

MARK4 ablation suppresses MHC class II-associated microglial responses in a tauopathy mouse model

#1229

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Key findings: *Mark4* deletion suppresses MHC-II-associated microglial activation and mitochondrial gene signatures in PS19 mice.

Background

We previously showed that deletion of *Mark4* attenuates tau pathology, neurodegeneration, and behavioral deficits in PS19 tauopathy model mice (Sultanakhmetov et al., 2024). However, the cell-type-specific effects of MARK4 loss remain unclear.

Methods

Single-cell RNA-seq analysis

Fixed cortical cells from four mice/genotype were analyzed using the 10x Genomics Chromium Flex platform. Data were processed with Cell Ranger and Seurat.

qPCR analysis of isolated microglia

CD11b-positive microglia were isolated by magnetic sorting and analyzed by qPCR.

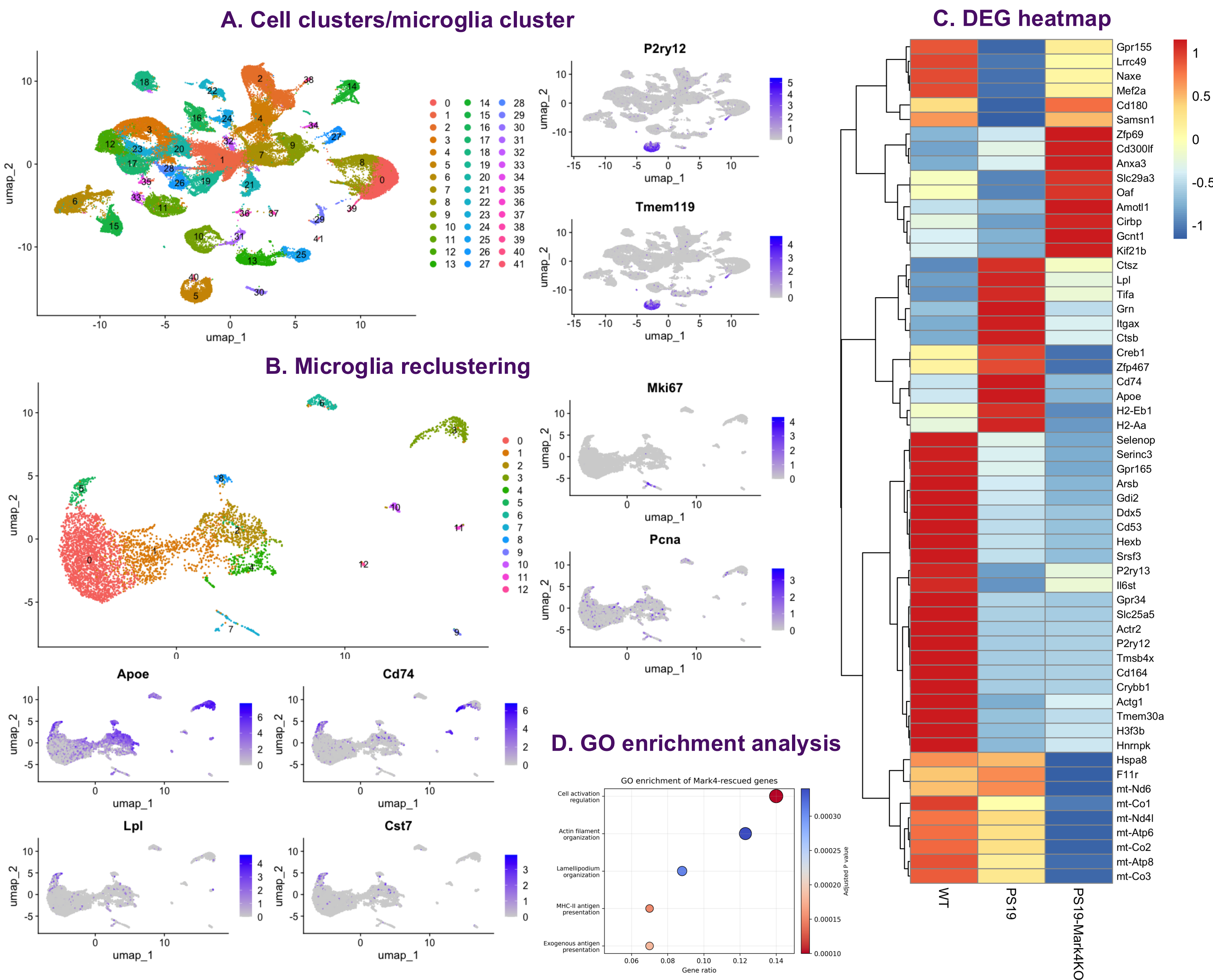
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Results

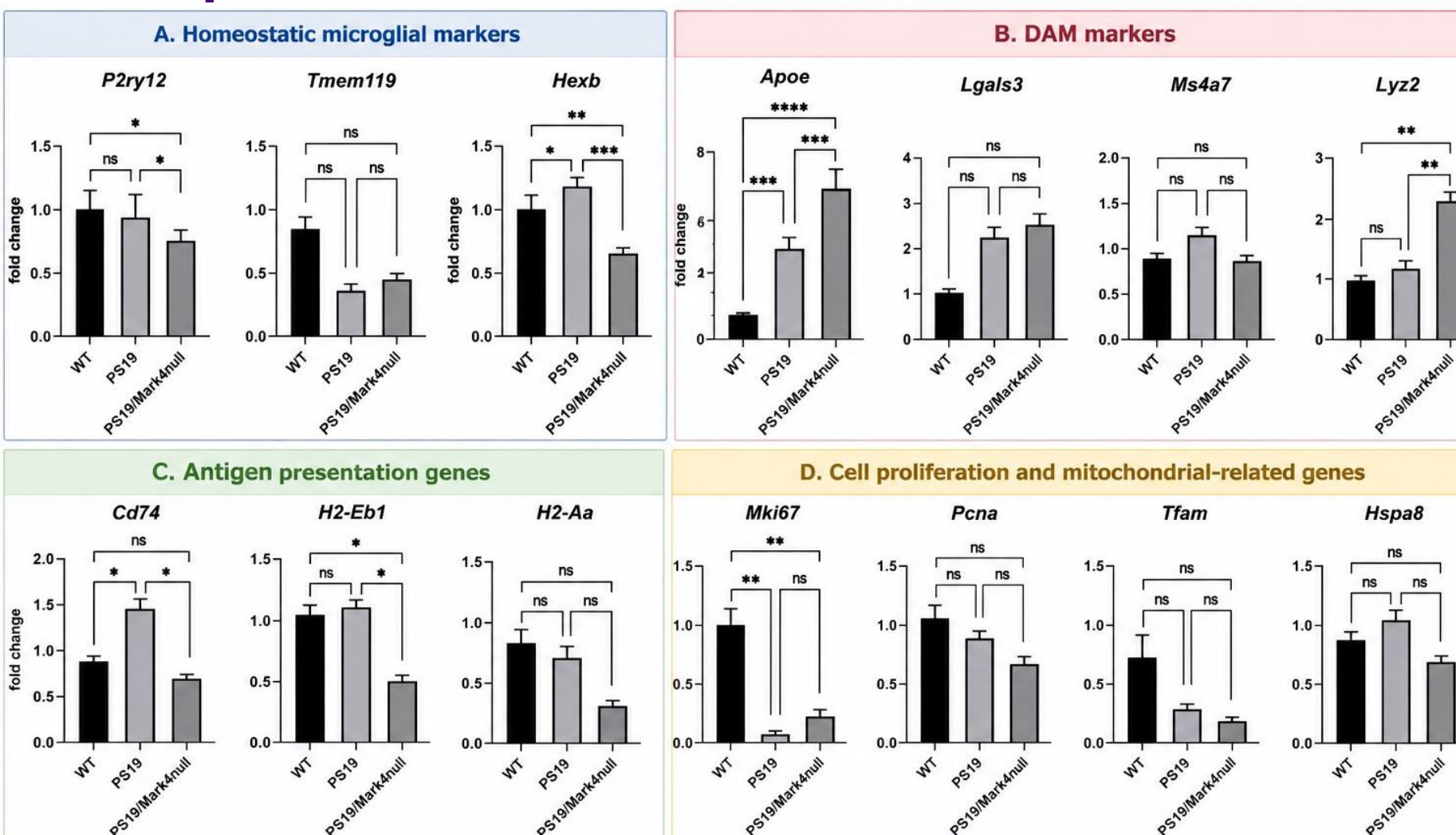
Single-cell RNA-seq identifies reduced MHC-II-associated microglial activation after *Mark4* deletion

Figure 1. Single-cell RNA-seq revealed disease-associated microglial subpopulations and reduced MHC-II antigen presentation after *Mark4* deletion.



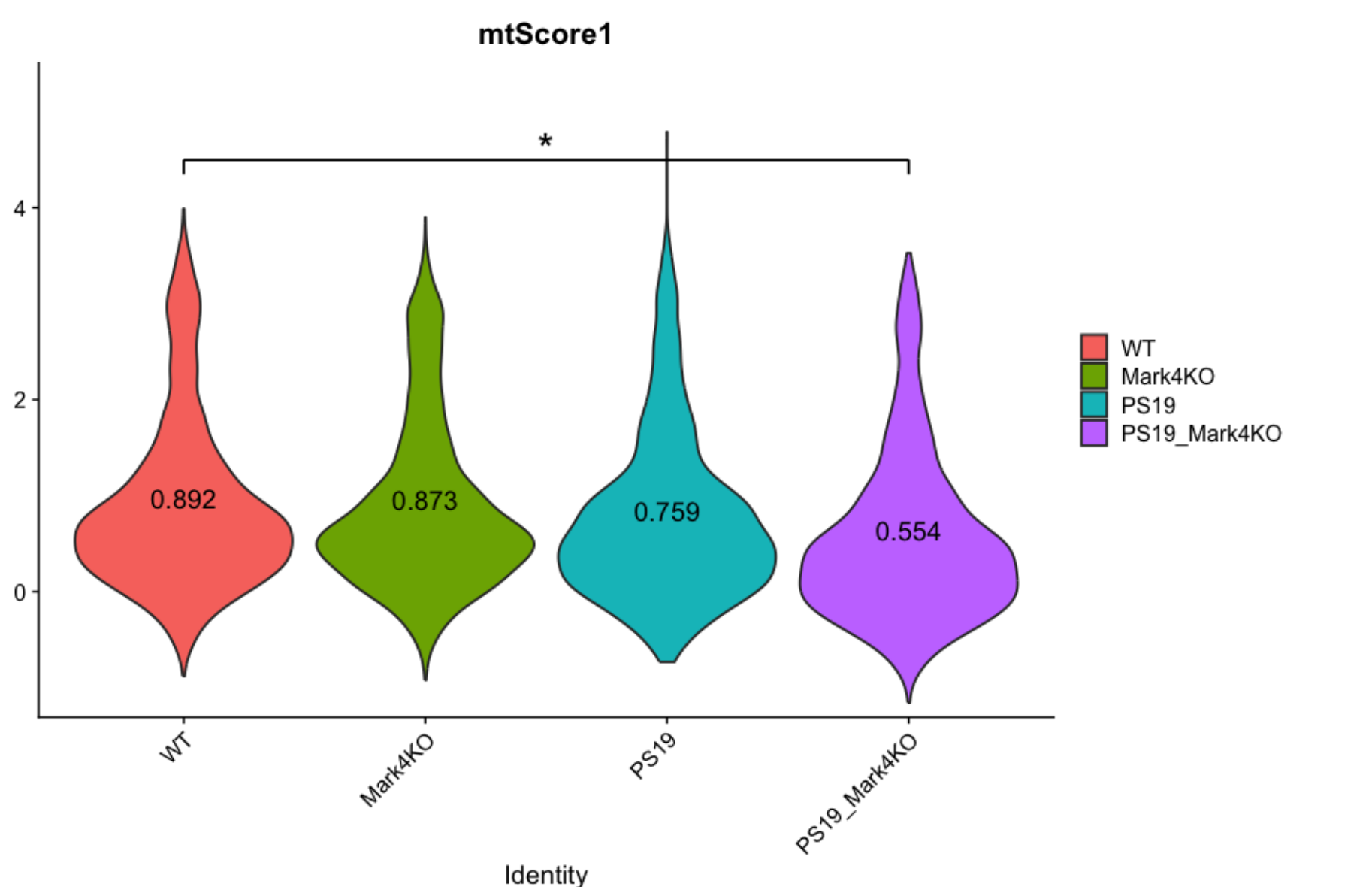
qPCR validation

Figure 2. qPCR confirmed reduced Cd74 and H2-Eb1 expression after *Mark4* deletion.



Mitochondrial gene signature

Figure 3. *Mark4* deletion reduced mitochondrial gene signature scores in PS19 microglia.



Conclusions

- *Mark4* deletion reduced expression of MHC-II-associated genes.
- qPCR validated reduced Cd74 and H2-Eb1 expression.
- *Mark4* deletion reduced mitochondrial gene signatures associated with microglial activation.

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