**Sample Extraction:**WT, Abca7-V1599M, 5xFAD and 5xFAD;Abca7-V1599M female and male mice were selected for quantitative immunohistochemical analysis of various markers at 4 and 12 months. At the above ages, mice were euthanized via CO2 inhalation. After intracardial blood collection, mice underwent transcardial perfusion with 1X phosphate buffered saline (PBS). Brains were removed and hemispheres separated along the midline. The right hemisphere was fixed in 4% paraformaldehyde overnight at 4°C and cryopreserved in 10% and later in 30% sucrose.

**Sample Preparation:** 40 μm coronal slices of the right hemisphere was prepared using a sliding microtome with a freezing stage and the tissues were stored in 1X PBS in 12-well plates and kept in 4℃ until further use for immunofluorescent staining. Free-floating sections were washed three times with 1X PBS and for Thiosflavin-S staining, 10 min incubation in 0.5% Thio-S (1892; Sigma-Aldrich, St. Louis, MO) diluted in 50% ethanol followed. Sections were then washed 2X for 5 min each in 50% ethanol and one 10-min wash in 1xPBS. Sections were immersed in normal blocking serum solution (5% normal goat serum with 0.2% Triton X-100 in 1X PBS) for 1 hr before overnight incubation at 4°C in primary antibodies diluted in normal blocking serum solution.

Brain sections were stained following a standard indirect technique as described (Forner et al., 2021; Javonillo et al., 2021) with the following primary antibodies:

* Anti-Iba1 (1:2000; 019-19741; Wako)
* Anti-GFAP (1:1000; AB134436; Abcam)
* Anti-S100β (1:200; AB41548; Abcam)
* Anti-LAMP1 (1:200; AB25245; Abcam)
* Anti-Nfl (1:200; 171 002; Synaptic Systems)
* Anti-OC (1:1000; AB2286; Abcam)

The secondary antibodies (1:200) used are:

* Goat Anti-Rabbit Alexa Fluor 635 (A31577, Invitrogen)
* Goat Anti-Chicken Alexa Fluor 555 (A21437, Invitrogen)
* Goat Anti-Rat Alexa Fluor 555 (A21434, Invitrogen)
* Goat Anti-Rabbit 488 (A11034, Invitrogen)

**Analysis:** High-resolution fluorescence images were obtained using a Leica TCS SPE-II confocal microscope and LAS-X software. For confocal imaging, one field of view (FOV) per brain region (cortex and subiculum) was captured per mouse using the Allen Brain Atlas to capture comparable brain regions. 20X z-stack images were acquired and later analyzed using the Imaris v9.7 software (Biplane Inc. Zürich, Switzerland). Immunohistochemical data were analyzed using Student’s t- test, one-way ANOVA, or two-way ANOVA via Prism v.9 (GraphPad, La Jolla, CA). Bonferroni- Šídák and Tukey’s post hoc tests were utilized to examine biologically relevant interactions from the two-way ANOVA. Where sex-differences are apparent, a Student’s t-test was used within genotype group. \*p ≤ 0.05, \*\* p ≤ 0.01, \*\*\*p ≤ 0.001, \*\*\*\*p ≤ 0.0001. Data are presented as raw means and standard error of the mean (SEM).