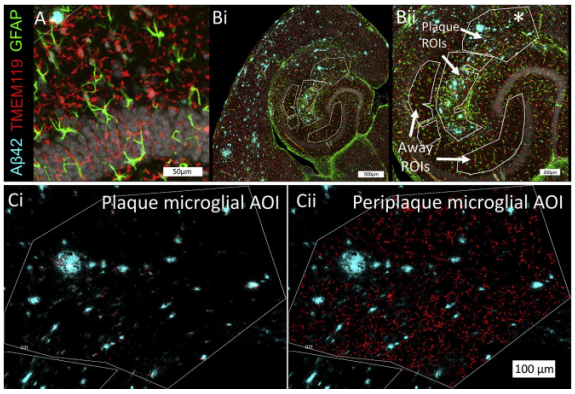
The microglial response to amyloid pathology depends on proximity to plaques and Trem2 expression

Background

- Several variants of TREM2 have been shown to increase the risk of developing Alzheimer's
- TREM2 pushes microglia an anti-inflammatory phagocytic phenotype and has been reported to be instrumental in the increased density of microglia around plaques
- The App$^{NL\text{-}F/NL\text{-}F}$ (NLF) mouse is a better model of sporadic AD than the more commonly used NLGF mouse because plaques develop later in life in the NLF mouse

Research Question

Does gene expression differ in microglia based on proximity to Ab plaques?



Experimental Setup

Instrument	GeoMx® DSP
Sample Type	FFPE
Tissue Type	Mouse Brain
Assay	Mouse Whole Transcriptome Atlas
Analytes	RNA
Readout	NGS

"With the introduction of spatial cell type-enriched transcriptomics, more subtle and direct analysis of plaque-induced microglial gene expression changes becomes possible, without the diluting effects of bulk analysis."

-Wood et al.

Geometric regions of interest (ROIs) were selected based on positive or negative staining for Ab plaques and were further segmented based on colocalization of microglia with Ab within or outside of a region with plaques. Figure reproduced with permission from Wood et al. Cell Rep. 2022 Nov 22;41(8):111686 under the **Creative Commons license.**

Results & Conclusions

- Expression of 38/55 plaque-induced genes (PIGs) have plaque-induced microglial upregulation, with a subset only upregulating in microglia directly contacting plaques.
- For seven PIGs, including Trem2, this upregulation is prevented in APP$^{NL\text{-}F/NL\text{-}F}$Trem$^{2R47H/R47H}$ mice.
- These TREM2-dependent genes are all involved in phagocytic and degradative processes that correspond to a decrease in phagocytic markers and an increase in the density of small plaques in Trem2-mutated mice.
- TREM2 protein levels and microglial density are still marginally increased on plaques.
- Microglial contact with plaques and functioning TREM2 are necessary for microglia to respond appropriately to amyloid pathology.

Wood et al. Cell Rep. 2022 Nov 22;41(8):111686. ***https://doi.org/10.1016/j.celrep.2022.111686***

For more information, please visit nanostring.com/geomx

NanoString Technologies, Inc.
530 Fairview Avenue North
Seattle, Washington 98109
T (888) 358-6266
F (206) 378-6288
nanostring.com
info@nanostring.com

Sales Contacts
United States **us.sales@nanostring.com**
EMEA: **europe.sales@nanostring.com**
Asia Pacific & Japan **apac.sales@nanostring.com**
Other Regions **info@nanostring.com**

MARCH 2023 MK55484