

- Single-cell transcriptomics of around 247,000 temporal cortex nuclei identified oligodendrocytes and OPCs as major hubs of LOAD-associated molecular dysregulation, with glial cells being key contributors to disease pathology.
- Across ancestries, there was consistent upregulation of ribosomal and protein translational pathways in oligodendrocytes, with an increased expression in ribosomal genes such as RPS15, RPS11, and RPL7, suggesting alterations in protein machinery.
- Oligodendrocyte ribosomal and protein translation pathways and networks were a prominent male-associated LOAD signature across ancestries.
- Female LOAD brains exhibited prominent neuroinflammatory and immune-associated glial signatures, contrasting with the translation and proteostasis pathways that were prominent in the male brains
- Sex dependent effects frequently exceeded (meaning more distinctions across the two sexes within an ancestry) ancestry-dependent effects, emphasizing sex as a critical determinant