Characterizing the Role of Trem2 in Alzheimer's Disease (AD)

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Alzheimer’s disease (AD) is a neurodegenerative disorder characterized pathologically by amyloid-beta plaques. Variants in the Trem2 gene confer increased risk for developing AD. Myeloid cells can alter AD pathology through inflammation or plaque clearance. It was previously found in Trem2 WT and KO AD mouse models that Trem2 is expressed on plaque-associated myeloid cells and is necessary for the recruitment of myeloid cells to plaques. We explored mechanisms in Trem2 WT and KO AD models as potential explanations for reduced myeloid-cell number around plaques. Cell proliferation was measured using bromodeoxyuridine (BrdU). Using immunohistochemistry (IHC), brain tissue was co-stained for BrdU and the immune-cell marker Iba1. Colocalization was measured in the cortex and the hippocampus, brain regions where amyloid pathology is prevalent. Colocalization was significantly reduced in both the hippocampus ($p<0.01$) and cortex ($p<0.001$). Cell death was similarly quantified with IHC using Cleaved-caspase 3, a cell-death marker, and Iba1. While there were no significant differences, there was a strong trend towards increased cell death in the KOs. These findings suggest that reduced myeloid-cell numbers in the KOs is at least partially explained by both reduced proliferation and increased death of myeloid cells. Next, we assessed if change in myeloid-cell number affected general myeloid-cell functions related to AD. Phagocytosis between the two models was examined using a slice-phagocytosis assay, which measures phagocytosis of florescent beads in live-brain cells, however there was no significant change in phagocytosis between the KO and WTs. Understanding how Trem2 affects myeloid-cell number and phagocytosis may help to elucidate Trem2’s role as an AD risk factor.

Awards Won: