



Not all amyloid-depositing models are the same when considering CAA – implications for the study of CAA-related events



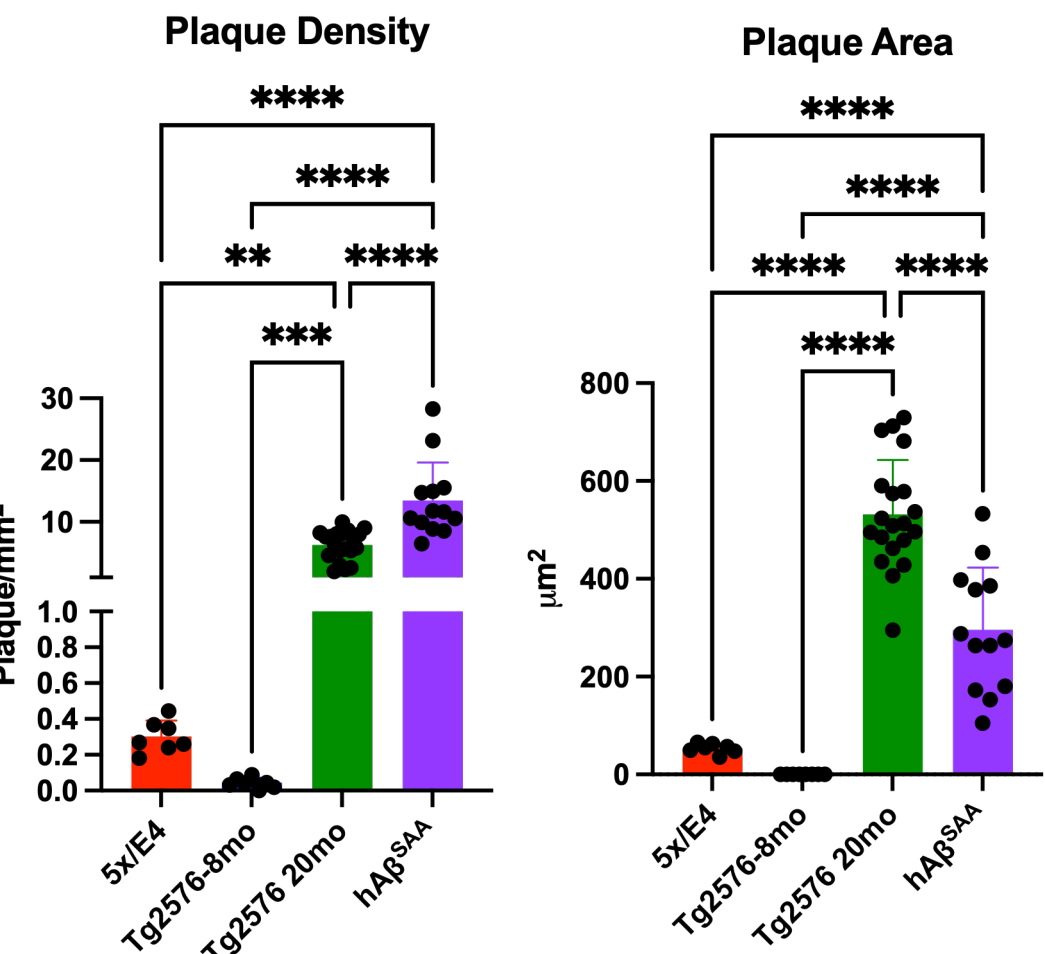
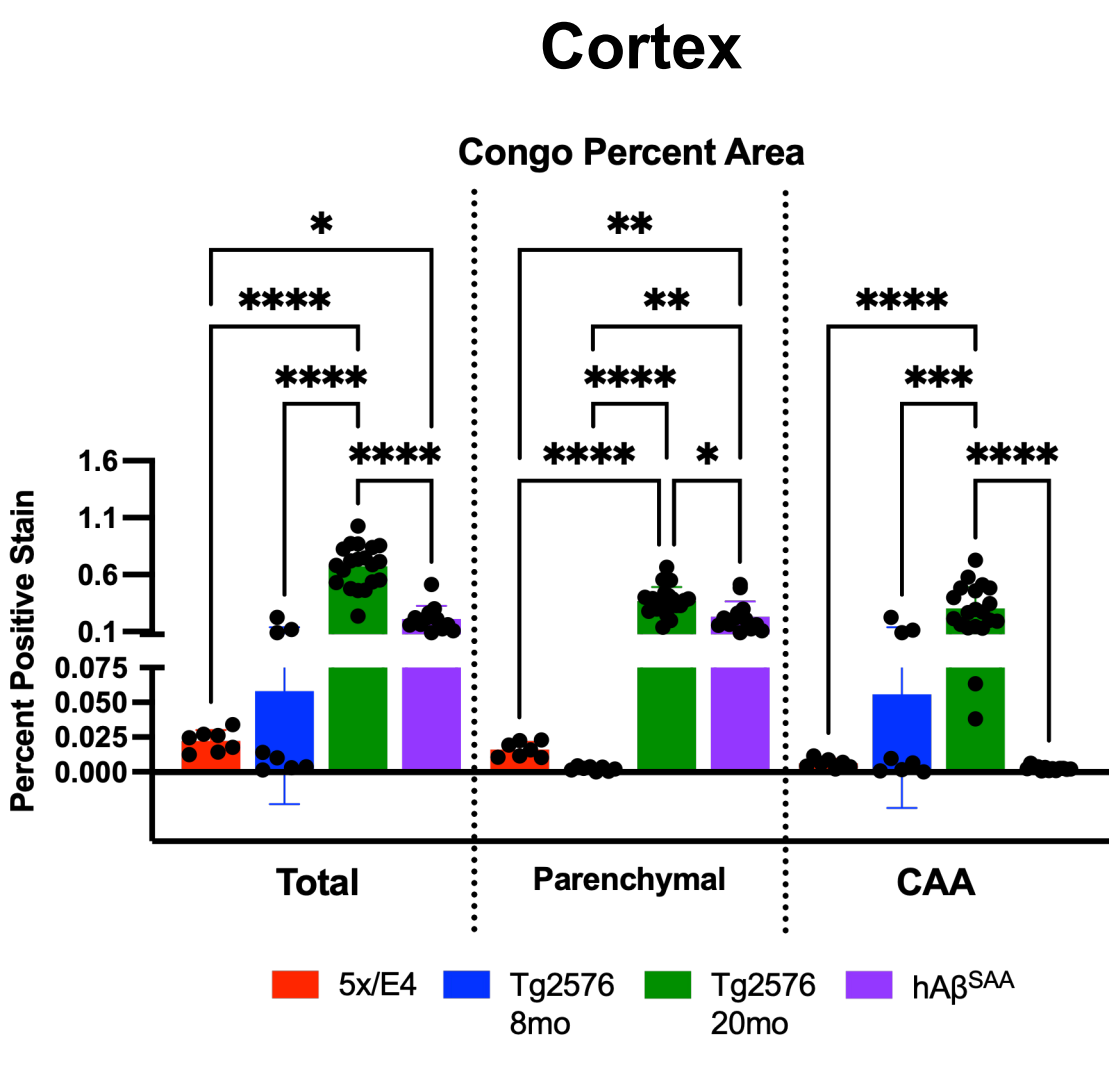
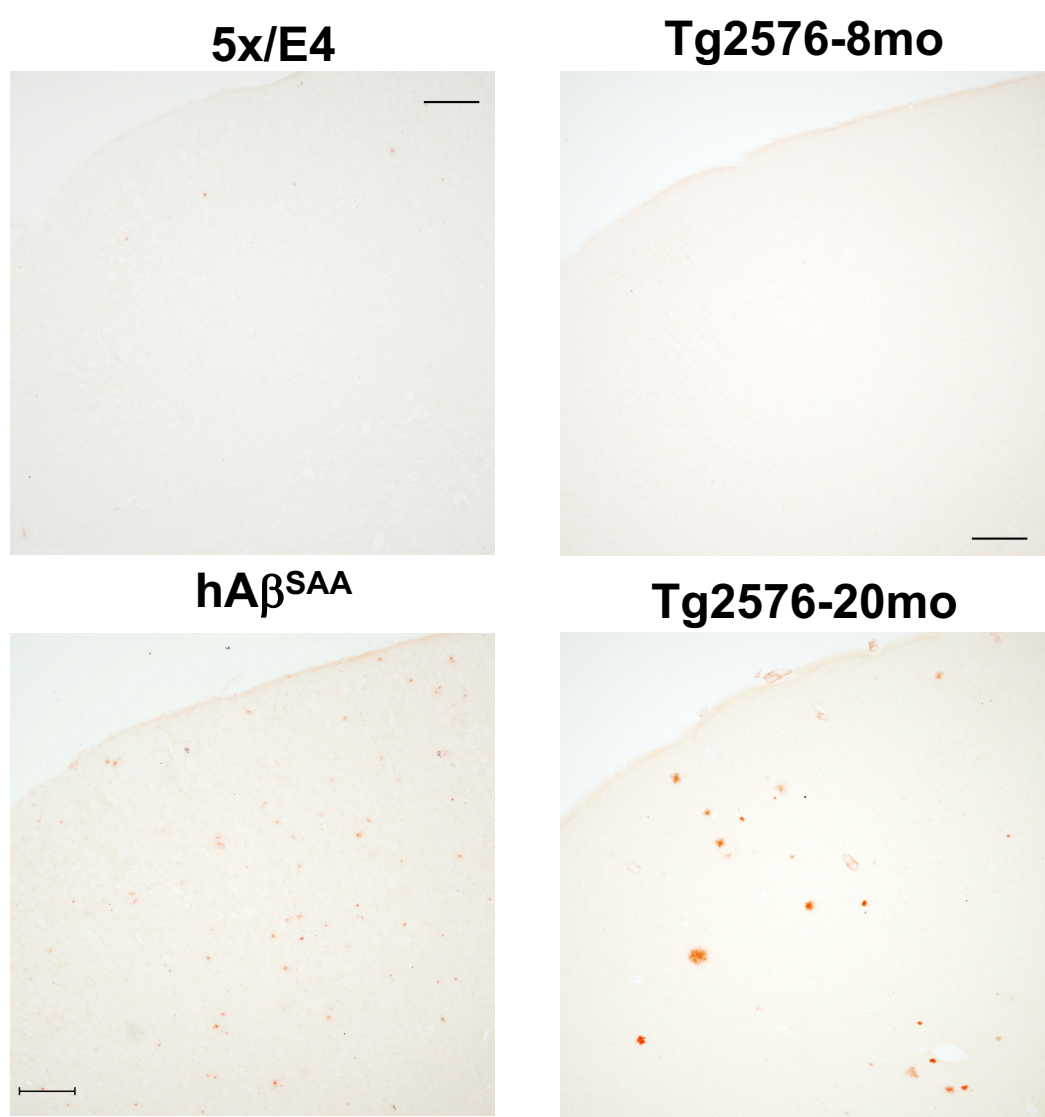
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Cerebral Amyloid Angiopathy

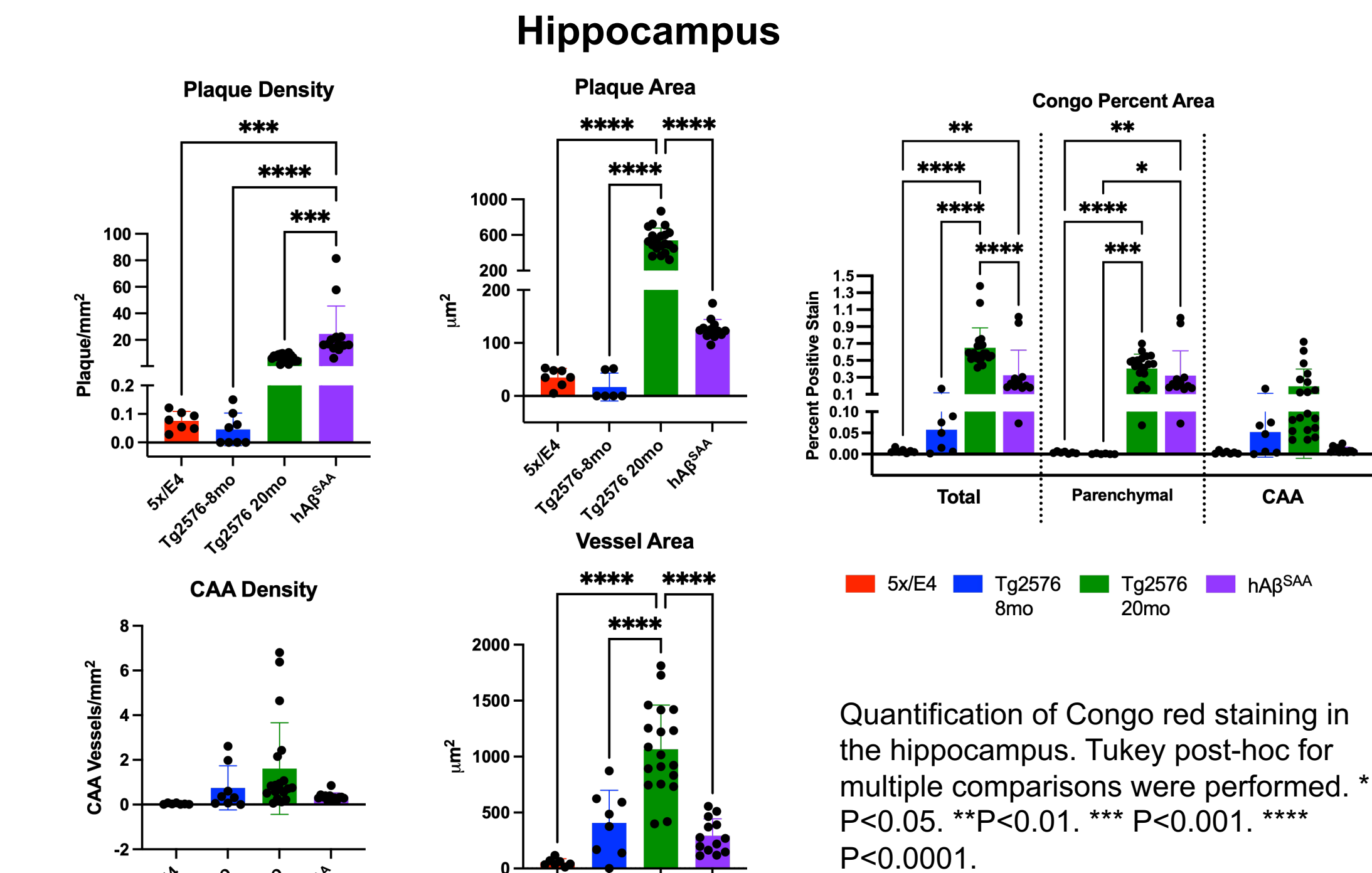
- Cerebral amyloid angiopathy (CAA) occurs when amyloid-beta builds up within the vessel wall of arteries.
- CAA is present in roughly 80% of Alzheimer's disease cases and is a significant risk factor for the development of ARIA during immunotherapy treatment, making it critical to understand mechanisms of CAA.
- To understand the differences in CAA across animal models of amyloid deposition, we investigated plaque/CAA levels, microglia morphology and astrocyte levels in 8-month-old 5xFAD/ApoE4 (5x/E4) mice, 8-month-old Tg2576 mice, 20-month-old Tg2576 mice and 22-month-old hAβ^{SAA} mice.

Tg2576 mice develop the highest levels of cortical CAA

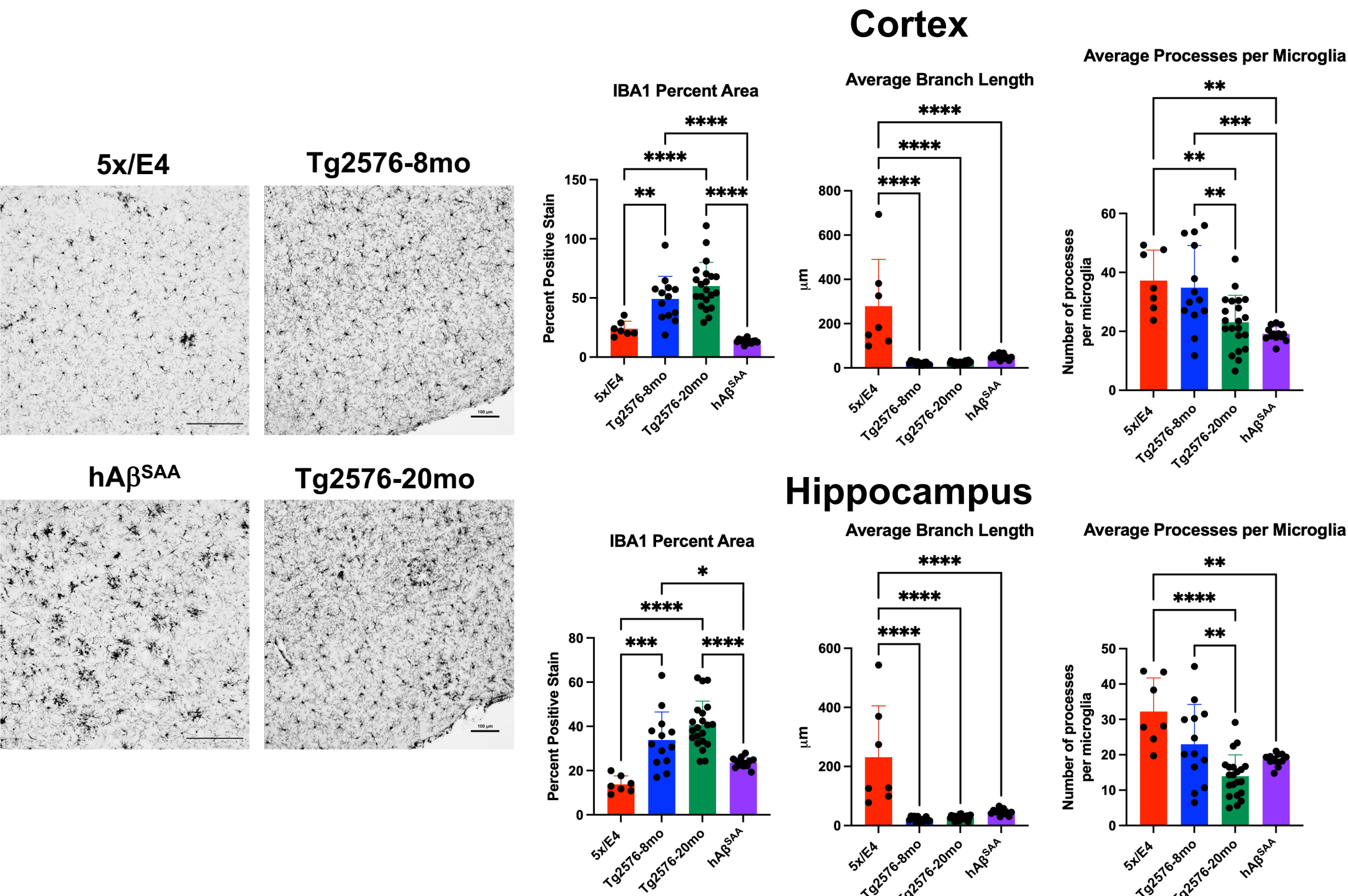


Representative images of Congo red staining in the cortex of 8mo 5x/E4, 8mo Tg2576, 20mo Tg2576 and 22mo hAβ^{SAA} mice. Scale bars = 200µm. Quantification of Congo red staining in the cortex. Tukey post-hoc for multiple comparisons were performed. * P<0.05. **P<0.01. *** P<0.001. **** P<0.0001.

Tg2576 mice and hAβ^{SAA} mice develop similar plaque levels in the hippocampus

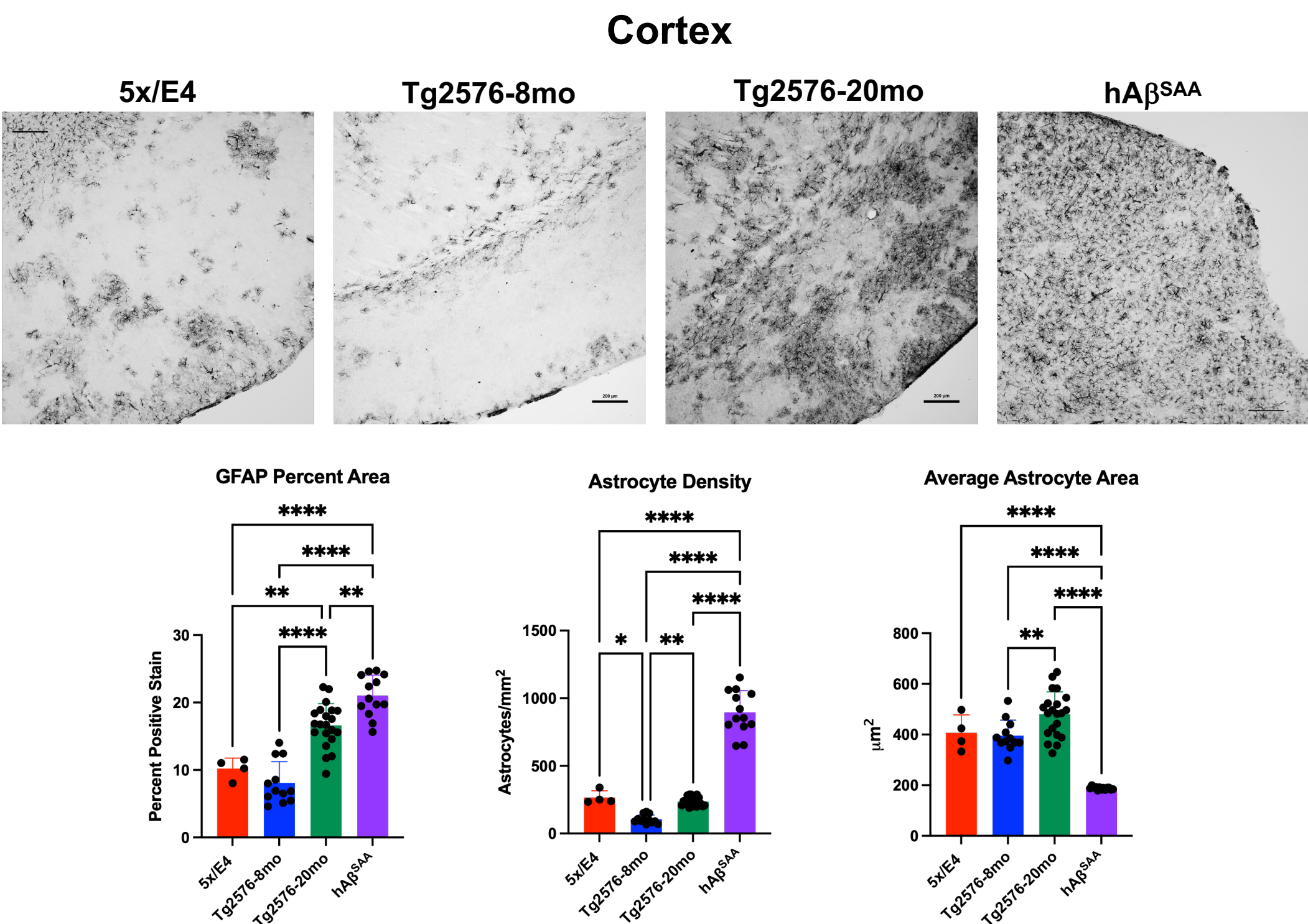


Microglia morphology reflects activation in Tg2576 and hAβ^{SAA} mice



Representative images of IBA1 staining in the cortex of 8mo 5x/E4, 8mo Tg2576, 20mo Tg2576 and 22mo hAβ^{SAA} mice. Scale bar in 5x/E4 and hAβ^{SAA} = 200µm. In Tg2576 = 100µm. Quantification of IBA1 staining in the cortex and hippocampus. Tukey post-hoc for multiple comparisons were performed. * P<0.05. **P<0.01. *** P<0.001. **** P<0.0001.

hAβ^{SAA} mice have high levels of cortical astrocyte activation



Representative images of GFAP staining in the cortex of 8mo 5x/E4, 8mo Tg2576, 20mo Tg2576 and 22mo hAβ^{SAA} mice. Scale bars = 200µm. Quantification of GFAP staining in the cortex. Tukey post-hoc for multiple comparisons were performed. * P<0.05. **P<0.01. *** P<0.001. **** P<0.0001.

Summary

- Tg2576 mice develop the highest levels of CAA as well as the largest plaques.
- While hAβ^{SAA} mice have low CAA levels, they develop multiple smaller plaques than Tg2576 mice.
- 5x/E4 mice have significantly lower levels of IBA1 staining with increased branch length, suggesting homeostatic microglia.
- hAβ^{SAA} mice have significantly higher levels of cortical GFAP staining, due to higher number of astrocytes.

Conclusion

Each mouse model presents differing levels of plaques vs CAA as well as morphology of plaques. The glial responses are also altered due to these differing forms of amyloid deposition. It is critical that we continue to understand underlying pathology in models of Alzheimer's disease to select the correct tool for investigating hypotheses.

Acknowledgements

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