



Supplementary Figure 4: The inhibition of carbonic anhydrases attenuates microglial A β accumulation and caspase-3 activation in CA1 area. **A)** Representative immunofluorescence images indicating abundant microgliosis (IBA1, microglia marker in blue), A β (red) deposition and active caspase-3 (green) in Tg animals, rescued by CAIs. Original magnification, 60x. Scale bar, 10 μ m. On the right, microgliosis measured as %IBA1 area per acquisition field. WT, TgSwDI and MTZ: N=5, ATZ: N=4, n \geq 8 measurements/group. Arrows indicate microglial A β accumulation colocalized with active caspase-3. The magnified images show A β within IBA1+ microglia (signals overlap in magenta), microglial caspase-3 activity (signals overlap in cyan), or A β colocalizing with active caspase-3 (yellow). On the right, plots represent the percentage of A β and active caspase-3 signals overlapping with IBA1. For A β /IBA1 overlap. WT, TgSwDI and MTZ: N=5, ATZ: N=4, n \geq 8 measurements/group. For active caspase-3/IBA1 overlap, WT, TgSwDI and MTZ: N=5, ATZ: N=4, n \geq 8 measurements/group. **B)** Representative immunofluorescence images of microglia (IBA1 marker, cyan) for analysis of resting, amoeboid and bushy morphology. On the right, plots represent the different microglial phenotypes in each treatment group, in cortex. WT mice have resting microglia as the most numerous subpopulation. TgSwDI have bushy microglia as most represented microglial type. ATZ- and MTZ-treated mice have similar amounts of resting and bushy microglia. WT, TgSwDI and MTZ: N=5 ATZ: N=4, n \geq 8 measurements/group. **C)** Comparison of cortical resting, amoeboid and bushy microglia between the different groups. The number of resting microglia in MTZ- and ATZ-treated mice is significantly higher than in Tg animals, and is similar to WT mice. The amount of cortical amoeboid and bushy microglia does not change in Tg treated and untreated mice. WT, TgSwDI and MTZ N=5, ATZ N=4, n \geq 8 measurements/group. **D)** Microglia (IBA1+ cells) counts in cortex. TgSwDI and CAIs-treated Tg animals show between 2 and 2.5folds higher number of microglia, compared to WT mice. WT, TgSwDI and MTZ: N=5, ATZ: N=4, n \geq 8 measurements/group. In **(A-D)**, one-way ANOVA and Tukey's post-hoc test: * and + p<0.05, ** and ++ p<0.01, *** and +++ p<0.001, **** and ++++ p<0.0001. Data are expressed as mean \pm SEM.