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MEETING ABSTRACT

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CD8$^+$ T-cell-mediated contribution to neuropathology in a transgenic Alzheimer's disease mouse model

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Background: Neuroinflammation is a major contributor to disease progression in Alzheimer's disease (AD) and is characterized by the activity of brain-resident glial cells, in particular microglia cells, and by the infiltration of peripheral immune cells. The role of T lymphocytes in the AD brain and their beneficial or detrimental contribution to AD pathology are still controversially discussed. We recently identified CD8$^+$ T cells in the brain parenchyma of APP-PS1 transgenic mice forming strong immune interactions with microglia.
Methods: To address their functional relevance in AD, we ablated the pool of CD8$^+$ T cells from APP-PS1 transgenic mice for a total of 4 weeks using an anti-CD8 antibody treatment.
Results: Here, we demonstrate successful ablation of the CD8$^+$ T-cell pool in the blood and from the brains of the animals. While there were no changes in plaque pathology and only minor changes in neuroinflammation, RNASeq analysis revealed highly altered neuronal gene expression in the hippocampus of CD8$^+$ T-cell-ablated APP-PS1 transgenic mice. We identified a variety of significantly differentially expressed genes in APP-PS1 mice treated with anti-CD8 antibody. Gene expression for immediate early genes (IEGs) such as activity-regulated cytoskeleton-associated protein (Arc) and neuronal PAS domain protein 4 (Npas4) was upregulated in APP-PS1 transgenic mice lacking CD8$^+$ T cells in the brain. Gene ontology enrichment analysis revealed that biological processes such as "neuronal synaptic plasticity" were over-represented in the hippocampus upon CD8$^+$ T-cell ablation.
Discussion: Therefore, we assume that CD8$^+$ T cells contribute to neuronal dysfunction in modulating synaptic plasticity along AD. Further analysis will be essential to uncover the exact mechanism of how CD8$^+$ T cells contribute to AD pathology and to develop new treatment options.
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