# SINGLE-CELL RNA SEQUENCE ANALYSIS OF POST-MORTEM MIDBRAIN TISSUE REVEALS ALTERED GLIAL CELL FUNCTION IN PARKINSON'S DISEASE


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## ABSTRACT


Synucleinopathy marked by aberrant misfolding and aggregations of synuclein protein is a feature of many neurodegenerative disorders, particularly Parkinson's disease (PD) and Lewy Body Dementia (LBD). Neuroinflammation, characterized by reactive microglia and astrocytes are also a central marker of PD pathology. The inflammatory hypothesis suggests that dysregulated pathways in glial cells contribute to degeneration. Using a public dataset from Broad Institute, containing snRNA seq data from post-mortem midbrain tissue, we attempt to characterize functional alterations in several glial cell populations in Parkinson's disease. We specifically focus on functions that are associated with inflammation and damage response.


## METHODS

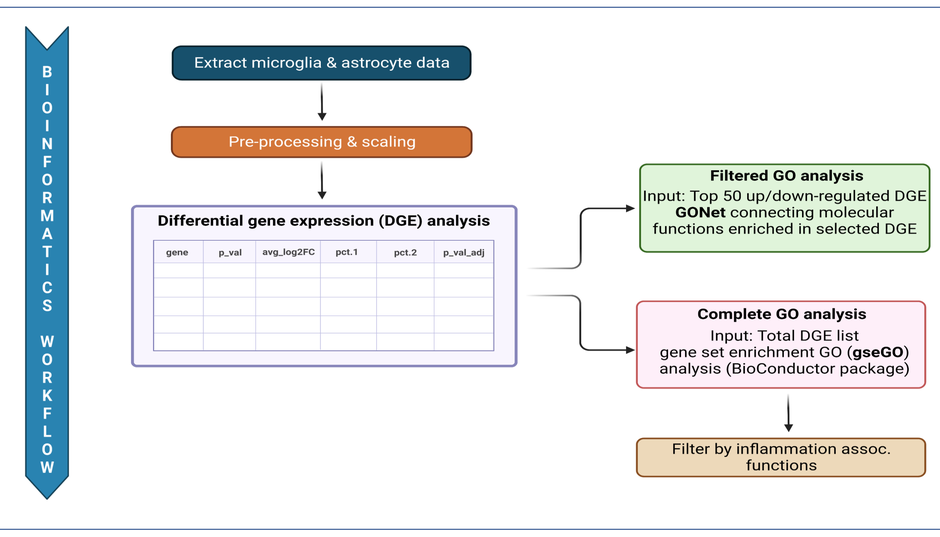
8 ctrl 6 PD 4 LBD

**Data source:** Single-cell genomic profile of human dopamine neurons identifies a population that selectively degenerates in Parkinson's disease (Kamath et al., 2022)

**Brain regions:** Caudate nucleus & substantia nigra

| Disease ontology | # of cells |
|---|---|
| normal | 231530 |
| Parkinson's disease | 135344 |
| Lewy body dementia | 67466 |

| Cell type | # of cells |
|---|---|
| dopaminergic neurons | 22048 |
| astrocytes | 33506 |
| microglia | 33041 |
| non-dopamine neurons | 91479 |
| oligodendrocytes | 178815 |
| oligo-progenitor cells | 13691 |
| endothelial cells | 14903 |




## RESULTS

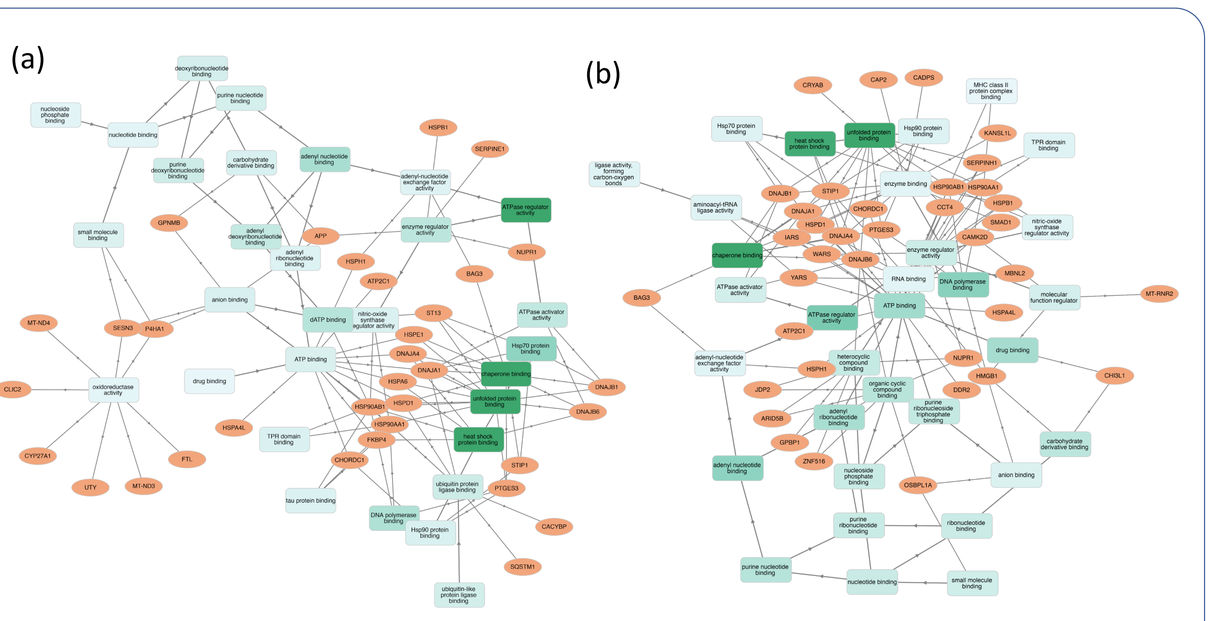



Figure 1: GONet enrichment plot of molecular functions associated with the 50 most upregulated genes in PD microglia (a) and PD astrocytes (b).

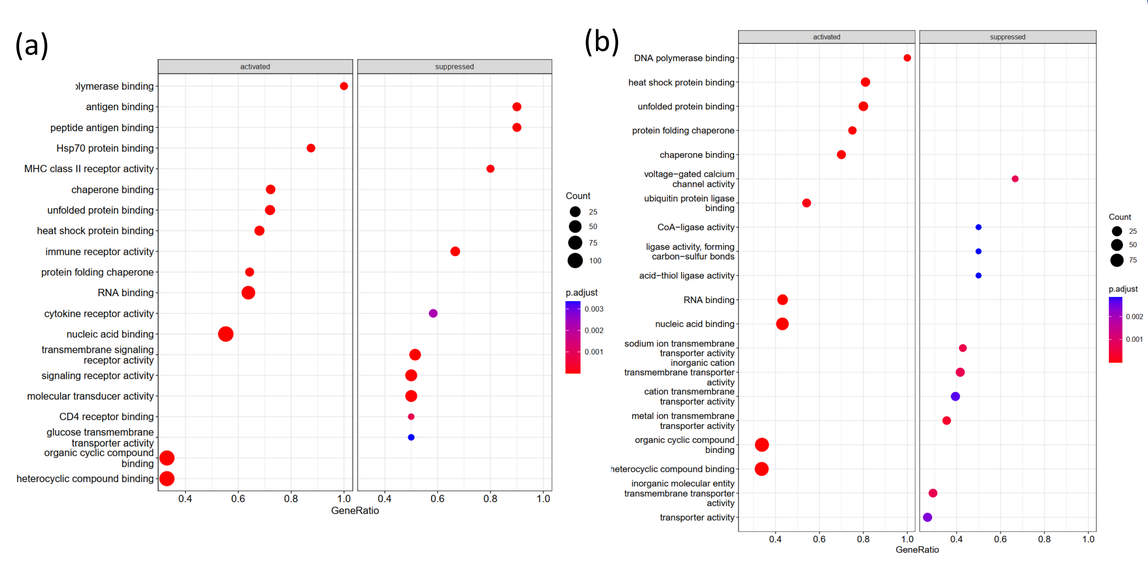



Figure 2: Dot plots of gseGO results showing the 10 most up and downregulated molecular functions in PD microglia (a) and PD astrocytes (b).

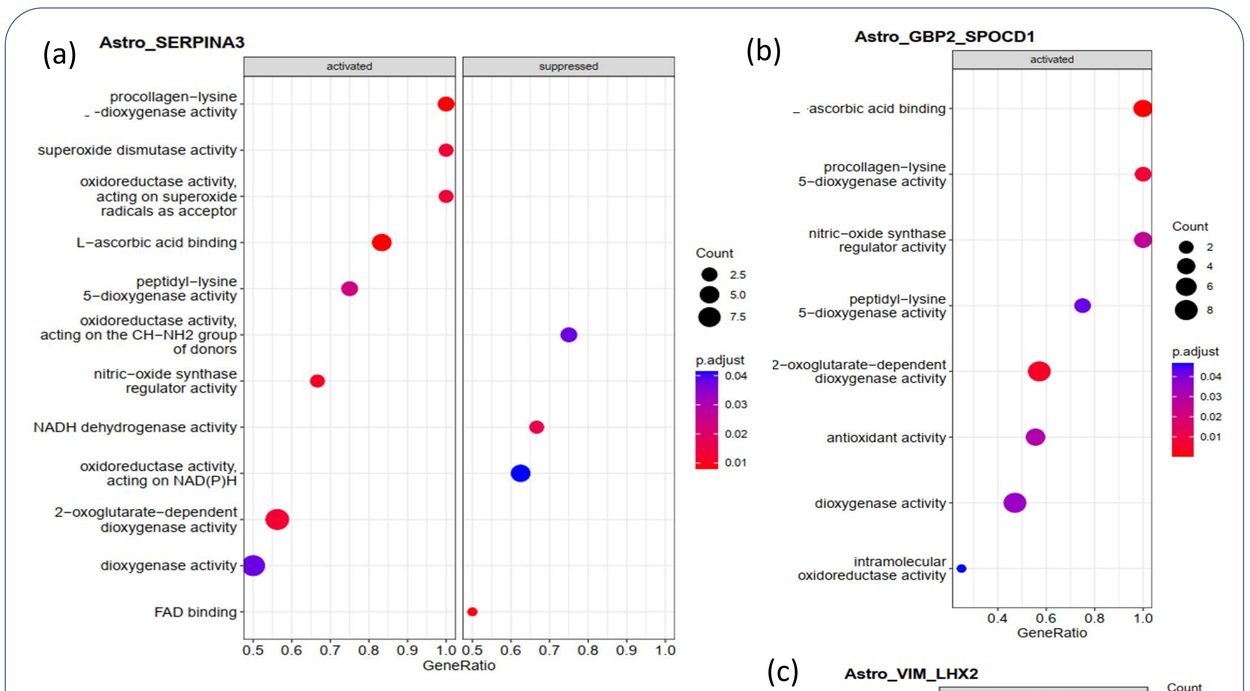



Figure 3: GseGO results for astrocyte subtypes filtered to show oxidoreductase activity related molecular functions in the three astrocyte subtypes that show increased expression in PD compared to control.

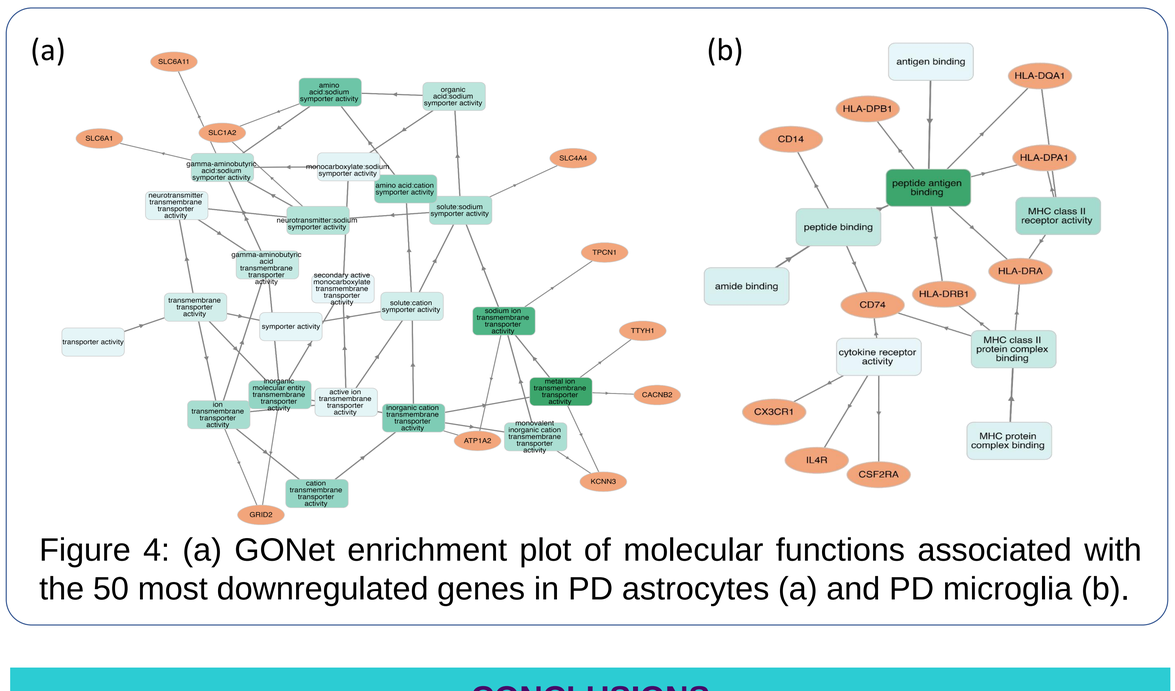



Figure 4: (a) GONet enrichment plot of molecular functions associated with the 50 most downregulated genes in PD astrocytes (a) and PD microglia (b).

## CONCLUSIONS

- Proinflammatory pathways are downregulated in microglia, suggesting alternate reactive states of microglia at different stages of PD.
- Upregulated oxidoreductase activity in both astrocytes & microglia suggest involvement in responding to oxidative damage.
- Chaperone binding and protein folding activity are strongly upregulated in PD for both microglia and astrocytes, possibly in an attempt to clear misfolded proteins.

## ACKNOWLEDGEMENTS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