Stem Cell Biology and Transcriptomics of Human White Matter Diseases

September 20

Tuesday, 12:30pm

Hybrid: Rosedale Room and Zoom

For Researchers

Speaker:

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Abstract

Multiple sclerosis (MS) is a common, debilitating, progressive and fatal neurological disease that targets myelinating oligodendrocytes. Although most likely driven by an autoimmune response, the effector mechanisms that cause inflammation and that lead to neurodegeneration are incompletely understood. Treatment options are limited and do not prevent the progressive phase. This talk will cover molecular, temporal and cellular diversity of glial cells in CNS development, and apply this perspective to understand what goes wrong in MS disease progression that: (1) causes inflammation in the brain, (2) death of neurons and brain shrinkage and (3) how to potentially enhance repair of lesions. In an effort to find biomarkers of disease progression and targets for new therapies, we have used transcriptomic approaches, stem cell models of oligodendrocyte disease that have highlighted a role for iron toxicity in cells of the oligodendrocyte lineage.

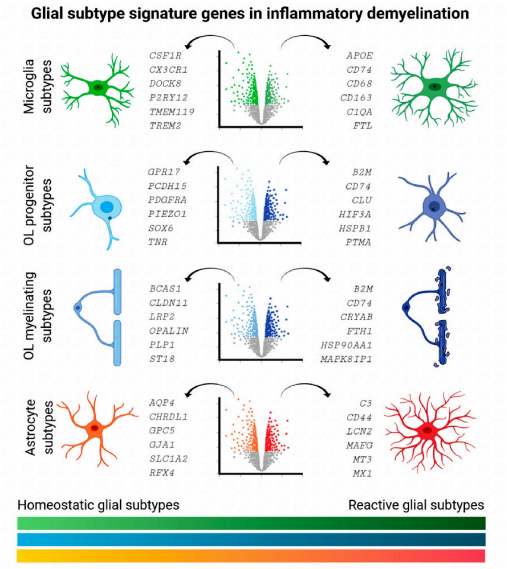

Figure 3. Human Transcriptomic Marker Genes Characterizing Homeostatic and Reactive Glial Subtypes.
Cartoon lists homeostatic (left) versus reactive (right) glial subtype signature genes by means of volcano plot visualization. Marker genes were selected by their specific enrichment in microglia, oligodendrocyte (OL) precursor, and myelinating cells, as well as astrocytes based on recent single-cell/nucleus RNA-sequencing (sc/snRNA-seq) studies from human control and multiple sclerosis (MS) tissues. See Boxes 2-4 in the main text for details about signature genes and their functional relevance. Note color spectrum on the bottom illustrates dynamic changes in gene expression between homeostatic and reactive glial subtypes according to cell type color code. This figure was created using BioRender (https://biorender.com/).

1. Diversity and Function of Glial Cell Types in Multiple Sclerosis. Schirmer L, Schafer DP, Bartels T, Rowitch DH, Calabresi PA. Trends Immunol. 2021 Mar;42(3):228-247. doi: 10.1016/j.it.2021.01.005. Epub 2021 Feb 13. PMID: 33593693 Free PMC article. Review.

2. Astrocyte layers in the mammalian cerebral cortex revealed by a single-cell in situ transcriptomic map. Bayraktar OA, Bartels T, Holmqvist S, Kleshchevnikov V, Martirosyan A, Polioudakis D, Ben Haim L, Young AMH, Batiuk MY, Prakash K, Brown A, Roberts K, Paredes MF, Kawaguchi R, Stockley JH, Sabeur K, Chang SM, Huang E, Hutchinson P, Ullian EM, Hemberg M, Coppola G, Holt MG, Geschwind DH, Rowitch DH. Nat Neurosci. 2020 Apr;23(4):500-509. doi: 10.1038/s41593-020-0602-1. Epub 2020 Mar 16. PMID: 32203496 Free PMC article.

3. Neuronal vulnerability and multilineage diversity in multiple sclerosis. Schirmer L, Velmeshev D, Holmqvist S, Kaufmann M, Werneburg S, Jung D, Vistnes S, Stockley JH, Young A, Steindel M, Tung B, Goyal N, Bhaduri A, Mayer S, Engler JB, Bayraktar OA, Franklin RJM, Haeussler M, Reynolds R, Schafer DP, Friese MA, Shiow LR, Kriegstein AR, Rowitch DH.Nature. 2019 Sep;573(7772):75-82. doi: 10.1038/s41586-019-1404-z. Epub 2019 Jul 17. PMID: 31316211 Free PMC article.

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