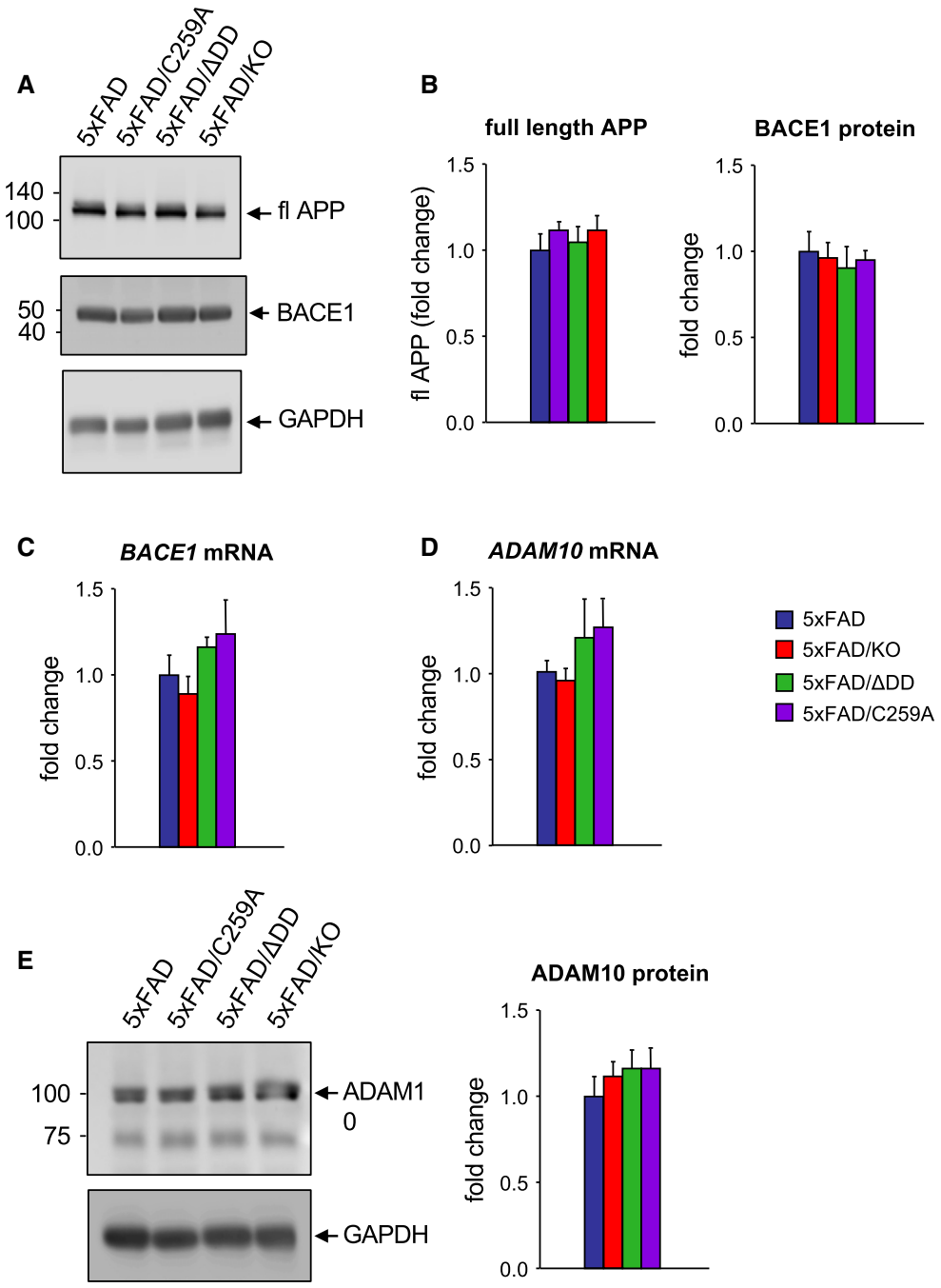


Figure EV2. Unaltered expression of full-length APP, ADAM10, and BACE1 in hippocampus of 9-month-old 5xFAD mouse strains.

A Western blot analysis of full-length APP (fl APP) and BACE1 expression (after reprobing of the same membrane) in hippocampal lysates of 5xFAD mice carrying different p75NTR alleles. Lower panel shows reprobing for GAPDH as control.

B Quantification showing mean ± SEM normalized to GAPDH expressed relative to 5xFAD levels. $N = 6$ mice per group.

C Expression of BACE mRNA in hippocampus of 5xFAD mice carrying different p75NTR alleles. $N = 6$.

D Expression of ADAM10 mRNA in hippocampus of 5xFAD mice carrying different p75NTR alleles assessed by qPCR, normalized to Gapdh mRNA, and expressed as fold change over 5xFAD. $N = 6$.

E Western blot analysis of ADAM10 expression in hippocampal lysates. ADAM10 precursor runs at ≈100kDa, processed ADAM10 at ≈75kDa. The lower panel shows reprobing for GAPDH. Quantification shown to the right normalized to GAPDH. $N = 6$ mice per group.

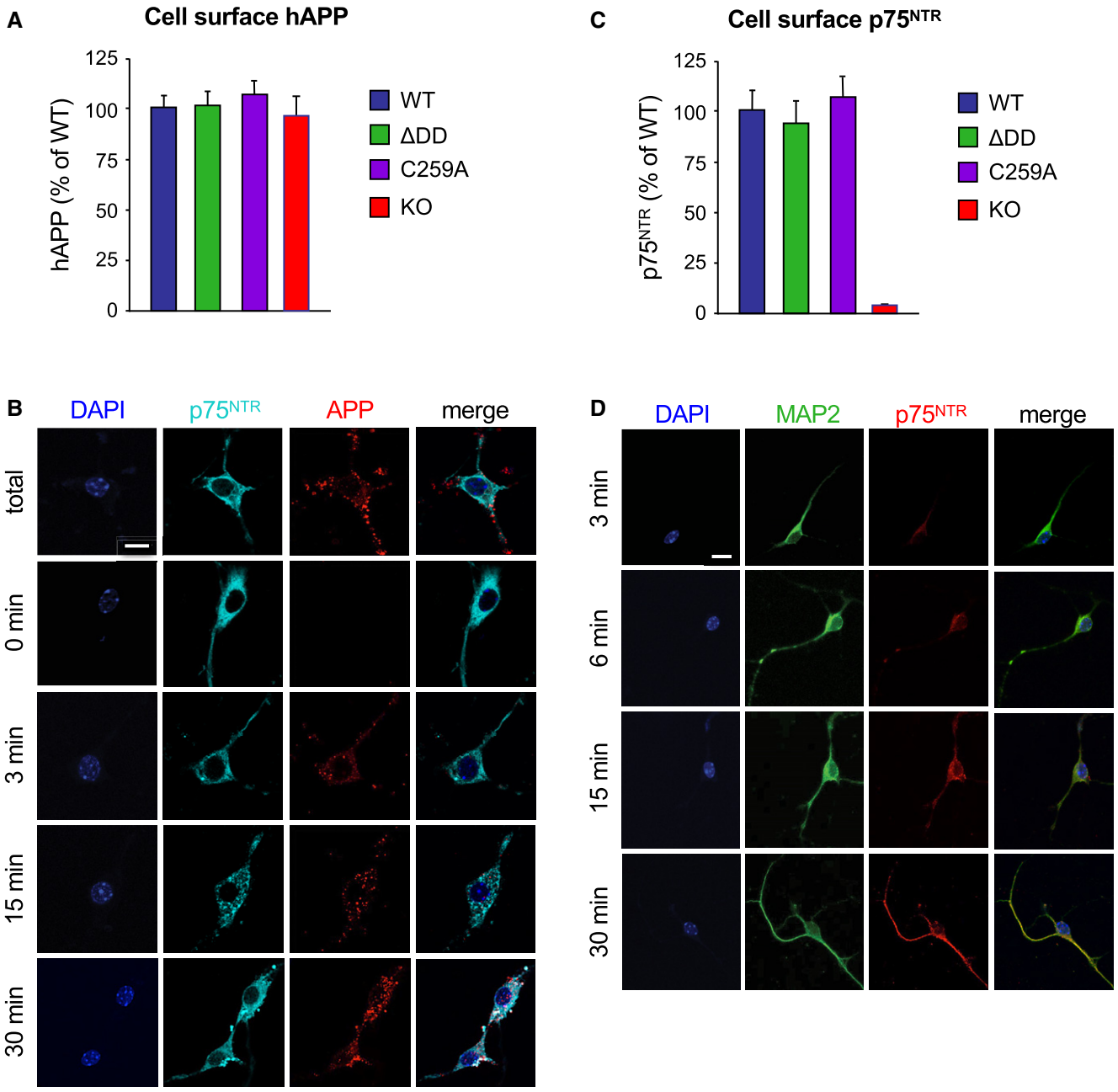


Figure EV3. Internalization of 5xFAD hAPP and p75NTR in wild-type mouse hippocampal neurons.

A Quantification of cell surface hAPP in wild type and p75NTR mutant neurons after 6E10 antibody feeding on ice followed by fixation. Values were normalized to levels in wild-type neurons and are expressed as percentage ± SEM. $N = 3$ independent experiments.

B Internalization of 5xFAD hAPP in wild-type mouse hippocampal neurons. Live neuron cultures were fed with anti-human APP antibodies (6E10) on ice, washed, and then placed at 37°C for different periods of time to allow internalization. The reaction was stopped by a quick acid wash followed by fixation. Total staining (100%) was determined by direct fixation after antibody feeding. Baseline ($t = 0$ min) was obtained by acid wash directly after antibody feeding. Counterstaining for p75NTR (antibody GT15057, see Table S1) and DAPI is also shown. Scale bar, 10 μm.

C Quantification of cell surface p75NTR in wild type and mutant neurons after antibody feeding on ice followed by fixation. Values were normalized to levels in wild-type neurons and are expressed as percentage ± SEM. $N = 3$ independent experiments.

D Internalization of p75NTR in wild-type mouse hippocampal neurons. Live neuron cultures were fed with anti-mouse p75NTR antibodies on ice, washed, and then placed at 37°C for different periods of time to allow internalization. Counterstaining for MAP2 and DAPI is also shown. Scale bar, 10 μm.

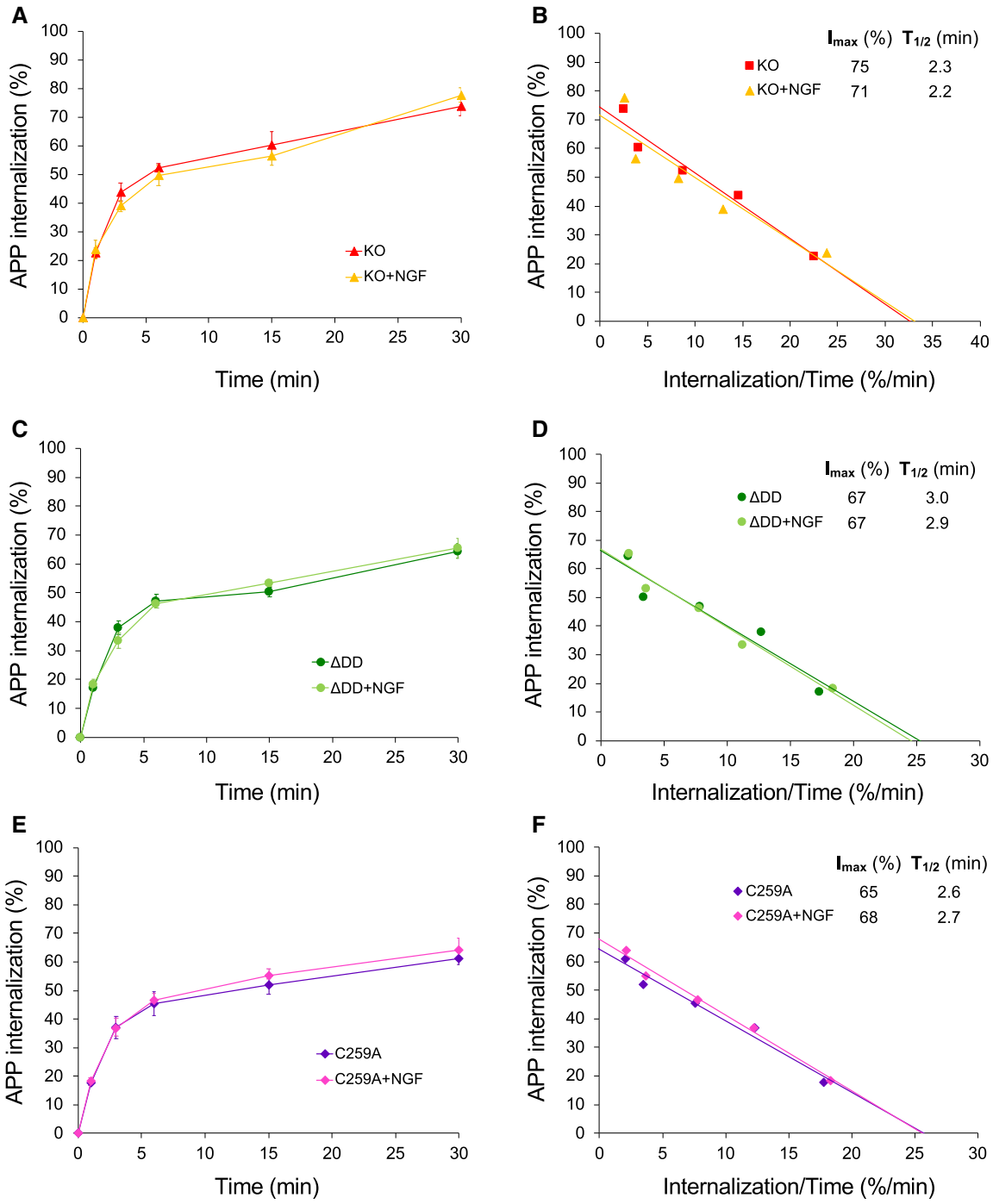


Figure EV4. Internalization of 5xFAD hAPP in mouse hippocampal neurons from p75NTR mutant mice in the presence and absence of NGF.

A, C, E Internalization of hAPP in hippocampal neurons from knock-out (A) ΔDD (C) and C259A (E) mice. Shown are averages ± SEM of percentage internalization of total surface hAPP (set to 100%). $N = 3$ independent experiments each performed in duplicate.

B, D, F Linear transformation of hAPP internalization kinetics shown in panels (A, C, and E), respectively. IMAX denotes maximal internalization in %. T1/2 denotes time for half maximal internalization (in minutes).