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# CIRCADIAN REGULATION OF MICROGLIAL FUNCTION IN ALZHEIMER'S DISEASE

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Alzheimer's Disease (AD) is the most common form of dementia and carries age as its number one risk factor. Neuronal damage caused by inflammation and oxidative stress are consistent hallmarks of AD. Microglia, the chief immune cells of the central nervous system, are principal contributors to, and under certain conditions can exacerbate, these effects. Furthermore, disruption of circadian rhythms and the molecular clock of CNS cells have been linked to the development and progression of AD. Thus, investigating circadian rhythm dysfunction in microglia and its impact on AD could elucidate the role of microglia in the neurodegeneration seen in AD.

To disrupt the microglial circadian clock, we used a microglial specific (Cx3cr1-linked) Cre recombinase to excise and knock out microglial *Bmal1*, a core clock gene, causing total loss of microglial molecular clock rhythms throughout the CNS. This Cre lineage was crossed to AD model mice (PS1/APP transgenic) and all mice were aged to 16-18 months. We quantified gene expression of various inflammatory and oxidative stress markers in cortical tissue via RT-qPCR. We then measured astrocyte and microglial activation and evaluated amyloid beta (A $\beta$ ) plaque load via immunohistological staining of brain tissue slices. In the PS1/APP-Cre+ mice, there was elevated expression of cytochrome b-245, beta chain (Cybb or NOX2), an oxidative stress marker, relative to that of the PS1/APP-Cre- mice. This suggests a potential role for the microglial circadian clock in regulating the oxidative stress response in AD.