



## **MICROGLIA RESISTANCE TO CSF1R INHIBITION**

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### Abstract

Microglia are immune cells that reside in all parts of the brain. Microglial survival depends on signaling through Colony Stimulating Factor 1 Receptor (CSF1R). However, there may be a subpopulation of unique microglia that survive without this signaling. We hypothesize that some microglia will still be present after CSF1R signaling is blocked, specifically residing in white matter tracts of the brain, which is where myelinated axons reside. After administration of an inhibitor of CSF1R signaling to Cx3cr1-GFP mice in which microglia are GFP labeled, we did find a subpopulation of microglia still present predominately in white matter tracts of corpus callosum and cerebellum. In contrast, CSF1R inhibition resulted in cell death for most microglia in the hippocampus and cerebral cortex. These data suggest that these cells represent a unique subpopulation that may be performing a distinct function.

### Introduction

Microglia are the resident immune cell of the central nervous system (CNS). Microglia have important functions during development<sup>1</sup>. In adult brain, microglia rely on a tyrosine kinase signaling pathway through colony stimulating factor 1 receptor (CSF1R) to survive<sup>2</sup>. Unpublished research from the Vetter Lab has shown that most microglia in the postnatal mouse retina do not require CSF1R signaling for survival and express a unique set of genes. A subset of microglia in the white matter tracts of the brain express similar genes<sup>3</sup>. Thus, we hypothesized that a subpopulation of CSF1R-independent microglia is present in the developing white matter tracts of the brain and that CSF1R independence may be linked to the expression of select genes.

### Hypothesis

We hypothesize that a subpopulation of microglia cells will survive CSF1R inhibition, and specifically reside in white matter tracts of the brain.

### Results/Conclusions

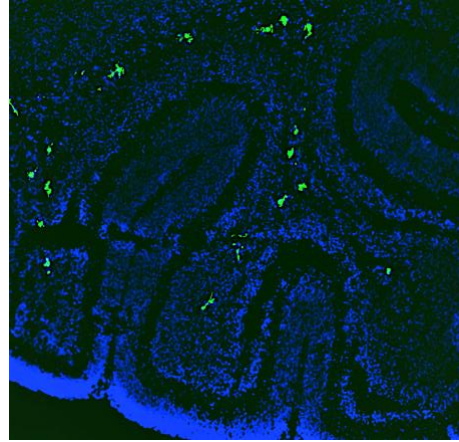
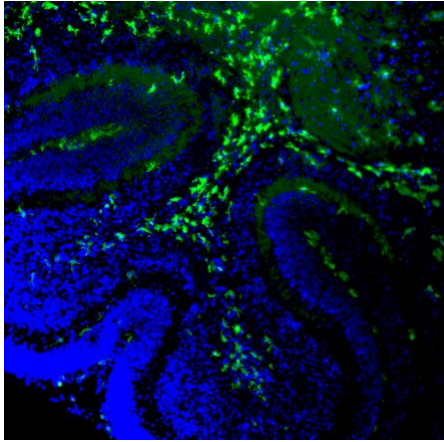
There is heterogeneity in developing brain microglia, with differences in CSF1R dependence across brain regions. Microglia in postnatal retina and brain white matter share similarities and may be performing related functions. More specifically, I have found that treatment with the CSF1R inhibitor PLX reduces brain microglia density, however, I observed a number of cells remaining in specific regions. Microglia in the white matter tracts of the brain, seem to be more resistant to inhibition of CSF1R at postnatal time periods.

Dapi = nuclei  
GFP = microglia

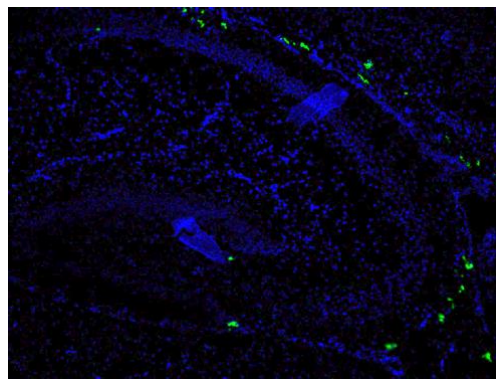
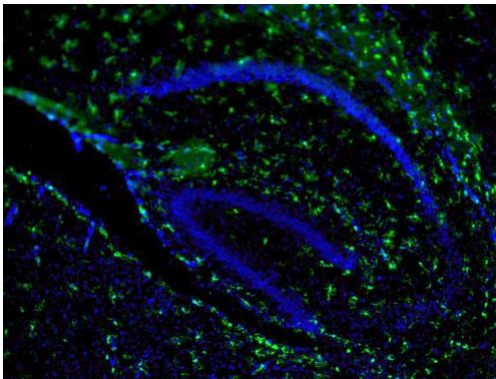
Vehicle

CSF1R Inhibitor

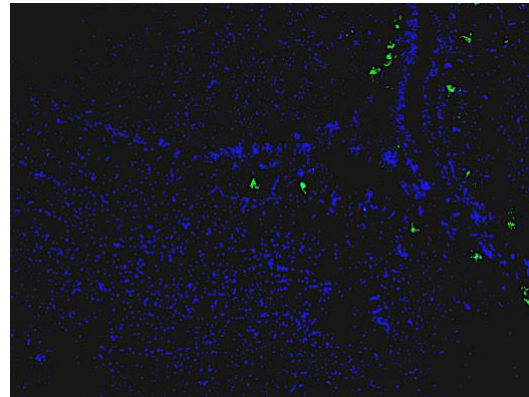
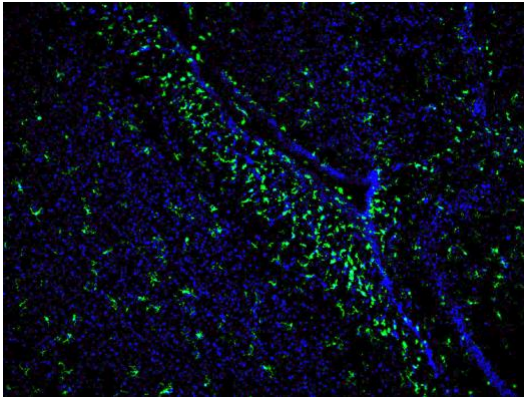
Cerebellum



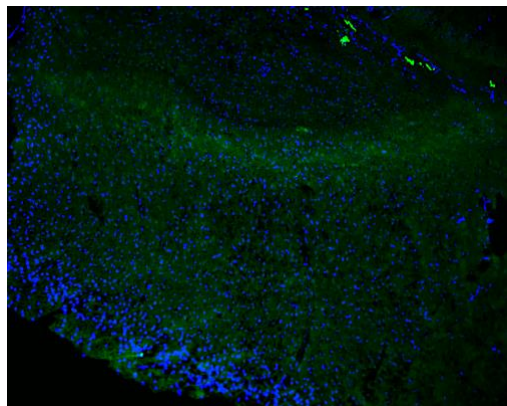
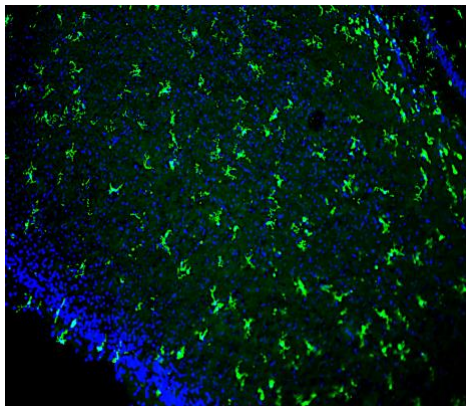
Hippocampus



Corpus  
Callosum



Cerebral  
Cortex



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