Title

Flow cytometry detection of inflammatory markers in glial cells and synaptosomes derived from AD cortex

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AAIC 2023 Abstract
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Background: Genetic studies of Alzheimer's disease (AD) have shown association with microglia in the brain. We probed microglia with markers against amyloid-associated (Clec7a, Axl), inflammatory M1 (CD86), alternatively activated M2 (CD206, CD163), and homeostatic (P2ry12, TMEM119) phenotypes in low plaque/tangle pathology controls (A-T-), high plaque/low tangle pathology controls (A+,T-), high plaque/high tangle pathology controls (HPCs) and late AD samples. We sought to determine how these microglial markers changed with clinical and neuropathological AD. *APOE* status was also explored as its associated with increased inflammation (suggesting M1 effects) and *APOE* is highly expressed by amyloid-associated microglia.
Method: Samples of parietal cortex from AD patients were cryopreserved in 0.32M sucrose + inhibitors and obtained from the UC Irvine ADRC. The tissue was later thawed, homogenized in 0.32M sucrose + inhibitors and then slow frozen to -80◦C. These samples were then processed and probed against targets of interest by western blotting.
Result: Preliminary data shows a 64.7% decrease in P2ry12 signal in late AD compared to A-T- controls that approaches significance, although TMEM119 shows no changes. A similar pattern is seen in *APOE4+(APOE3/4 and 4/4)* samples compared to ones that are *APOE3/3*, with P2ry12 showing a significant decrease while TMEM119 showing no change. CD206 shows a 44.8% decrease in late AD samples relative to A-T- controls, though CD163 shows no difference. CD206 and CD163 do not differ between HPC and late AD samples, nor are they modulated by *APOE* genotype.
Conclusion: Preliminary data suggests a decrease of homeostatic microglial signature with the presence of neuropathological, not clinical, AD, although one of the markers, TMEM119, showed no change. TMEM119 and P2ry12 are interesting markers of homeostasis that were characterized in mouse models of AD yet may have a more complicated connection to human disease (Zhou et. al., 2020). M2 microglial marker CD206 shows an increase with neuropathological, but not clinical, AD. Again, a complicated picture of M2 markers is seen, with CD206 showing change but not CD163. *APOE* genotype differences modulated the P2ry12 homeostatic signal, although no M2 changes were seen.