MicrogliaTRAP

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TREM2 Expression Analysis Across Hypothalamic Regions

Methods

TREM2 expression was analyzed across different hypothalamic regions using single-nucleus RNA sequencing data. Following quality control and normalization, we performed integrated analysis of multiple datasets (Figure 1).

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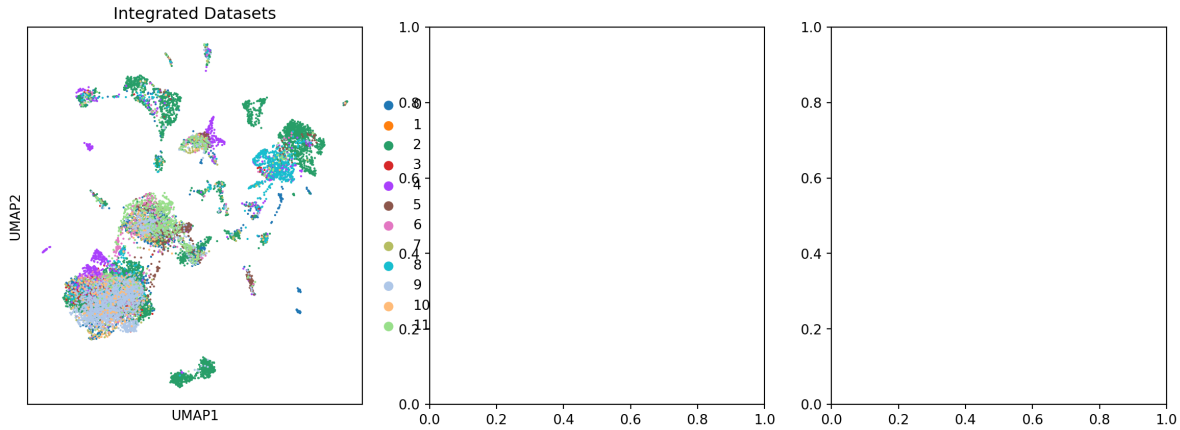

Figure 1: Analysis of batch-corrected microglial data. (A) UMAP visualization after integration shows reduced batch effects. (B) Refined clustering based on integrated data reveals distinct microglial subpopulations. (C) Distribution of cells by hypothalamic region demonstrates regional heterogeneity of microglia.

Initial clustering revealed distinct microglial populations across hypothalamic regions, which were further refined through batch correction and integration of multiple datasets.

Results

Regional Expression Patterns

Analysis of TREM2 expression revealed significant heterogeneity across hypothalamic regions (F = 302.35, p = 2.58e-4). Figure 2 shows the distribution of TREM2 expression across different regions.
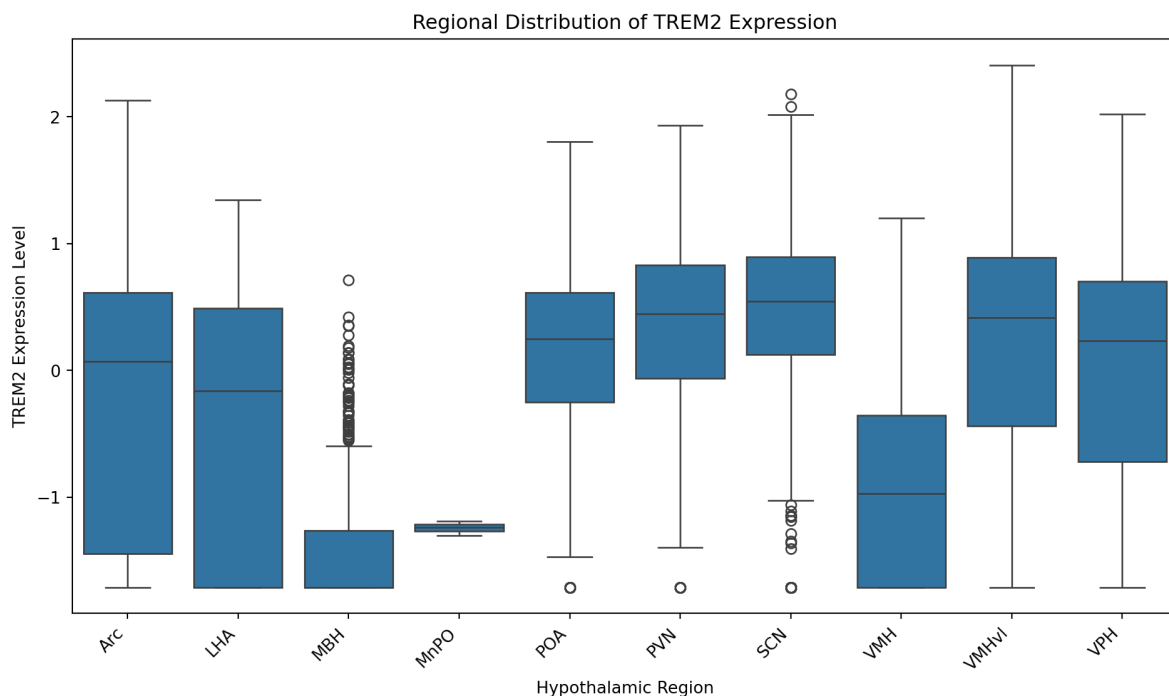

Figure 2: TREM2 expression levels across different hypothalamic regions. Box plots show the median, quartiles, and distribution of TREM2 expression in each anatomically distinct region. Whiskers extend to 1.5 times the interquartile range.

The highest TREM2 expression was observed in the SCN (mean = 0.436 ± 0.689), followed by the PVN (0.296 ± 0.799). In contrast, the MBH showed the lowest expression (-1.376 ± 0.604), followed by the MnPO (-1.241 ± 0.057).

Cluster-Specific Expression

TREM2 expression varied significantly across microglial clusters (Figure 3), suggesting functional heterogeneity within the microglial population.
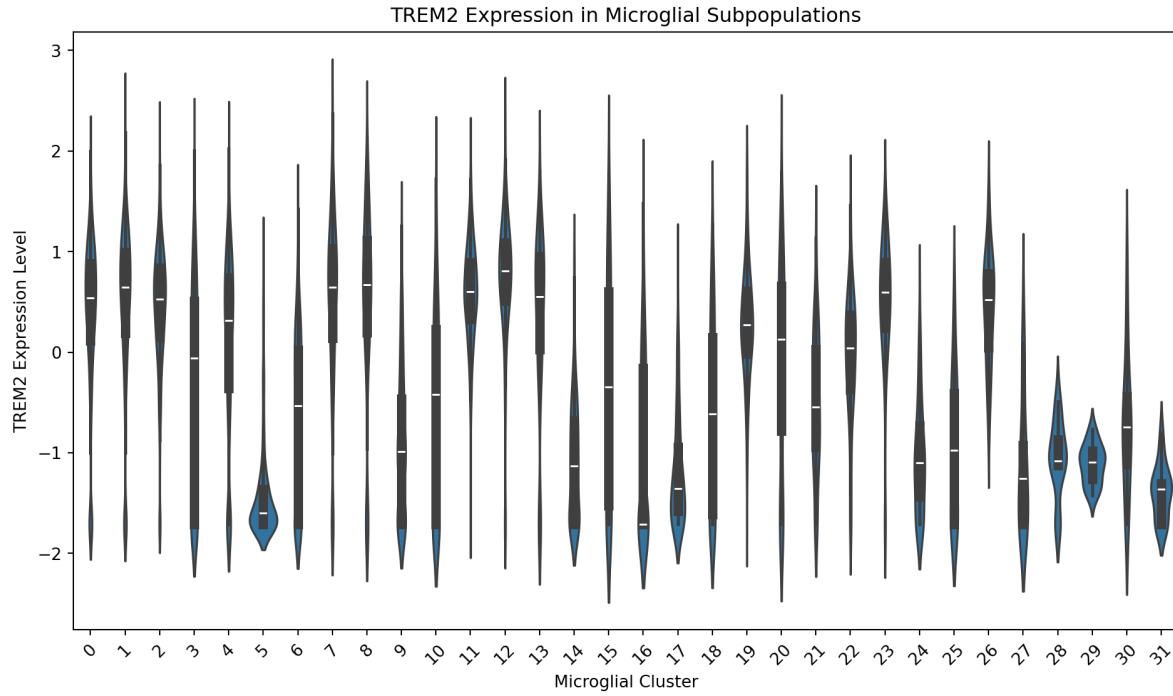
Figure 3: Distribution of TREM2 expression across identified microglial clusters. Violin plots demonstrate the full distribution of expression levels within each cluster, with embedded box plots showing median and quartile values.

Spatial Distribution

UMAP visualization of TREM2 expression (Figure 4) revealed distinct spatial patterns, indicating regional specialization of TREM2-expressing microglia.
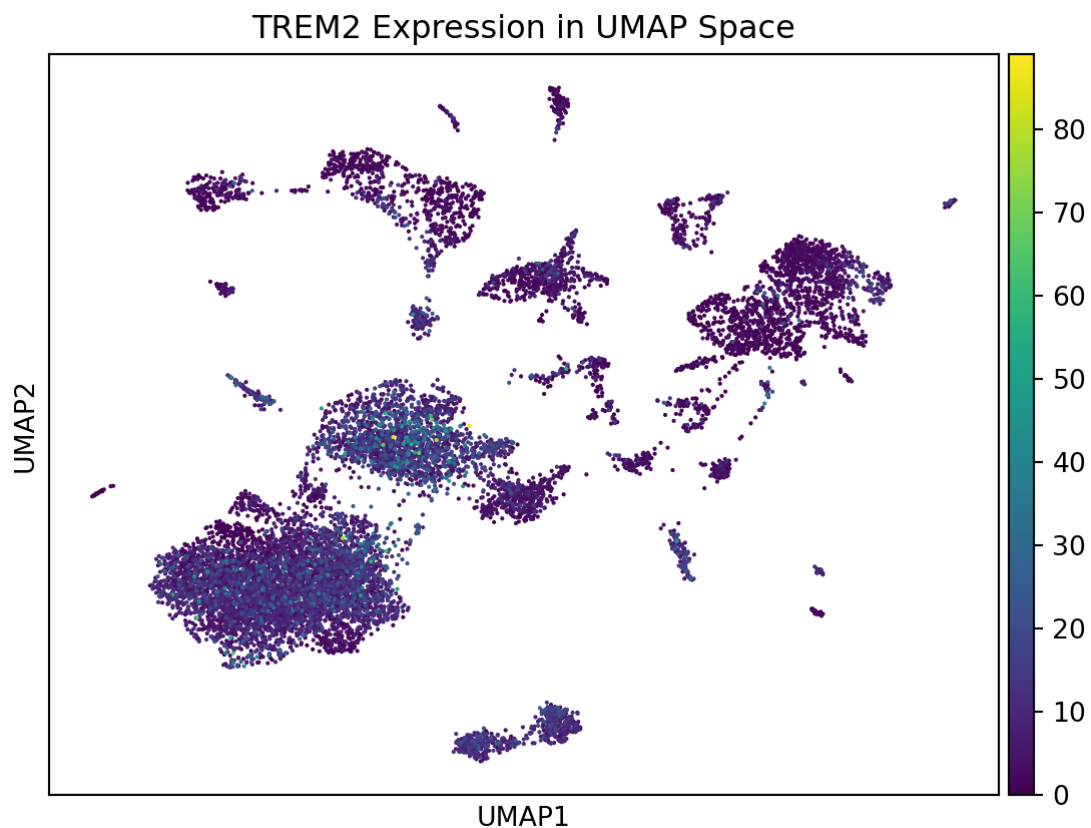
Figure 4: UMAP visualization of TREM2 expression across all microglia. Color intensity represents TREM2 expression level, showing the spatial distribution of TREM2-expressing cells in the reduced dimensional space.

Gene Co-expression Analysis

To understand the regulatory network associated with TREM2, we analyzed its correlation with other microglial markers (Figure 5).
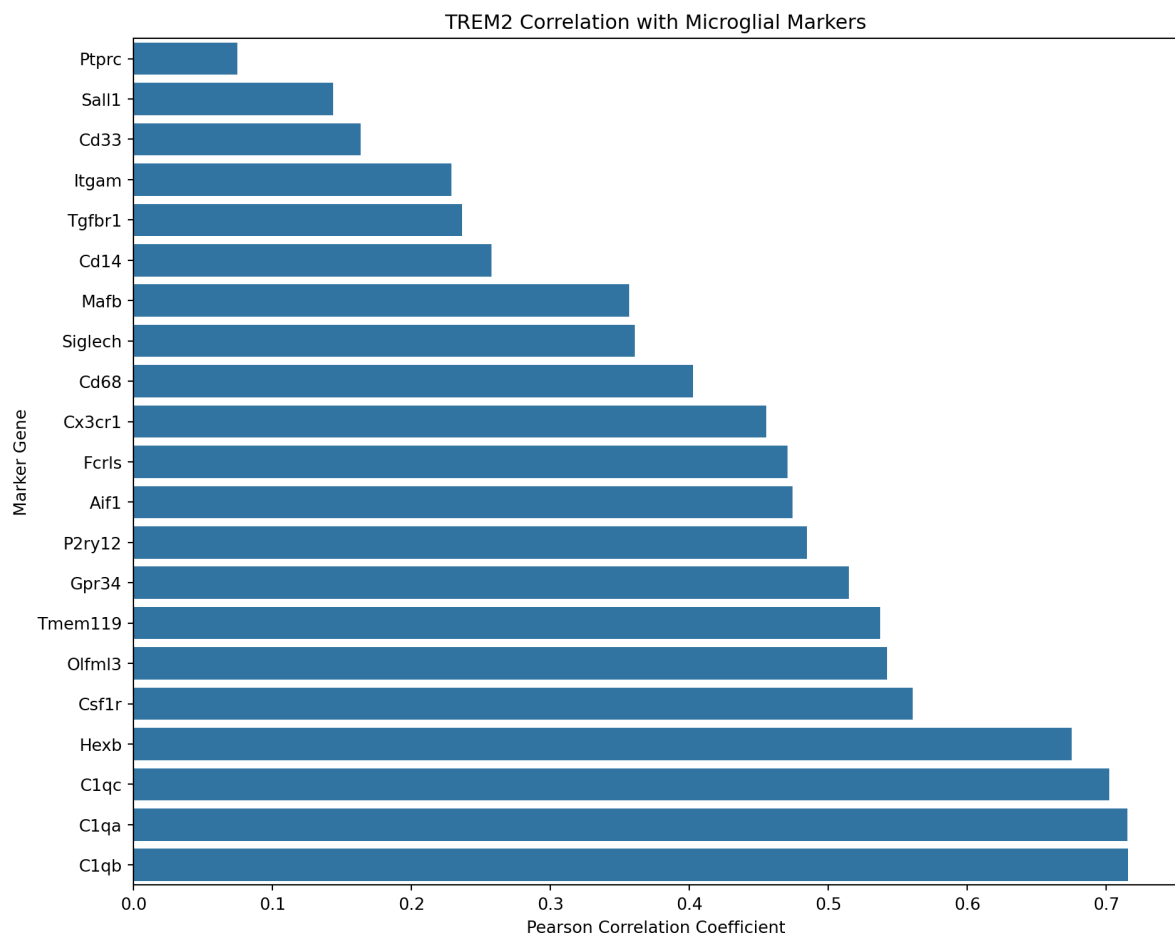
Figure 5: Correlation analysis between TREM2 and other microglial marker genes. Bar plot shows Pearson correlation coefficients, ordered by strength of correlation. Positive values indicate positive correlation, while negative values indicate inverse relationships.

Regional and Cluster-Specific Patterns

The heatmap analysis (Figure 6) revealed distinct patterns of TREM2 expression across both regions and clusters.

Figure 6: Regional and cluster-specific TREM2 expression patterns. Heatmap shows mean TREM2 expression levels across different microglial clusters (rows) and hypothalamic regions (columns). Color intensity represents expression level, with darker colors indicating higher expression.

Molecular Interactions

The co-expression network analysis (Figure 7) identified key molecular interactions of TREM2 with other genes.
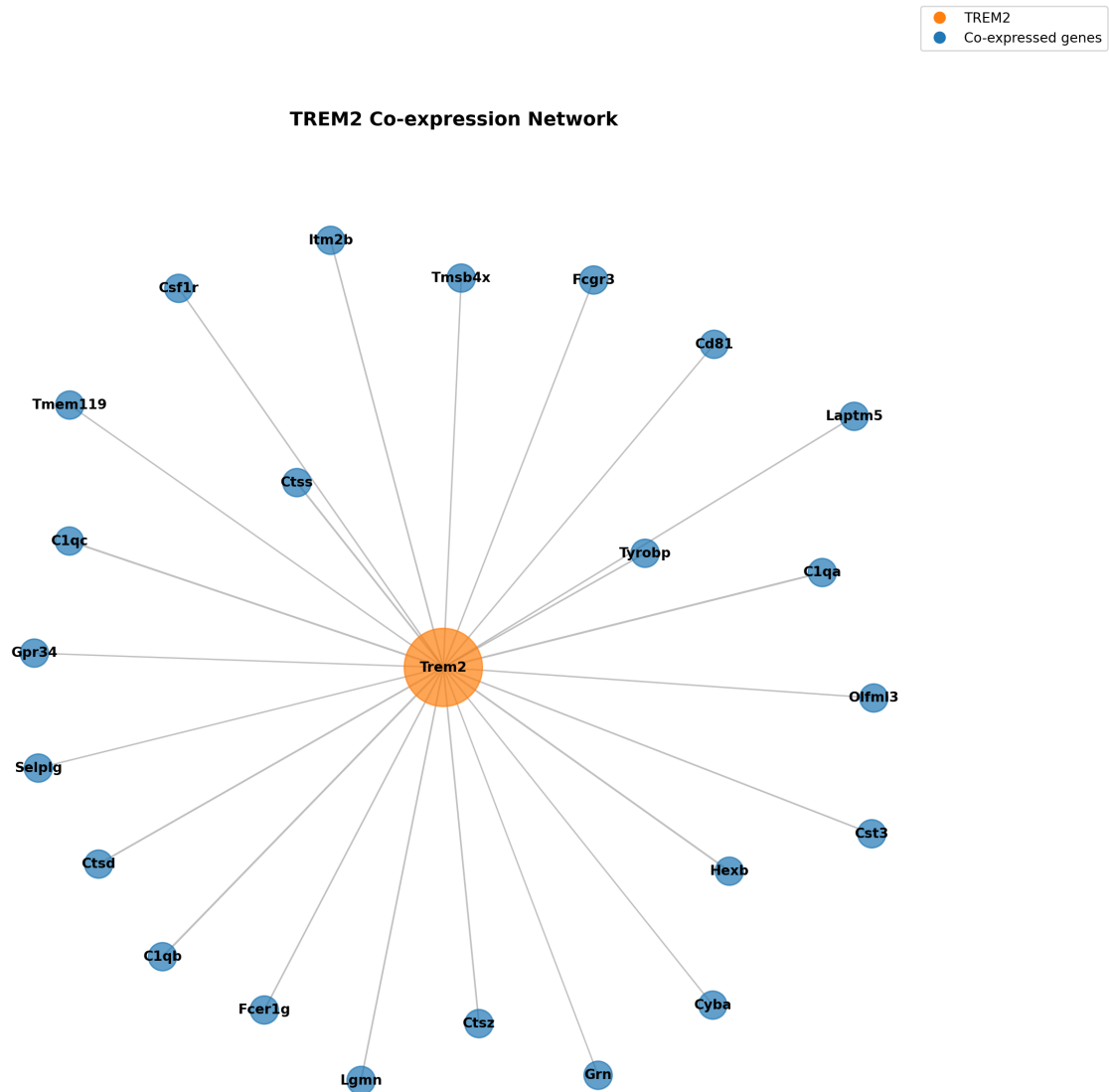
Figure 7: TREM2 co-expression network in hypothalamic microglia. Nodes represent genes, with TREM2 as the central hub. Edge weights represent the absolute Pearson correlation coefficient between gene pairs. Only correlations above 0.3 are shown.

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Network Statistics:
Number of co-expressed genes: 23
Number of connections: 23
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Network Metrics:
Network density: 0.083
Average clustering coefficient: 0.000
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Statistical Analysis

Statistical comparison across regions (Figure 8) revealed three distinct TREM2 expression domains:
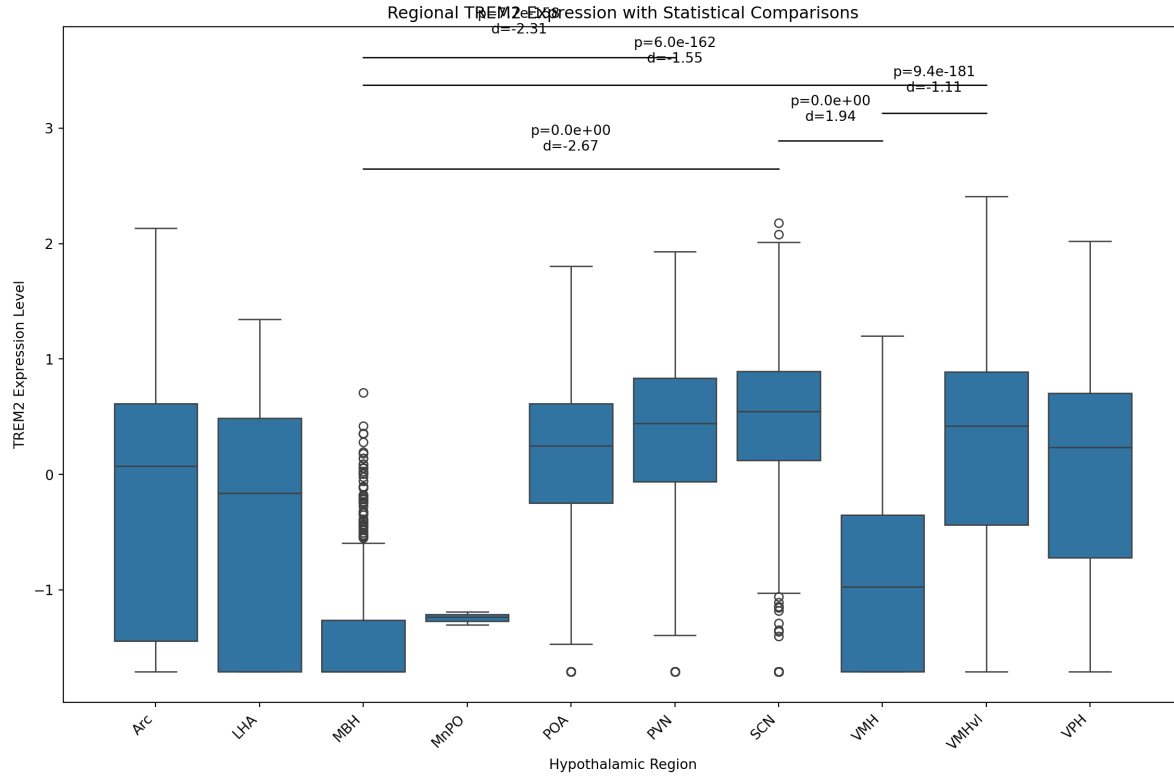

Figure 8: Statistical comparison of TREM2 expression across hypothalamic regions. Box plots show the distribution of TREM2 expression levels in each region. Significance bars indicate the top 5 most significant pairwise comparisons (FDR-corrected p-values). Cohen's d effect sizes are shown for each comparison, quantifying the magnitude of expression differences between regions.

1. High expression domain: SCN, PVN, VMHvl (means > 0.1)
2. Intermediate expression domain: POA, VPH, Arc (means between -0.3 and 0.1)
3. Low expression domain: MBH, MnPO, VMH (means < -0.9)

The most significant differences were observed between: - MBH and SCN (Cohen's d = -2.67, p-adj < 1e-300) - SCN and VMH (Cohen's d = 1.94, p-adj < 1e-300) - MBH and PVN (Cohen's d = -2.31, p-adj = 7.73e-158)

Interpretation

The observed regional heterogeneity in TREM2 expression suggests region-specific roles for microglial TREM2 signaling. The high expression in SCN and PVN, regions crucial for circadian rhythm and neuroendocrine function, indicates potential involvement of TREM2 in these processes. The co-expression analysis reveals potential molecular mechanisms through which TREM2 might influence microglial function in different hypothalamic regions.

These findings provide a comprehensive map of TREM2 expression across hypothalamic regions and suggest potential region-specific functions of TREM2-expressing microglia in the hypothalamus.