The role of microglia-oligodendrocyte interactions and the Type II Interferon Pathway in impaired myelination in the brain

Background

- Myelination of neuronal axons is required for optimal health and function of the CNS and many white matter disorders of the brain involve myelination.
- Oligodendrocytes are the myelinating cells of the CNS.
- In the human infant brain, microglia have been observed to be present in areas of poor myelination although the mechanism by which these cells are involved is not understood.

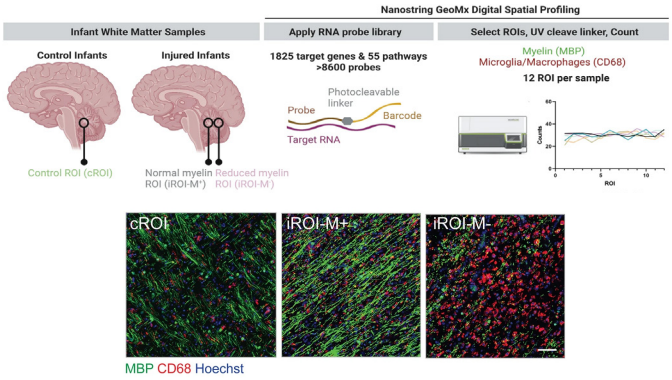
Research Question

What is the molecular mechanism underpinning the failure of developmental myelination, specifically in the human brain?

Experimental Setup

Instrument	GeoMx® DSP
Sample Type	FFPE
Tissue Type	Human Infant Brain
Assay	Cancer Transcriptome Atlas
Analyte	RNA
Readout	NGS

A comprehensive unbiased spatial transcriptomic analysis of human developing white matter with GeoMx DSP allowed for the identification of potential biomarkers for poor myelination.



Regions of interest (ROIs) were identified based on fluorescent antibody staining of myelin and inflammation markers. ROIs were taken from healthy control brain (cROI) and injured brains (iROI). In the injured brain, ROIs were taken from both normally myelinating regions (iROI-M+) and regions with reduced myelination (iROI-M-). Figure reproduced with permission from Holloway et al. Acta Neuropathologica Communications. (2023) 11:49 under the ***Creative Commons license.***

Results & Conclusions

- Oligodendrocyte progenitor cells were significantly reduced in injured brains compared to normal control brains.
- Oligodendrocyte maturation is not impaired in poorly myelinating regions but rather the ability to appropriately form myelin is affected.
- A molecular signature of myelination failure in the developing CNS of humans was identified.
- Interferon responsive microglia influence myelinating oligodendrocytes via an IFN-gamma independent mechanism.
- Enhanced Type II interferon signaling in microglia/macrophages is spatially associated with human developmental myelination.
- Osteopontin (SPP1) was identified as a potential biomarker of poor myelination in human developing white matter.

Holloway et al. Acta Neuropathologica Communications. (2023) 11:49. ***https://doi.org/10.1186/s40478-023-01543-8***

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**

FEB 2024 MK6279