Supplemental figures and legends

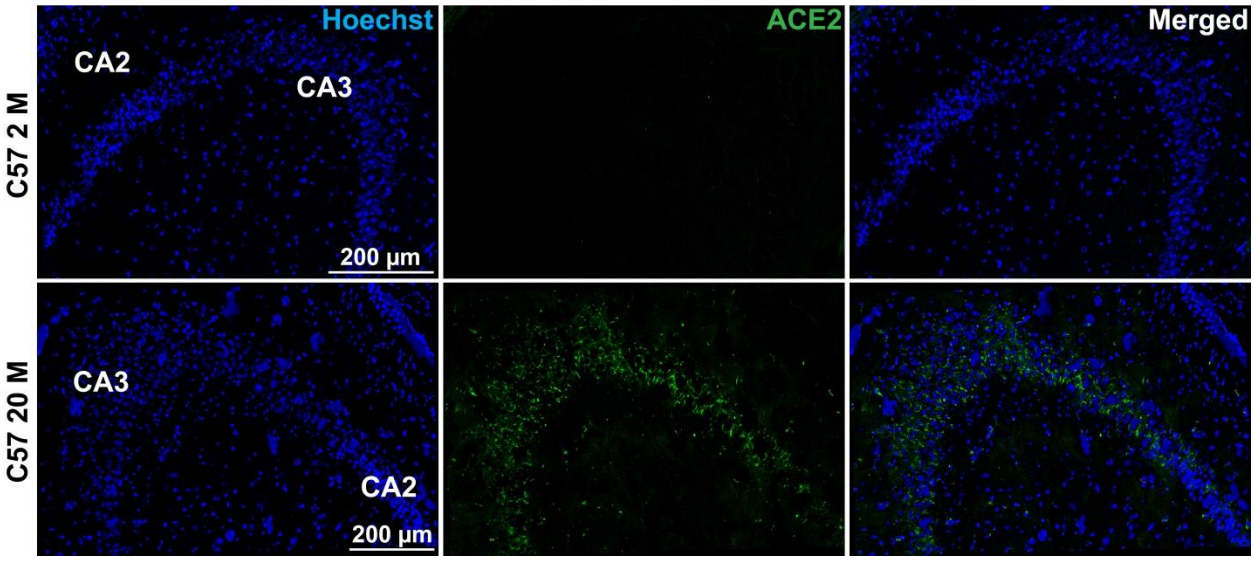


Fig. S1. ACE2 is increased with aging in wild-type mice. Immunofluorescence images of the CA2 and CA3 regions of C57BL/6J mice in low magnifications. Scale bar = 200 µm.

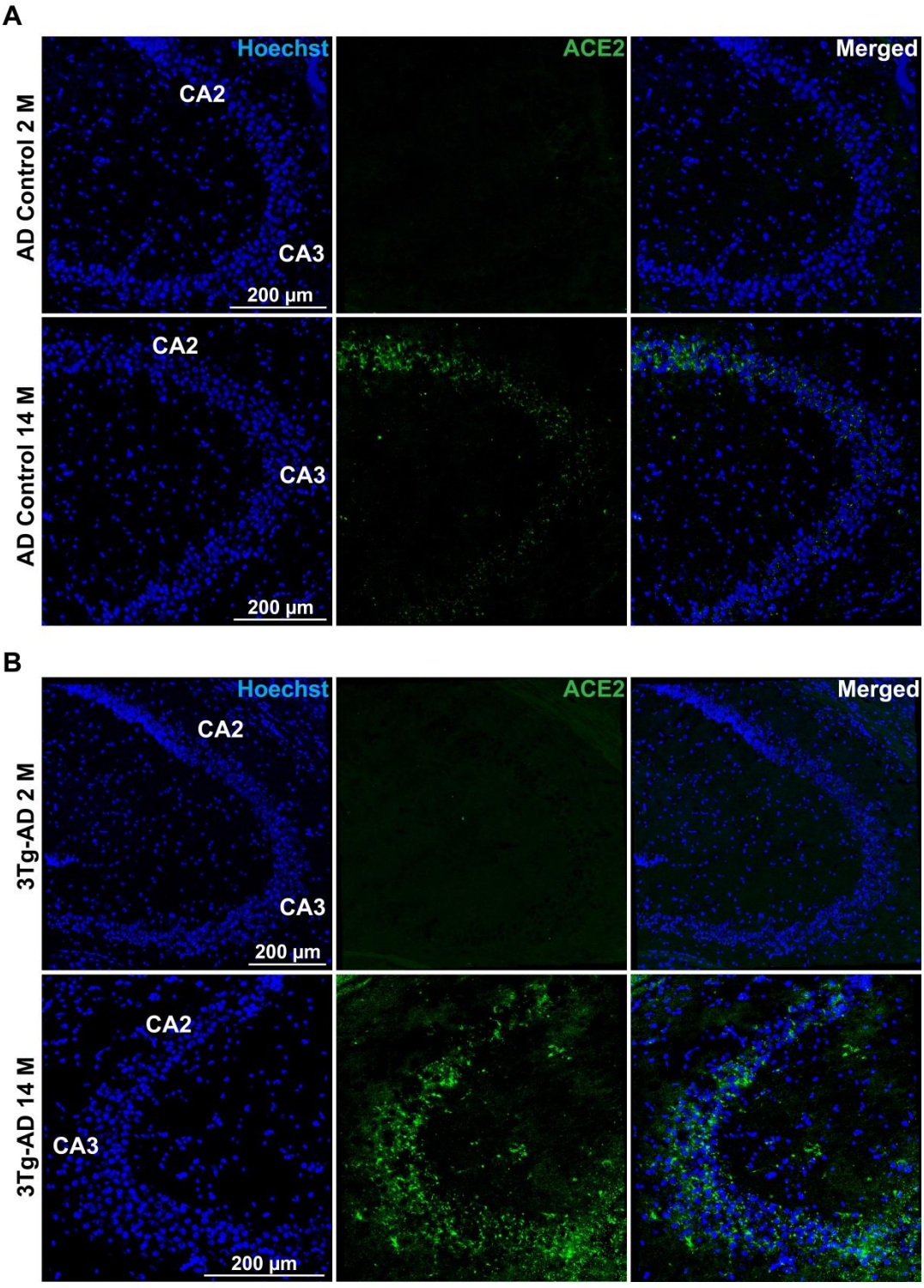


Fig. S2. ACE2 is increased with aging in mice with AD neuropathology. (**A**), Immunofluorescence images of CA2 and CA3 regions of control mice in low magnifications. Scale bar = 200 µm. (**B**), Immunofluorescence images of CA2 and CA3 regions of 3xTg-AD mice in low magnifications. Scale bar = 200 µm.

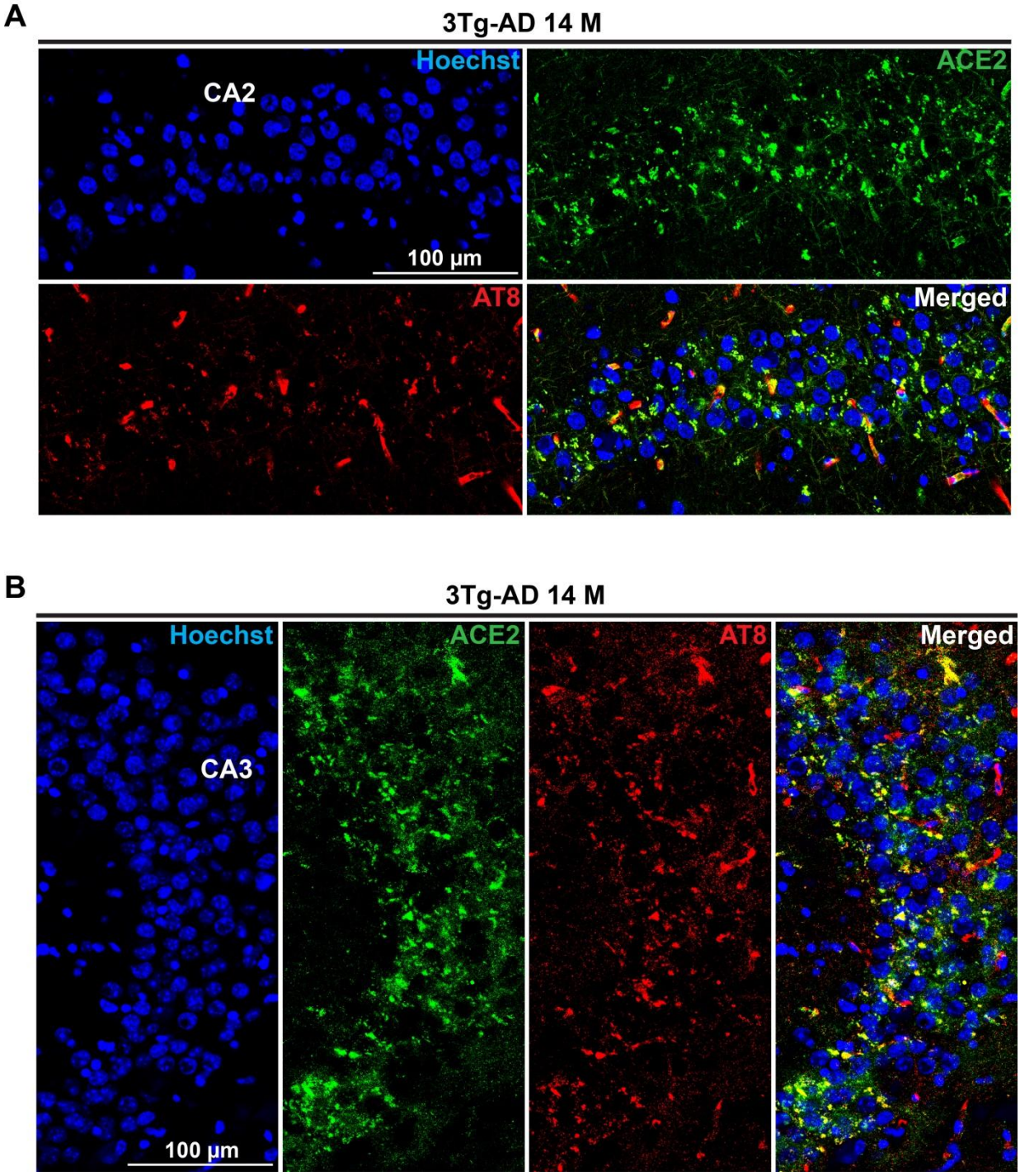


Fig. S3. ACE2 is in cells with hyperphospho-tau. (**A**), Immunofluorescence staining of ACE2 and hyperphospho-tau at ser 202 and thr 205 as detected by the AT8 antibody in the CA2 of 3xTg-AD mice in low magnifications. Scale bar = 100 µm. (**B**), Immunofluorescence staining of ACE2 and hyperphospho-tau at ser 202 and thr 205 as detected by the AT8 antibody in the CA3 of 3xTg-AD mice in low magnifications. Scale bar = 100 µm.

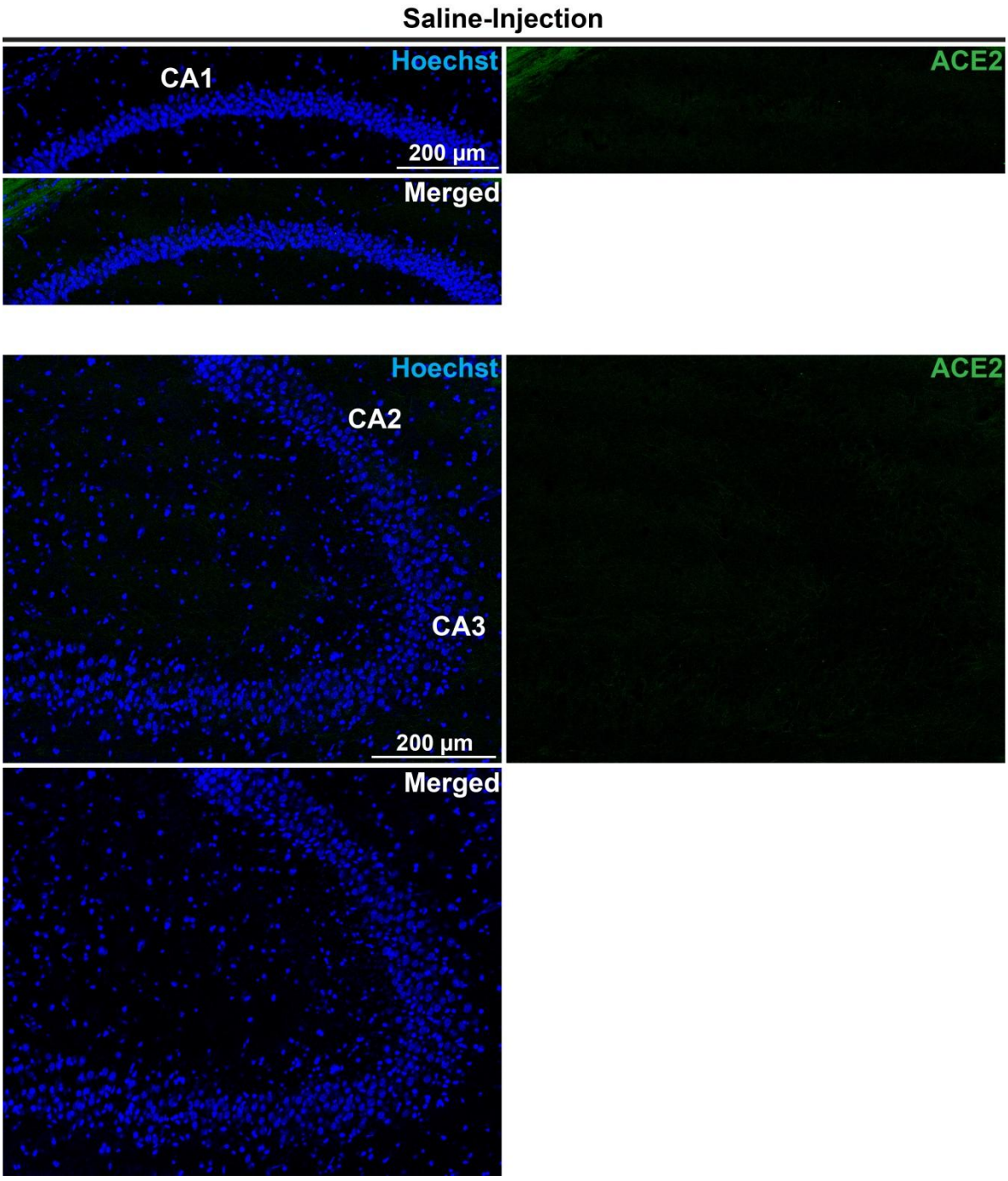


Fig. S4. ACE2 expression in 2-month old male C57BL/6J mice after receiving saline injection into the hippocampus. Immunofluorescence images of CA1, CA2 and CA3. Scale bar = 200 µm.

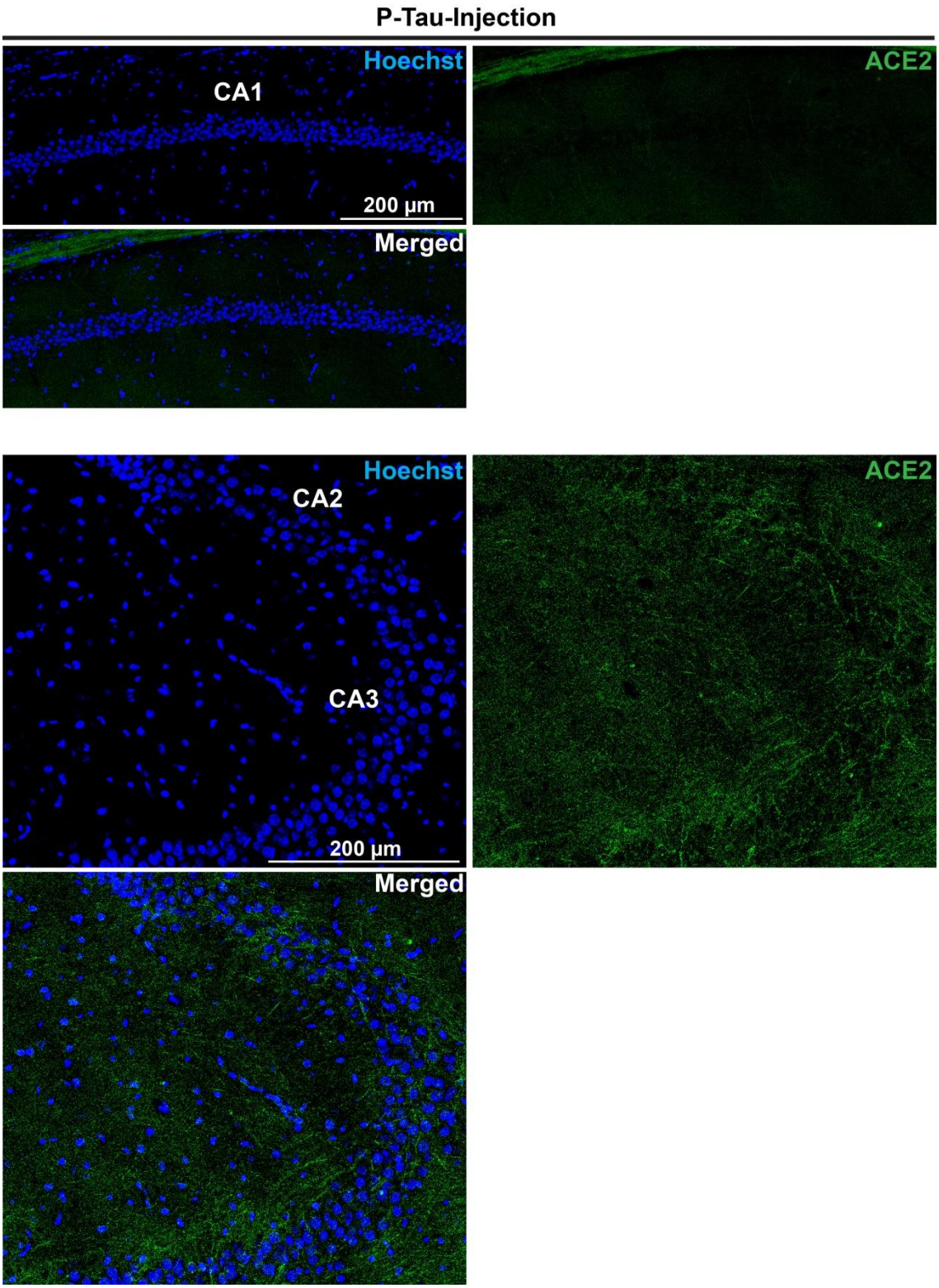


Fig. S5. ACE2 expression in 2-month old C57BL/6J mice after receiving phospho-tau fibril injection into the hippocampus. Immunofluorescence images of CA1, CA2 and CA3. Scale bar = 200 µm.

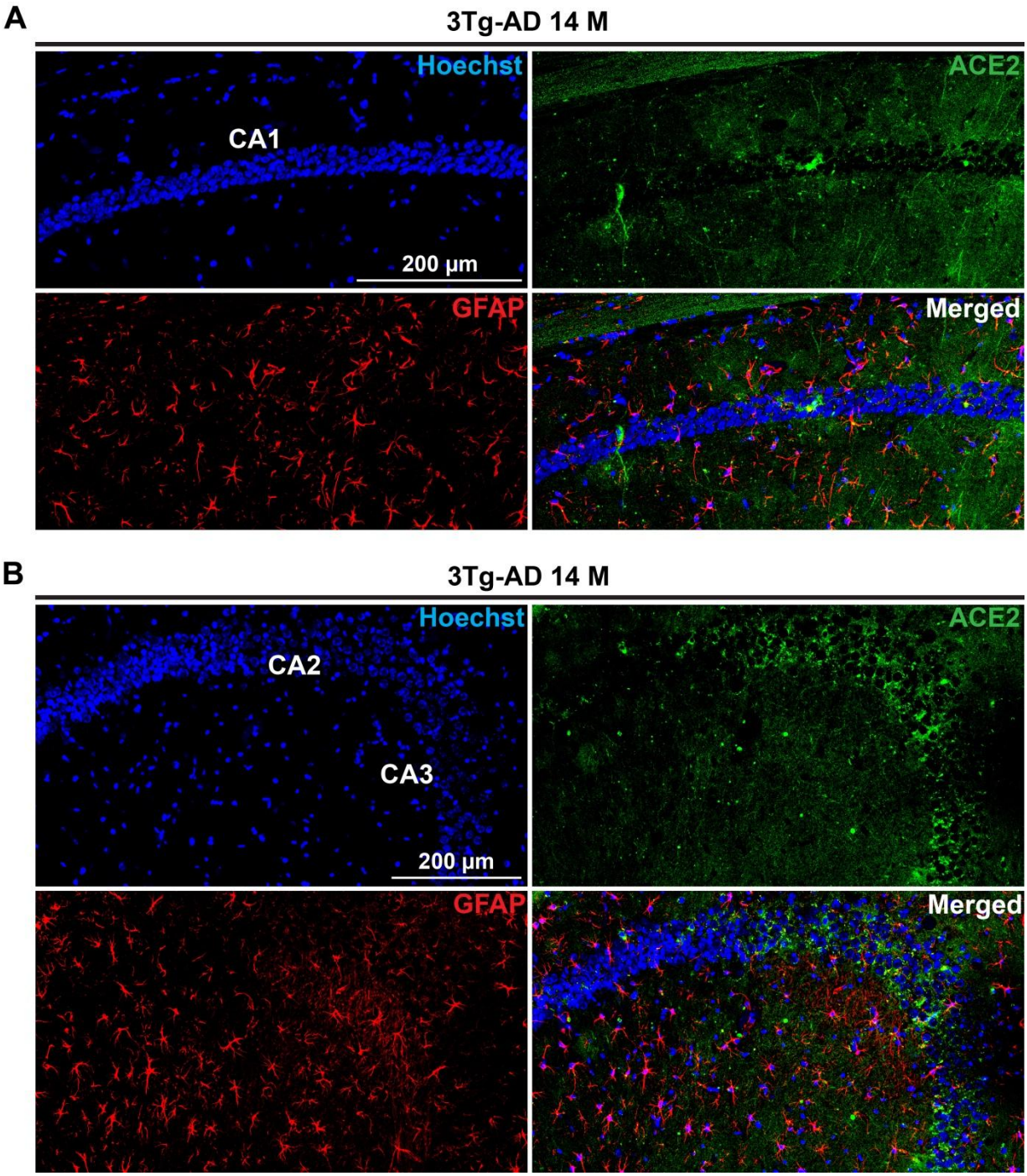


Fig. S6. ACE2 staining is not co-localized with the staining of GFAP in 3xTg-AD mice. (**A**), Immunofluorescence images of CA1. (**B**), Immunofluorescence images of the CA2 and CA3. Scale bar = 200 μm.

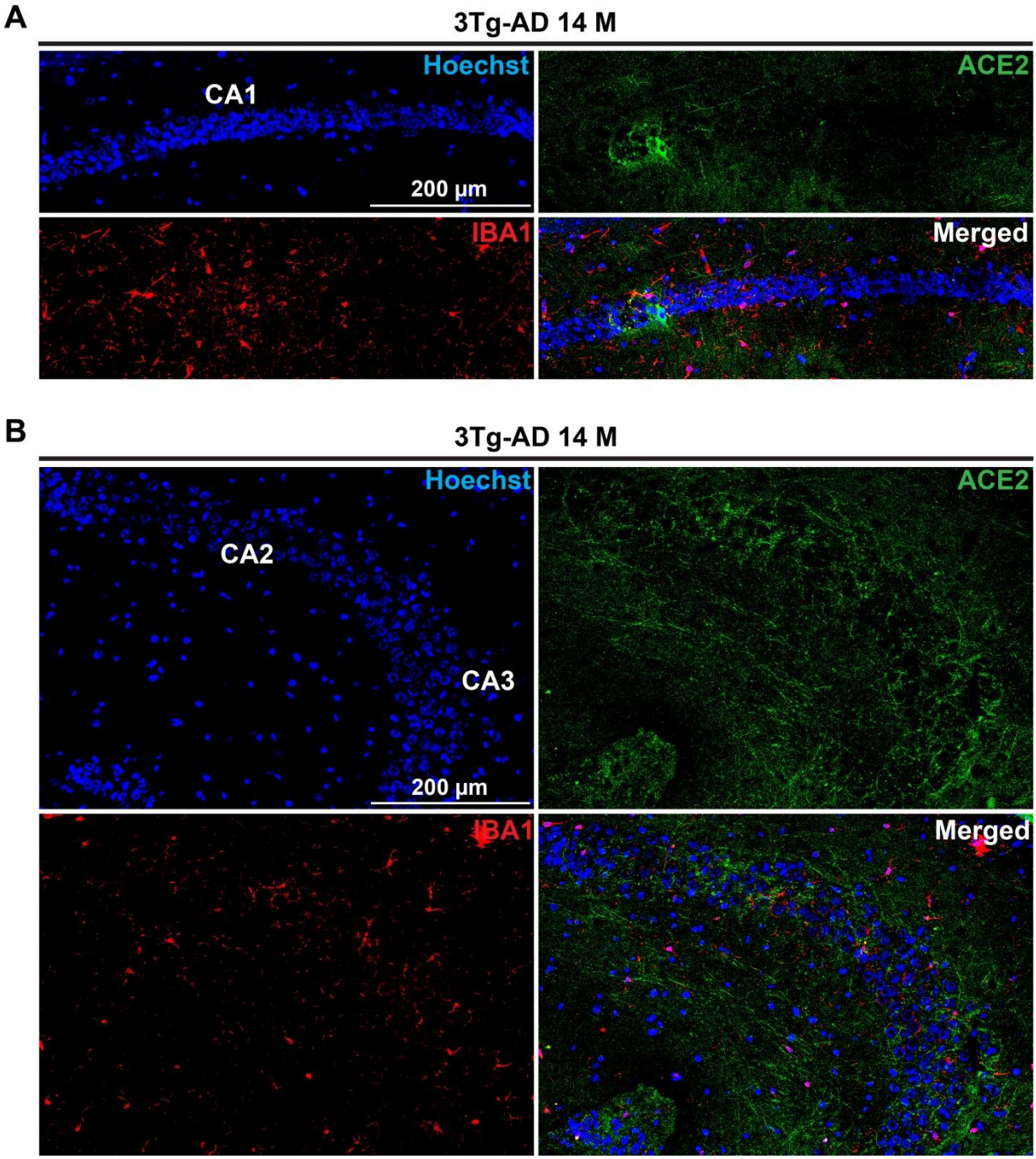


Fig. S7. ACE2 staining is not co-localized with the staining of Iba1 in 3xTg-AD mice. (**A**), Immunofluorescence images of CA1. (**B**), Immunofluorescence images of CA2 and CA3. Scale bar = 200 μm.

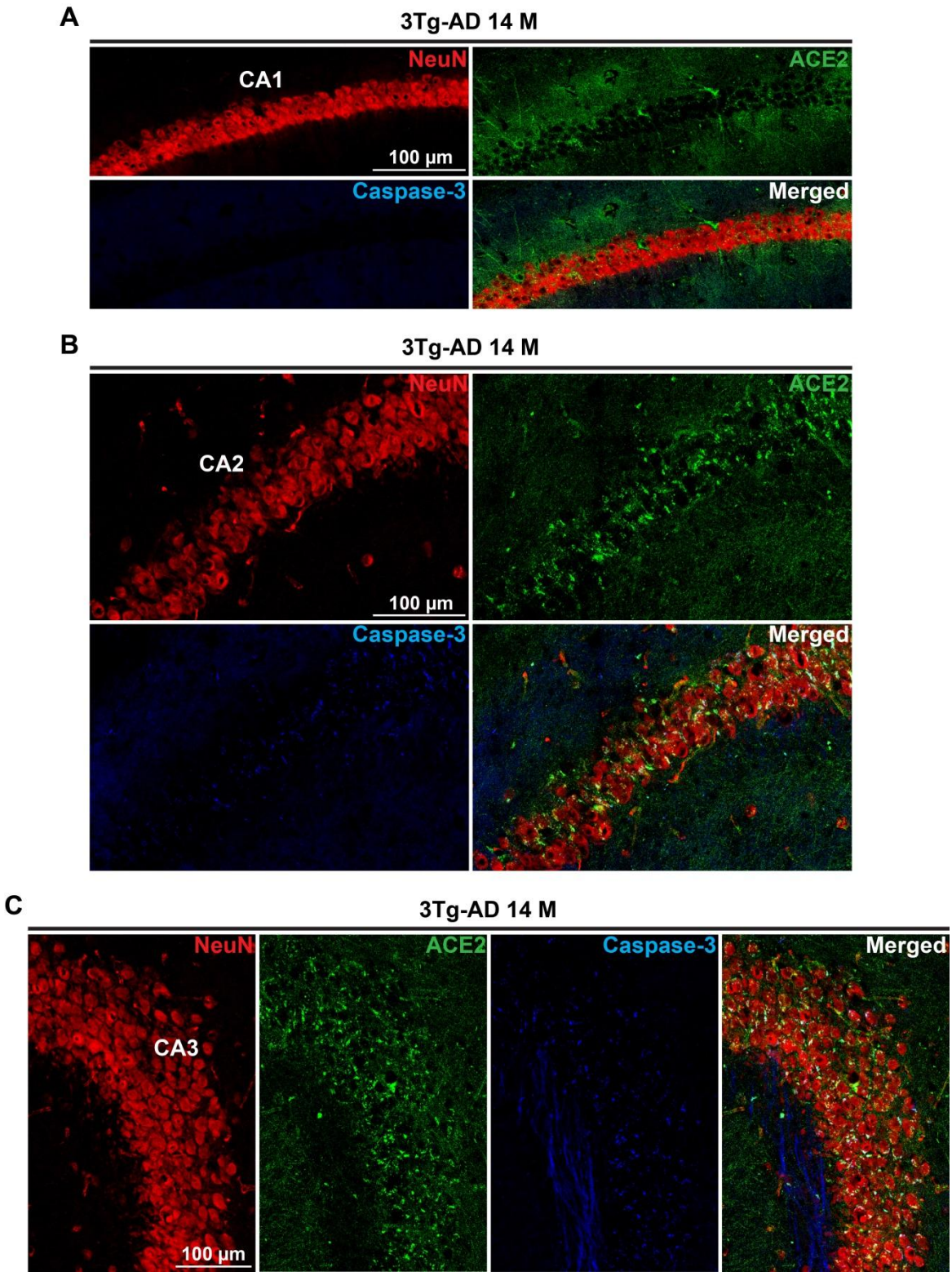


Fig. S8. ACE2 and cleaved caspase 3 staining in 3xTg-AD mice. (**A**), Immunofluorescence images of CA1. (**B**), Immunofluorescence images of CA2. (**C**), Immunofluorescence images of CA3. Scale bar = 100 μm.

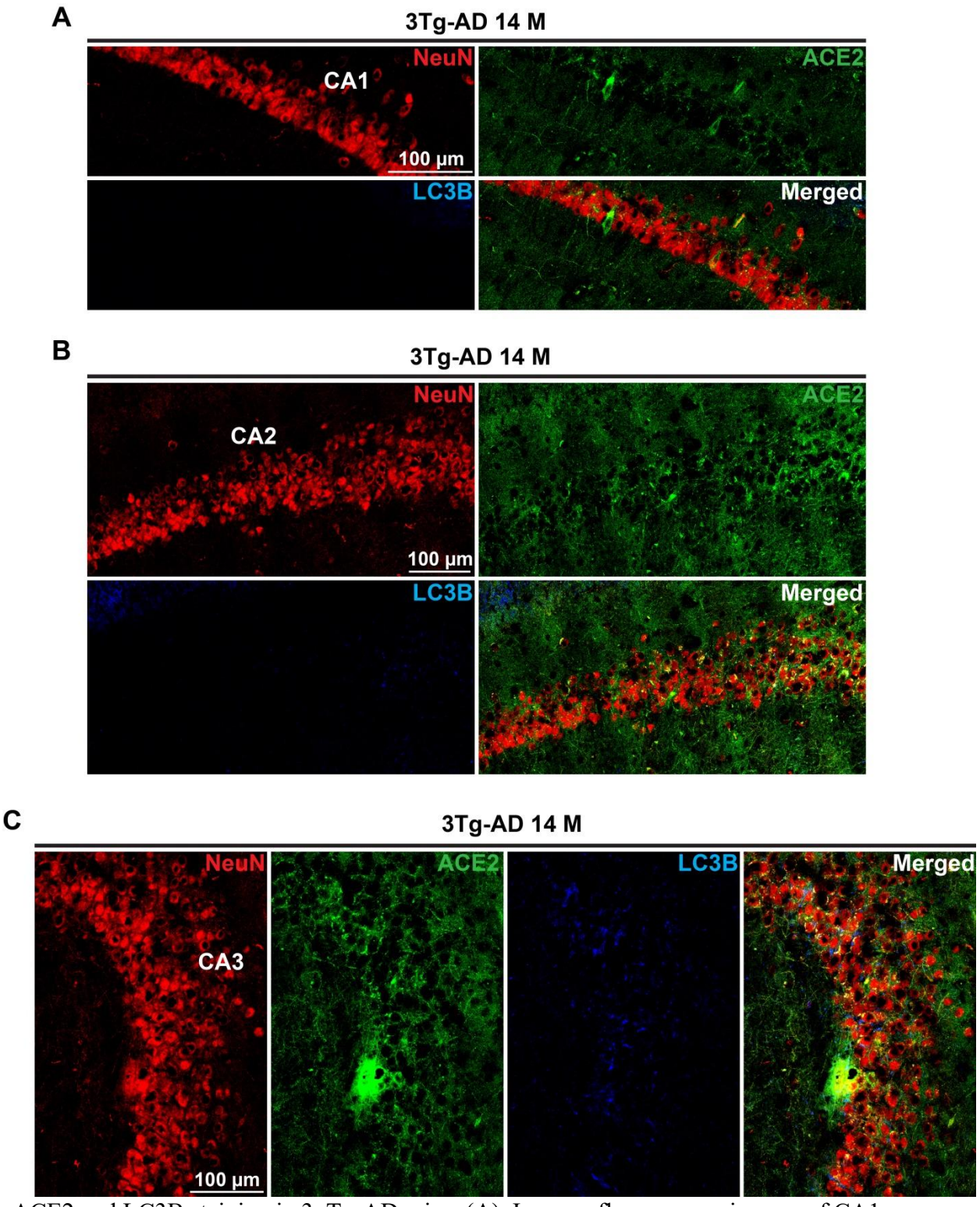


Fig. S9. ACE2 and LC3B staining in 3xTg-AD mice. (**A**), Immunofluorescence images of CA1. (**B**), Immunofluorescence images of CA2. (**C**), Immunofluorescence images of CA3. Scale bar = 100 μm.

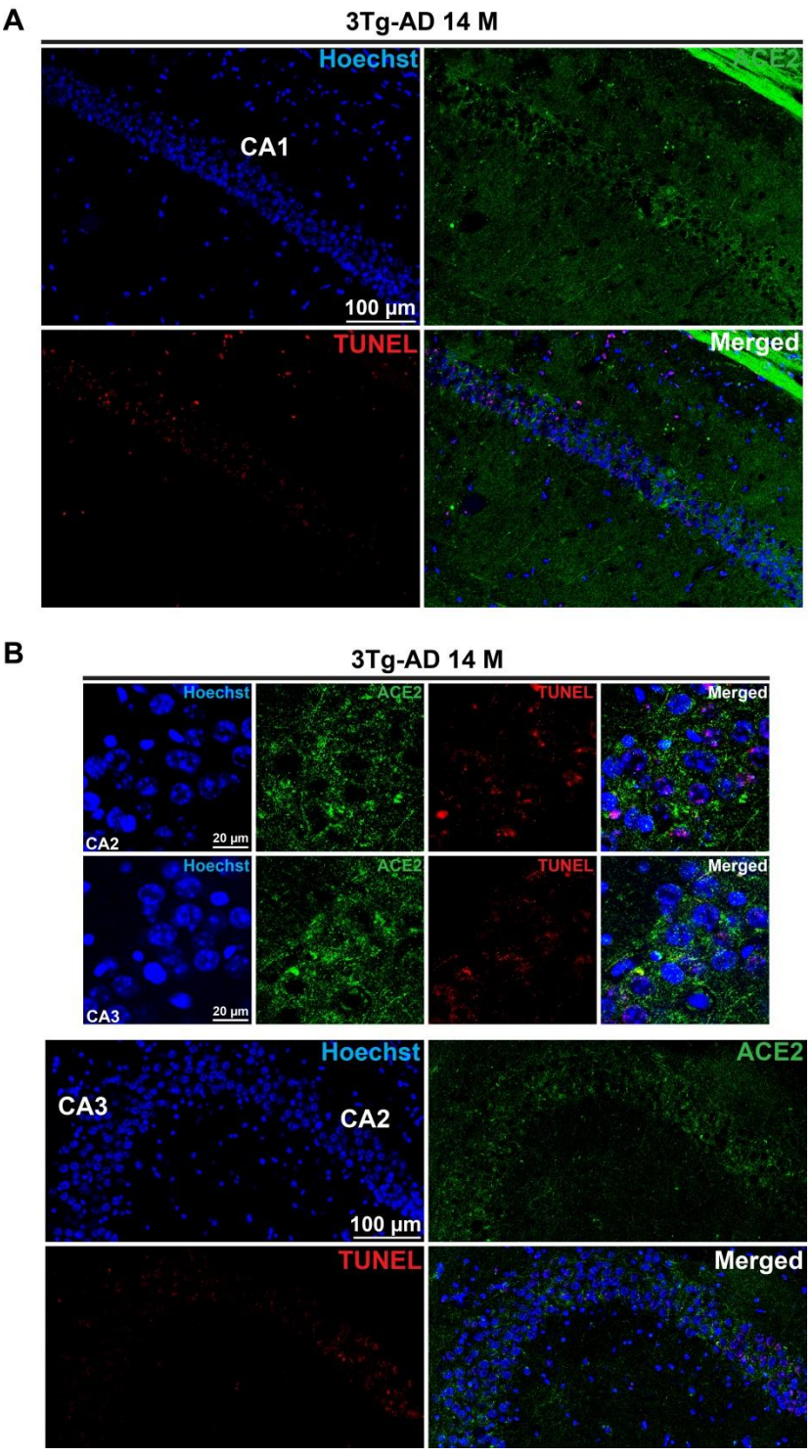


Fig. S10. ACE2 and TUNEL staining in 3xTg-AD mice. (**A**), Immunofluorescence images of CA1. Scale bar = 100 μm. (**B**), Immunofluorescence images of CA2 and CA3. Upper panel: images are in high magnifications (scale bar = 20 μm). Lower panel: images are in low magnifications (scale bar = 100 μm).

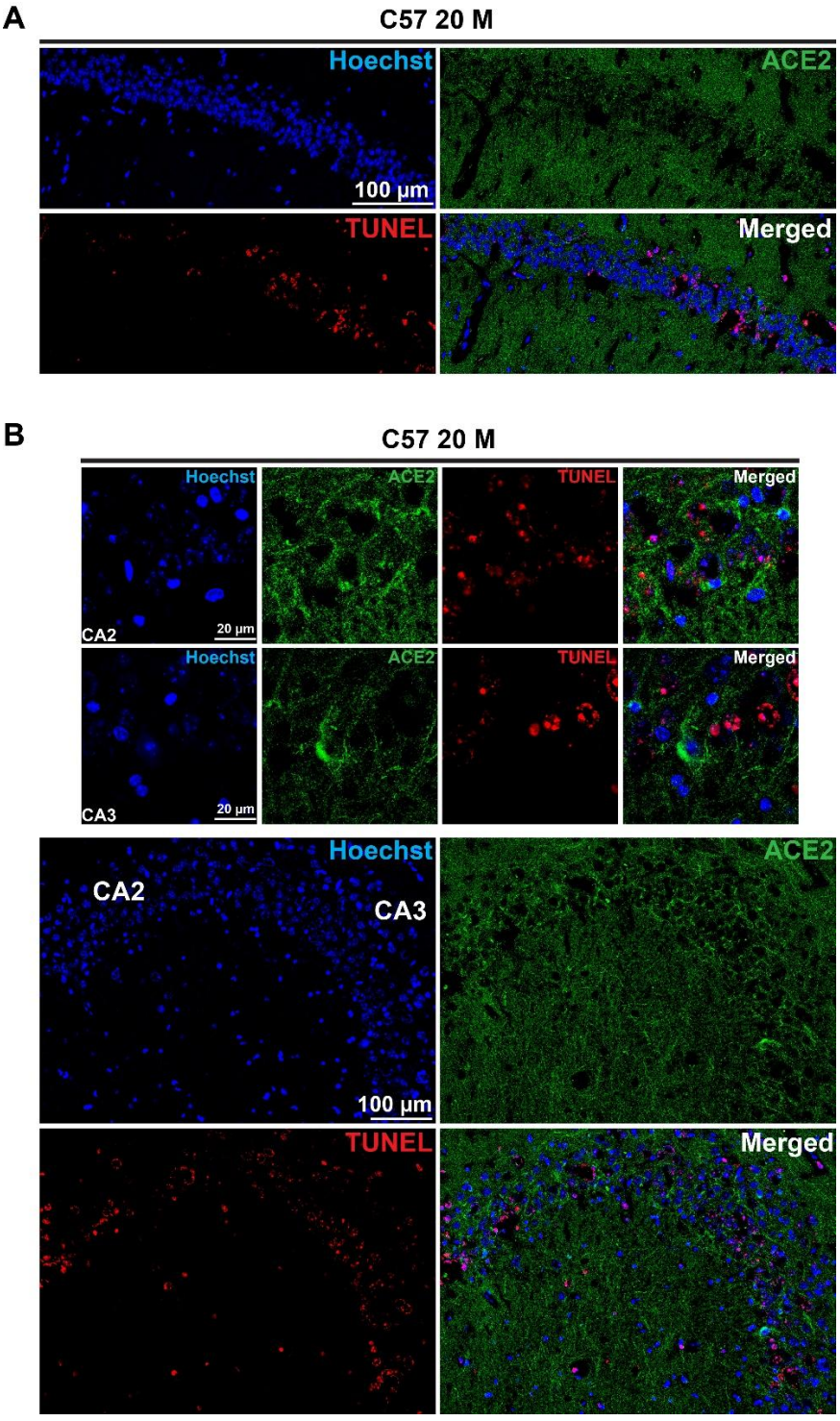


Fig. S11. ACE2 and TUNEL staining in old C57BL/6J mice. (**A**), Immunofluorescence images of CA1. Scale bar = 100 μm. (**B**), Immunofluorescence images of CA2 and CA3. Upper panel: images are in high magnifications (scale bar = 20 μm). Lower panel: images are in low magnifications (scale bar = 100 μm).

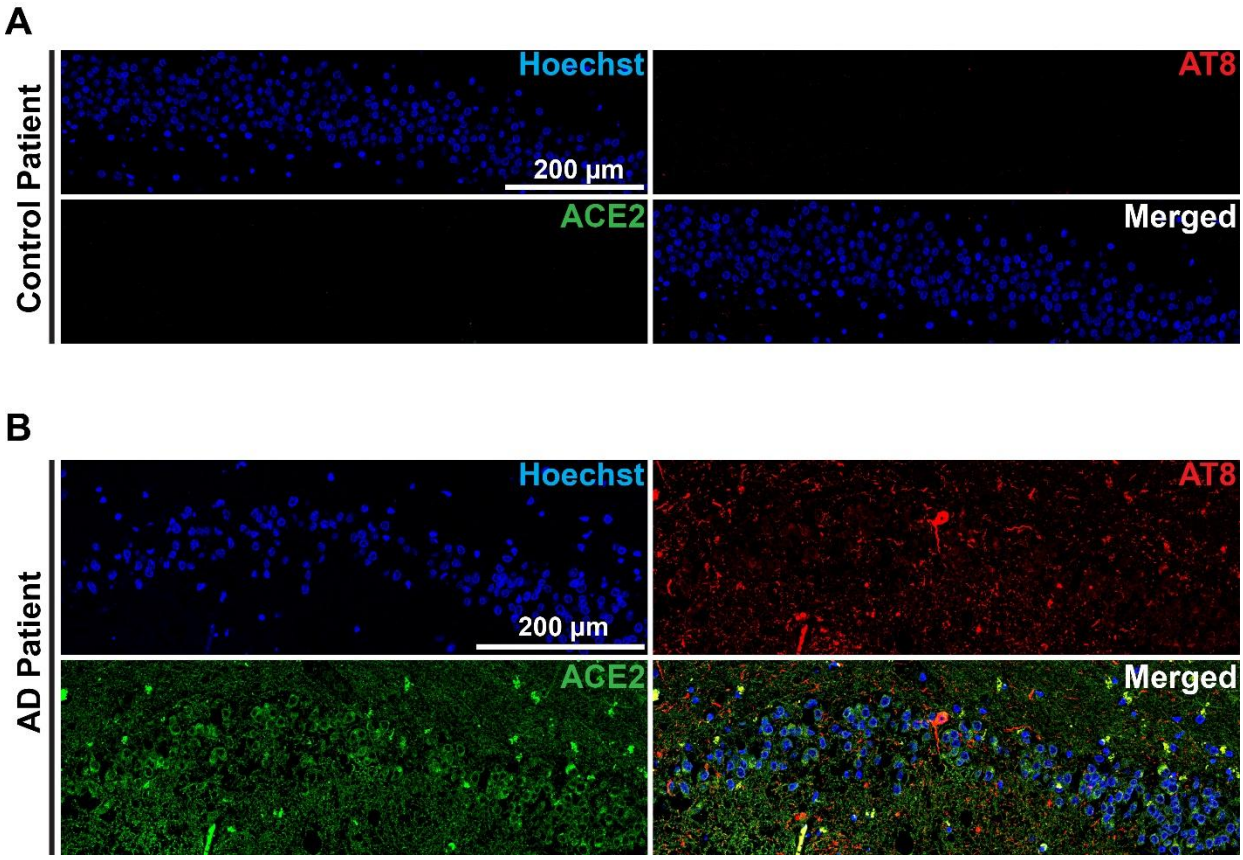


Fig. S12. ACE2 and phospho-tau staining in human hippocampus. (**A**), Immunofluorescence images of normal brain. Scale bar = 200 µm. (**B**), Immunofluorescence images of brain with AD neuropathology. Scale bar = 200 µm. Hyperphospho-tau at ser 202 and thr 205 is detected by the AT8 antibody

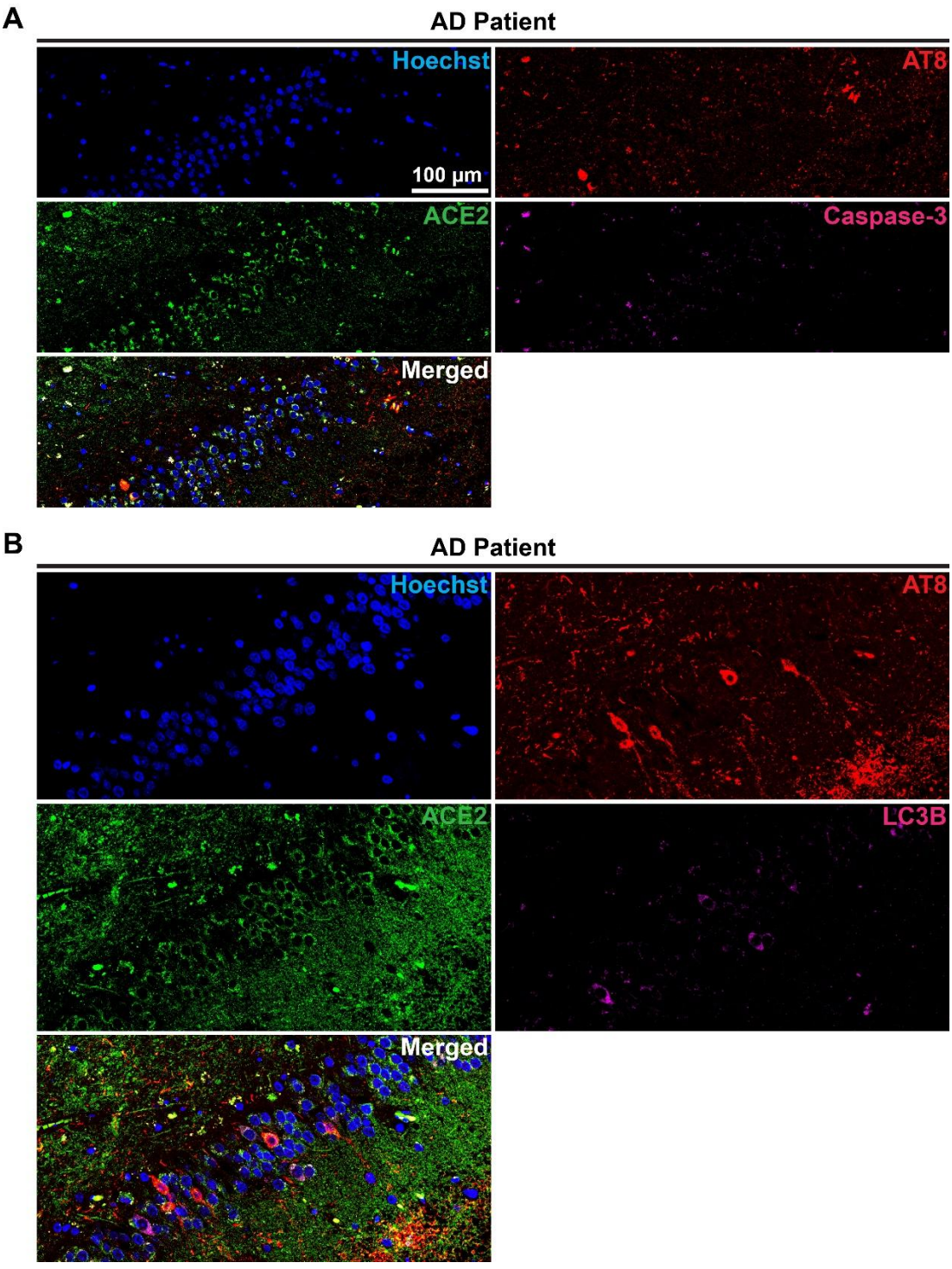


Fig. S13. ACE2, phospho-tau, cleaved caspase 3 and LC3B staining in human hippocampus. (**A**), Immunofluorescence images of triple staining of ACE2, phospho-tau and cleaved caspase 3 in brain with AD neuropathology. Scale bar = 100 µm. (**B**), Immunofluorescence images of triple staining of ACE2, phospho-tau and LC3B in brain with AD neuropathology. Scale bar = 100 µm.