

Macaca mulatta, 34 years-old
Sortilin labeling with Abcam antibody #ab16640

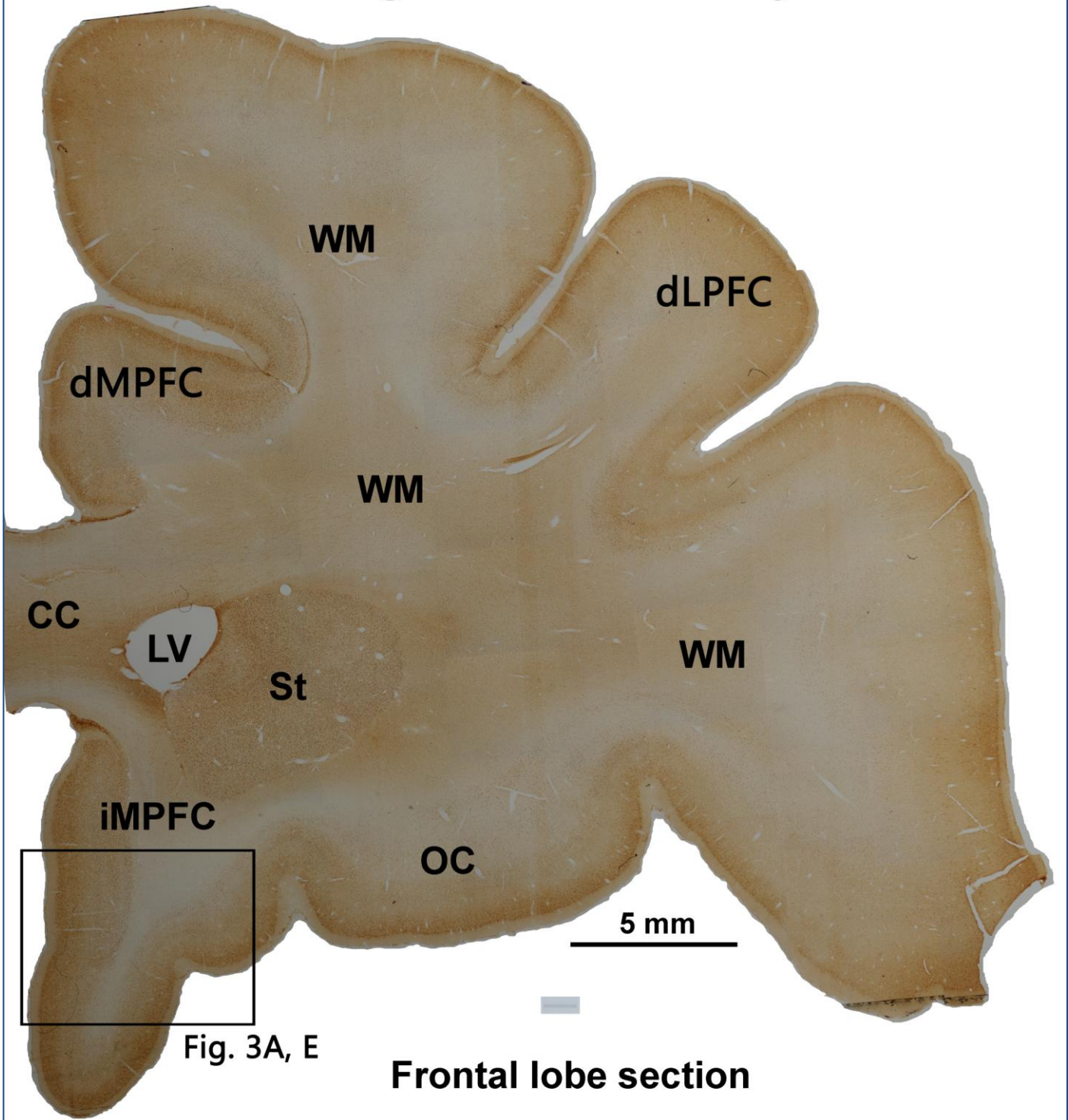


Figure S1: Sortilin immunolabeling with the C-terminal antibody in a frontal lobe section of an aged rhesus monkey at the level of the anterior end of striatum (St), as indicated. Note that there is no plaque-like extracellular labeling across the entire section. Also see labeling for β -amyloid, BACE1 and p-Tau in the sections at the same frontal level in Supplemental Figures 2-4. WM: white matter; iMPFC: inferior medial prefrontal cortex; dMPFC: dorsal medial prefrontal cortex; dLPFC: dorsal lateral prefrontal cortex; CC: corpus callosum; LV: lateral ventricle; OC: orbit cortex. The framed area is shown as Figure 3A, E in the paper. Scale bar = 5mm.

Macaca mulatta, 34 years-old
 β -Amyloid immunolabeling with 6E10

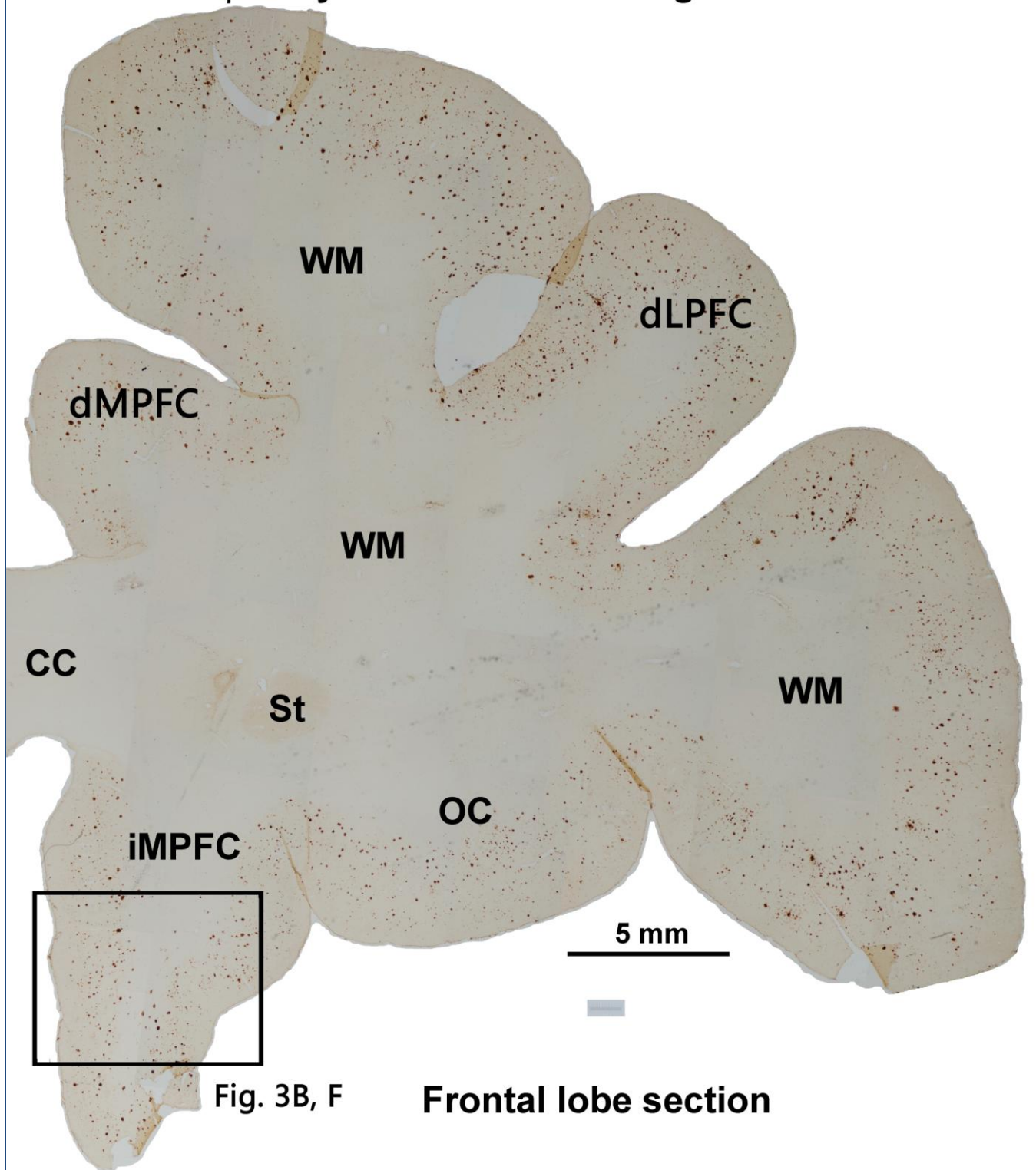


Figure S2: β -Amyloid ($A\beta$) immunolabeling with the monoclonal 6E10 antibody in a frontal lobe section of an aged rhesus monkey at the level of the anterior end of striatum (St), as indicated. Note the wide spread extracellular plaque labeling across the entire section. The framed area is shown as Figure 3B, F in the paper. Abbreviations are as defined in Supplemental Figure 1. Scale bar = 5mm.

Macaca mulatta, 34-years-old
BACE1 labeling with anti-BACE1 α (Zhang et al., 2009)

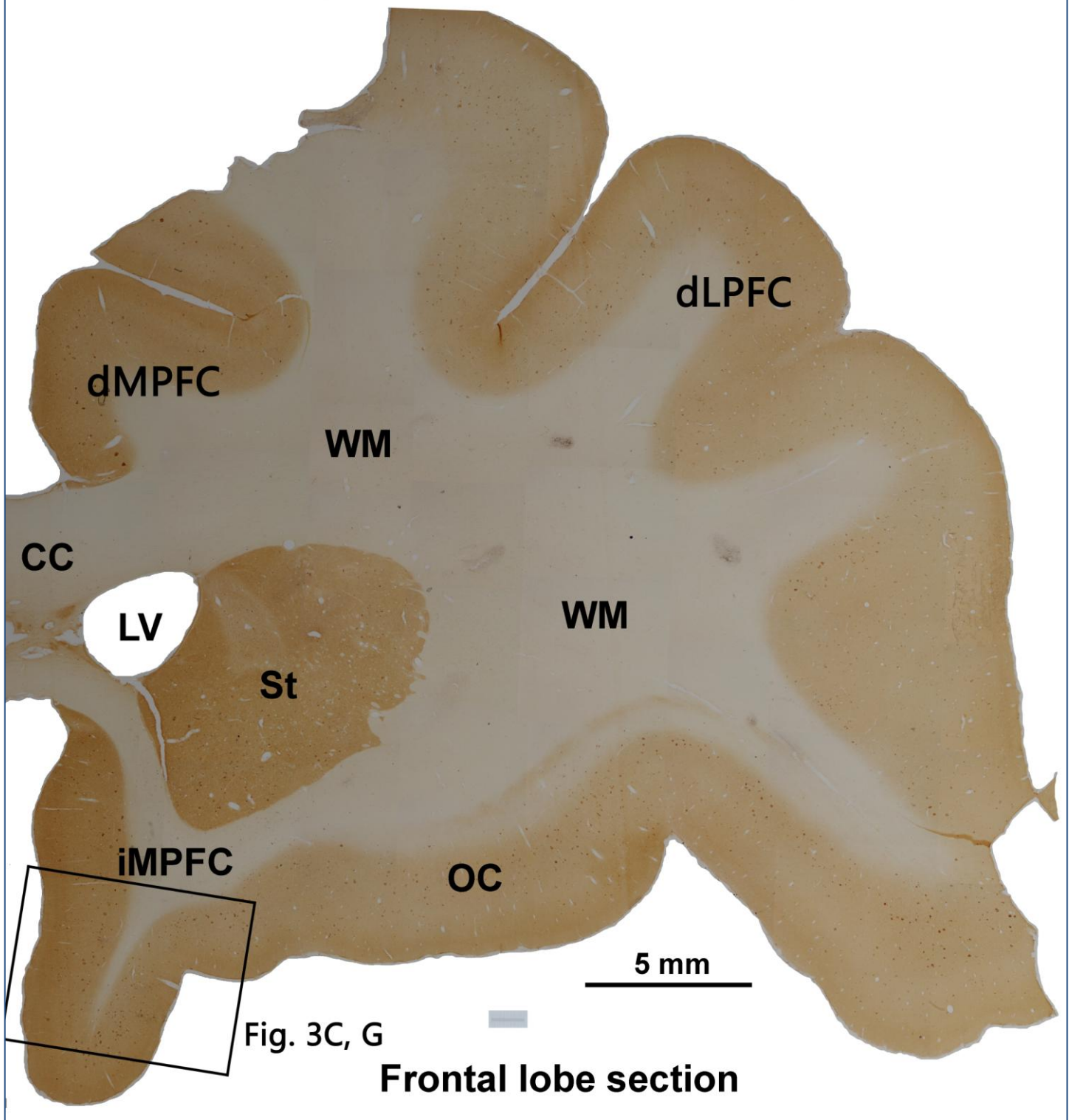


Figure S3: β -Secretase (BACE1) immunolabeling with a well characterized rabbit antibody in a frontal lobe section of an aged rhesus monkey at the level of the anterior end of striatum (St). The labeling exhibits a neuropil-like pattern over the cortex. By enlarging the image on the screen, clusters of dystrophic neurites are seen to show increased reactivity relative to background and they distribute over the cortex across the section. The framed area is shown as Figure 3C, G in the paper. Abbreviations are as defined in Supplemental Figure 1. Scale bar = 5mm.

**Macaca mulatta, 34 years-old
p-Tau labeling with the PHF1 antibody**

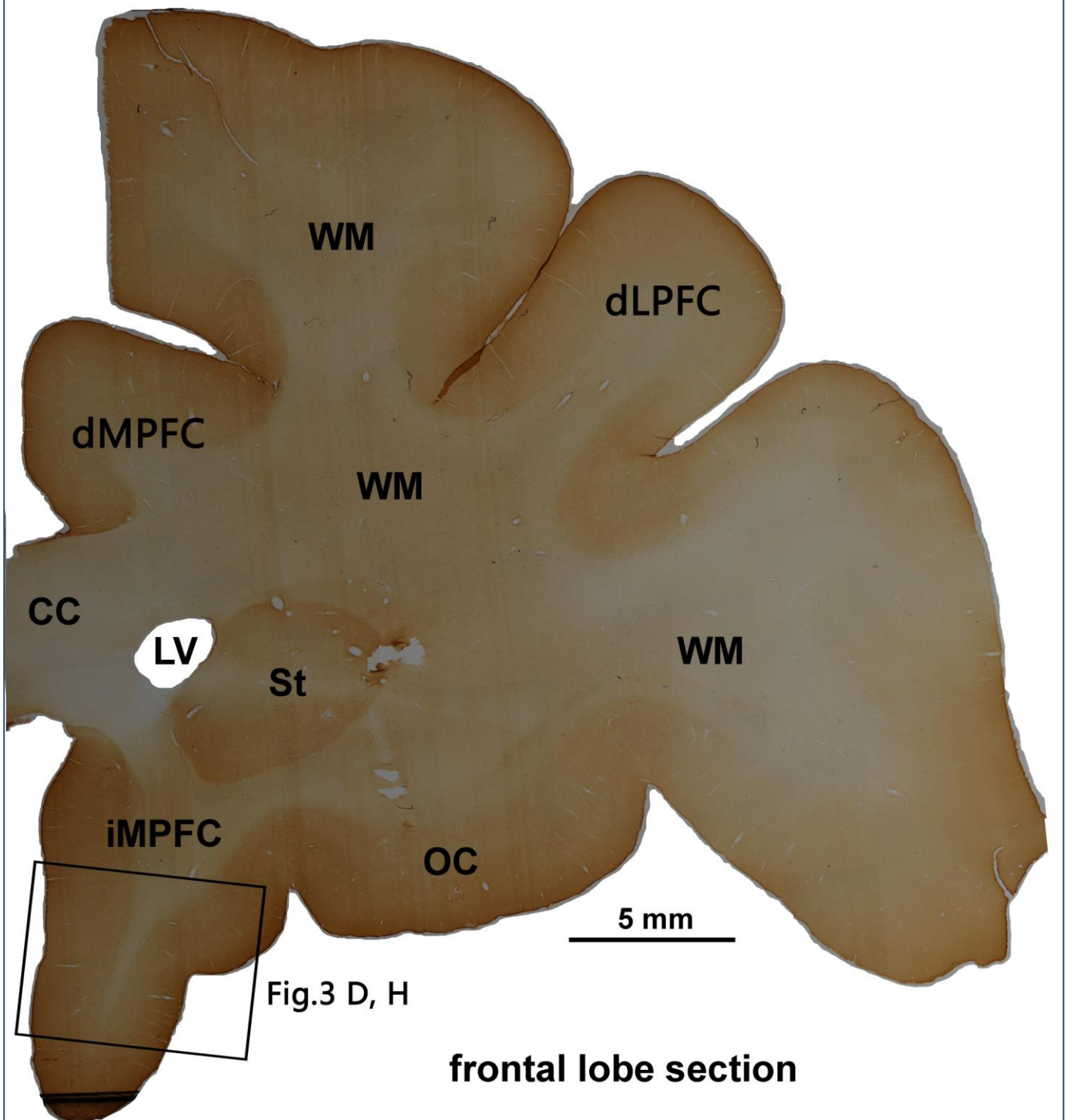


Figure S4: Pattern of labeling revealed with the PHF1 monoclonal phosphorylated tau antibody in a frontal lobe section of an aged rhesus monkey at the level of the anterior end of striatum (St). The labeling is background-like without any cellular profiles identifiable across the entire area of the section. The framed area is shown as Figure 3D, H in the paper. Abbreviations are as defined in Supplemental Figure 1. Scale bar = 5mm.

**Macaca fascicularis,
32 years-old
Sortilin labeling with
Abcam ab166440**

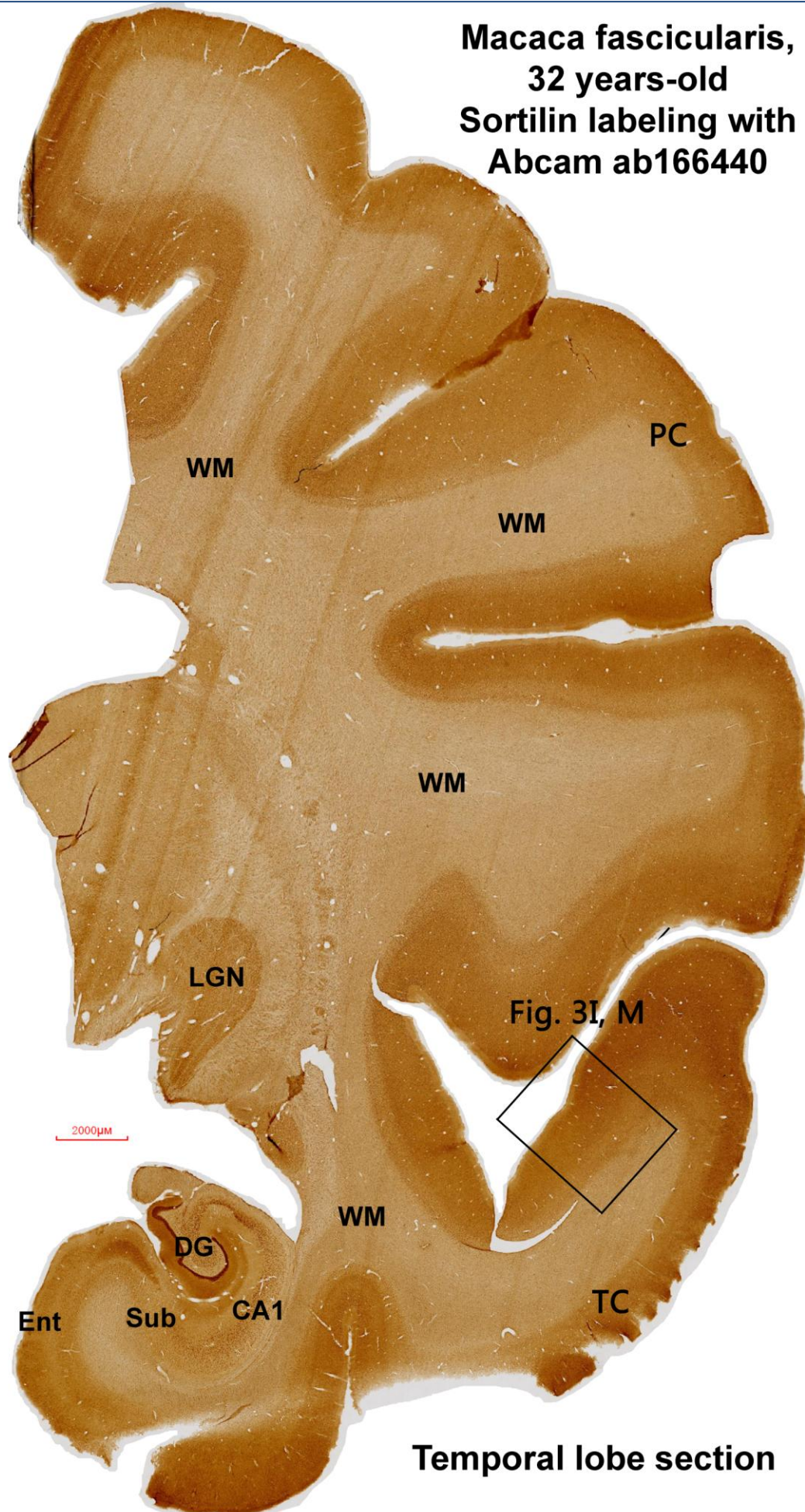


Figure S5: Sortilin immunolabeling with the C-terminal antibody in a temporal lobe section of an aged cynomolgus monkey at the level passing the anterior hippocampus and the lateral geniculate nucleus (LGN). As with the pattern seen in Supplemental Figure 1, there is no plaque-like extracellular labeling across the entire section. Note the strong labeling in the granule cell and molecular layer of the dentate gyrus (DG). Labeling for β -amyloid, BACE1 and p-Tau in adjacent the sections is shown as Supplemental Figures 6-8. WM: white matter; PC: parietal cortex; TC: temporal cortex; Ent: entorhinal cortex; Sub: subiculum; LV: lateral ventricle; OC: orbit cortex. The framed area is shown as Figure 3I and M in the paper. Scale bar = 2 mm.

**Macaca fascicularis,
32 years-old
 $A\beta$ immunolabeling
with 6E10**

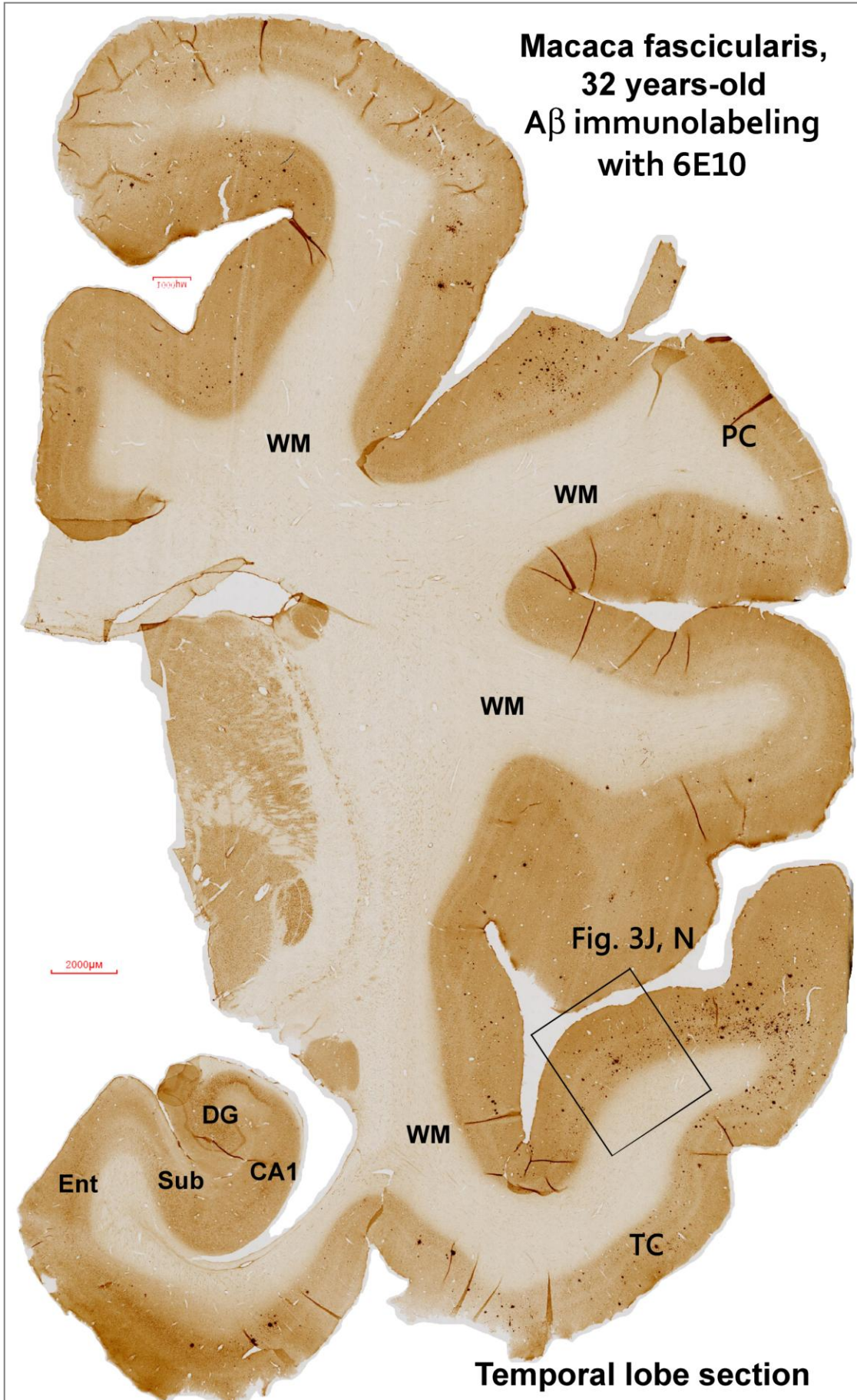


Figure S6: β -Amyloid ($A\beta$) immunolabeling with the monoclonal 6E10 antibody in a temporal lobe section of the aged cynomolgus monkey at the level of the anterior hippocampus. Extracellular amyloid plaques are present in a greater amount in the medial and lateral parts of the parietal neocortex (PC) and temporal neocortex (TC), relative to the entorhinal cortex (Ent). Very few plaques are seen in the hippocampal formation. The framed area with fairly dense plaques is shown as Figure 3J, N in the paper. Abbreviations are as defined in Supplemental Figure 5. Scale bar = 2 mm.

**Macaca fascicularis,
32 years-old
BACE1 labeling with
anti-BACE1 α**

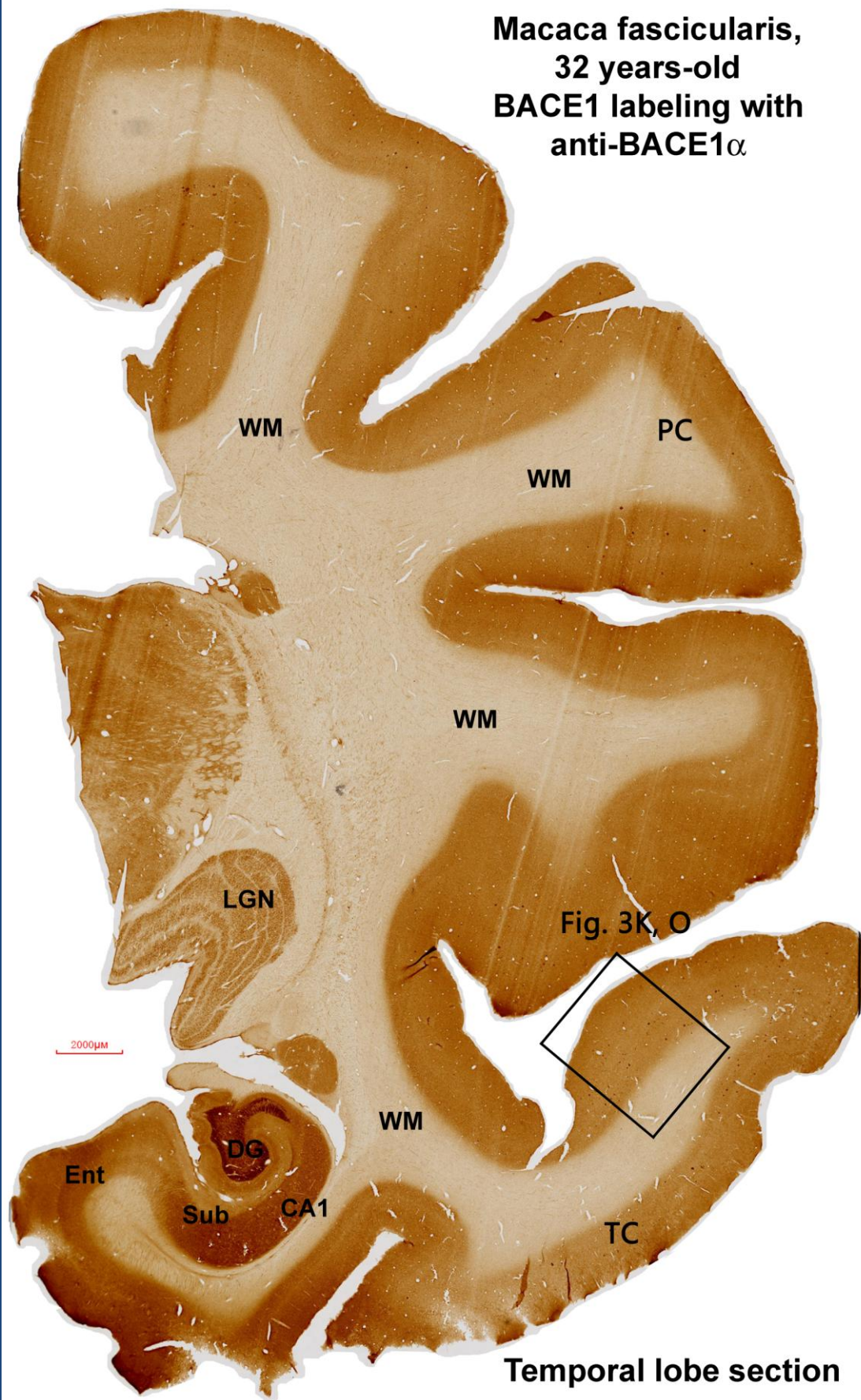


Figure S7:
 β -Secretase (BACE1) immunolabeling across the hemispheric section from the aged rhesus monkey passing the lateral geniculate nucleus (LGN) and anterior hippocampus. Neuropil-like reactivity is present over the cortical gray matter. Heavy labeling is present in the dentate gyrus (DG) in association with mossy fiber terminals. There are clusters of dystrophic neurites with increased reactivity relative to background, visible by enlarging the image. These neuritic profiles also appear more frequent in upper parts of the parietal neocortex and superior temporal neocortex. The framed temporal cortical area is shown as Figure 3K and O in the paper. Abbreviations are as defined in Supplementary Figure 5. Scale bar = 2 mm.

**Macaca fascicularis,
32 years-old
p-Tau labeling with
PHF1 antibody**

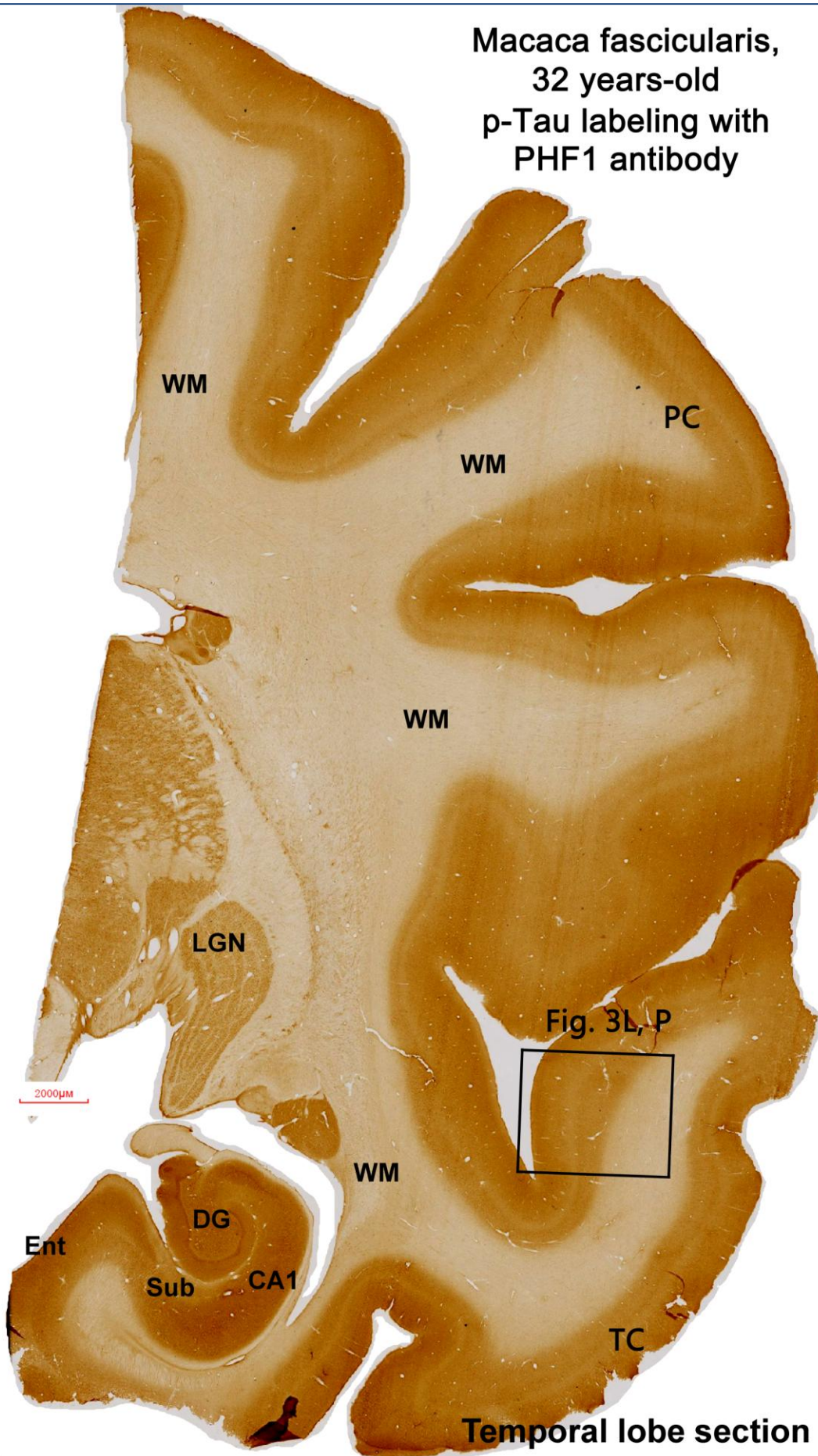


Figure S8: Non-edge montaged Motic-microscopic image covering the area of the entire hemispherical section from an aged cynomolgus monkey at the level passing the anterior hippocampus and the lateral geniculate nucleus (LGN). This figure illustrates the immunolabeling pattern revealed with the PHF1 monoclonal phosphorylated tau antibody. No cellular profiles resembling neurofibrillary tangle lesions seen in Alzheimer's disease human brain are detectable over the cerebral cortex or the hippocampal formation. The framed area of the temporal neocortex is enlarged and shown as Figure 3L, P in the paper. Abbreviations are as defined in Supplemental Figure 5. Scale bar = 2 mm.