

Immune–epithelial remodeling axis in the human choroid plexus in Alzheimer’s disease

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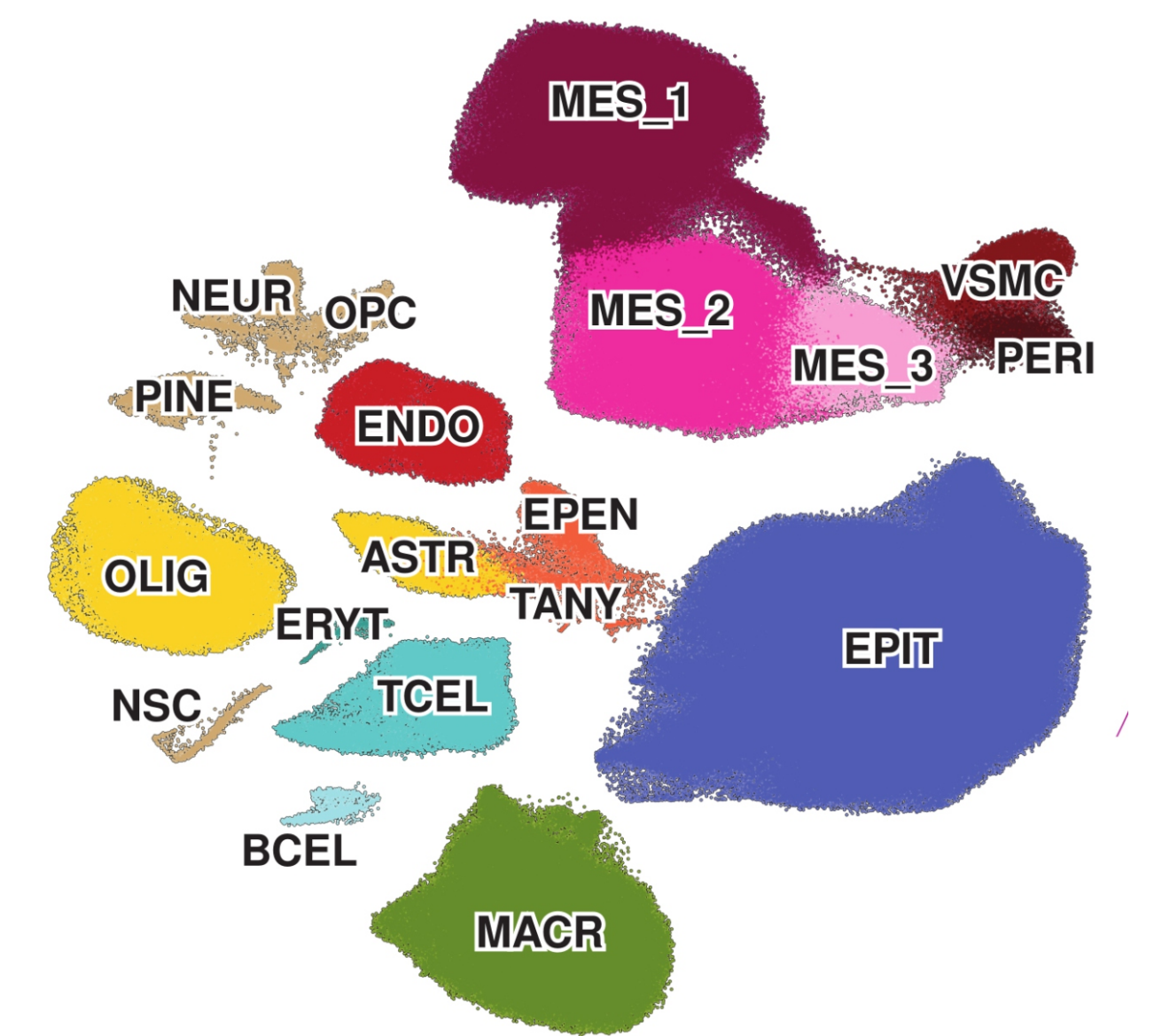
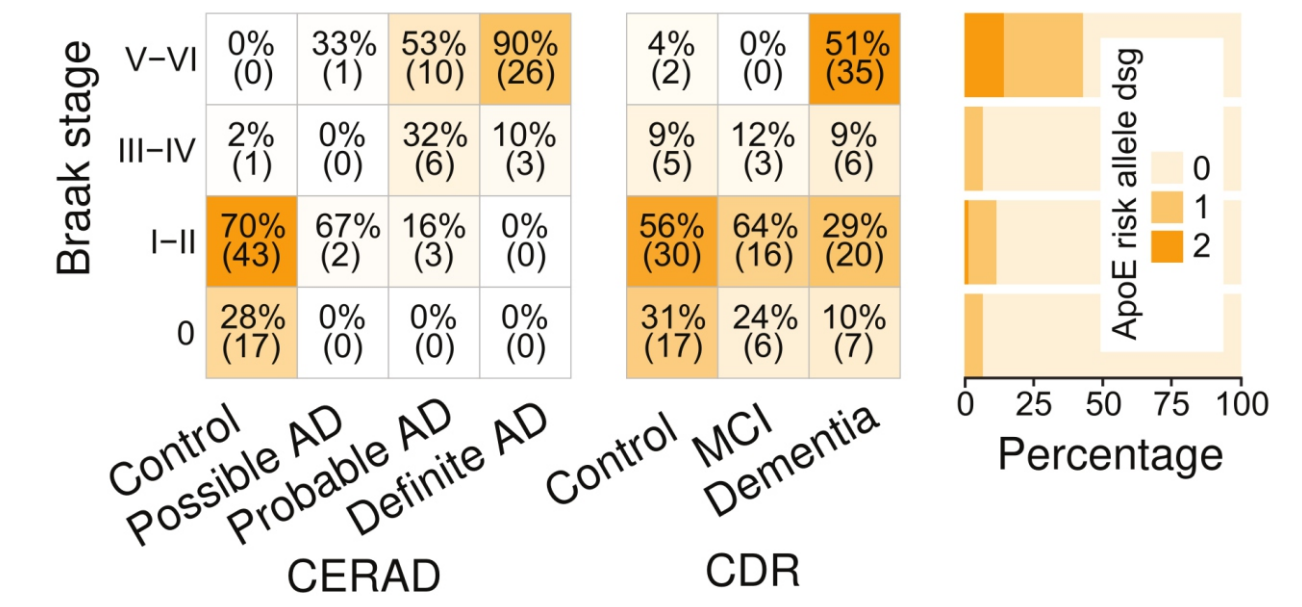
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snRNA-seq dataset

“Discovery” cohort

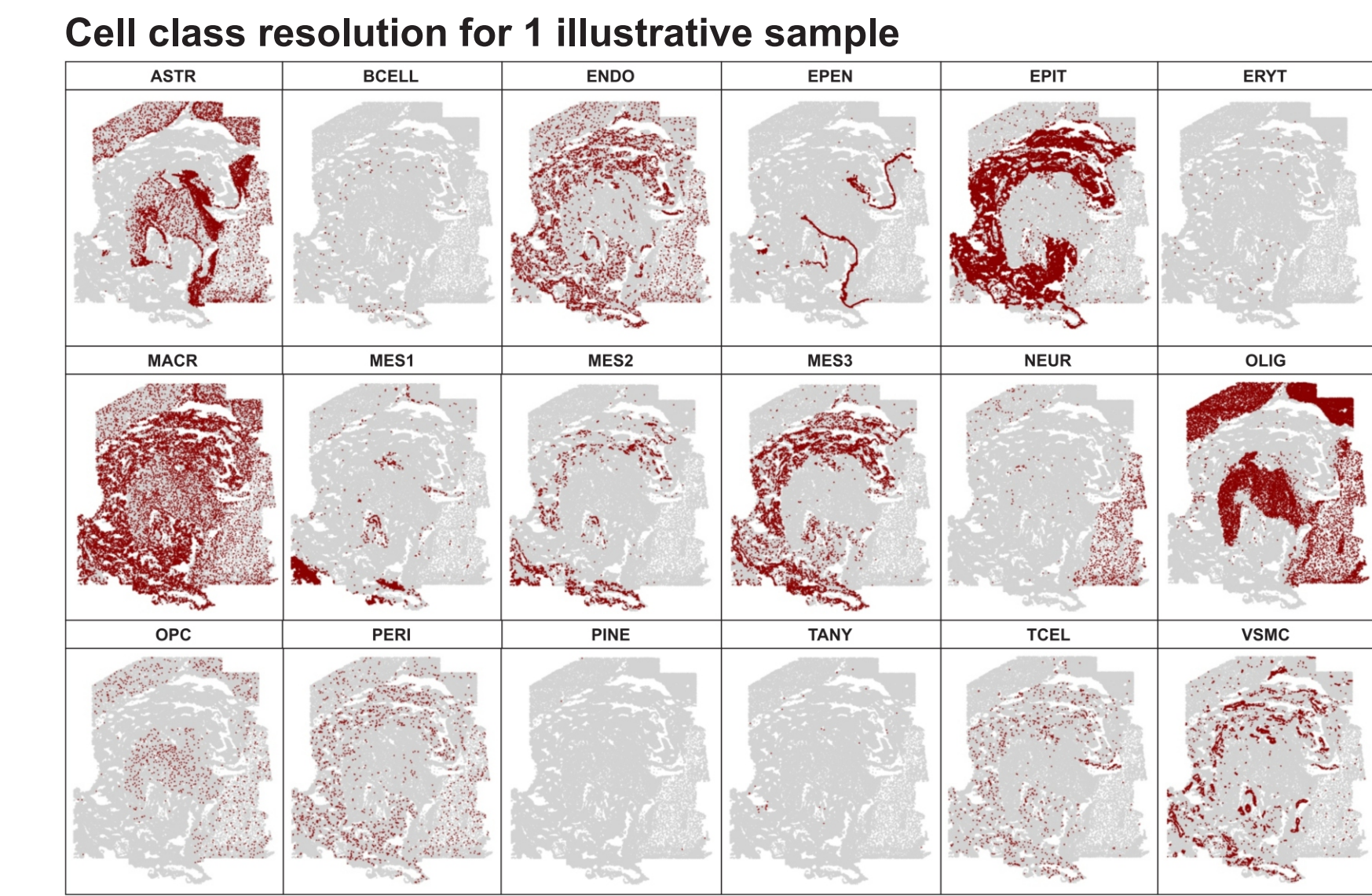
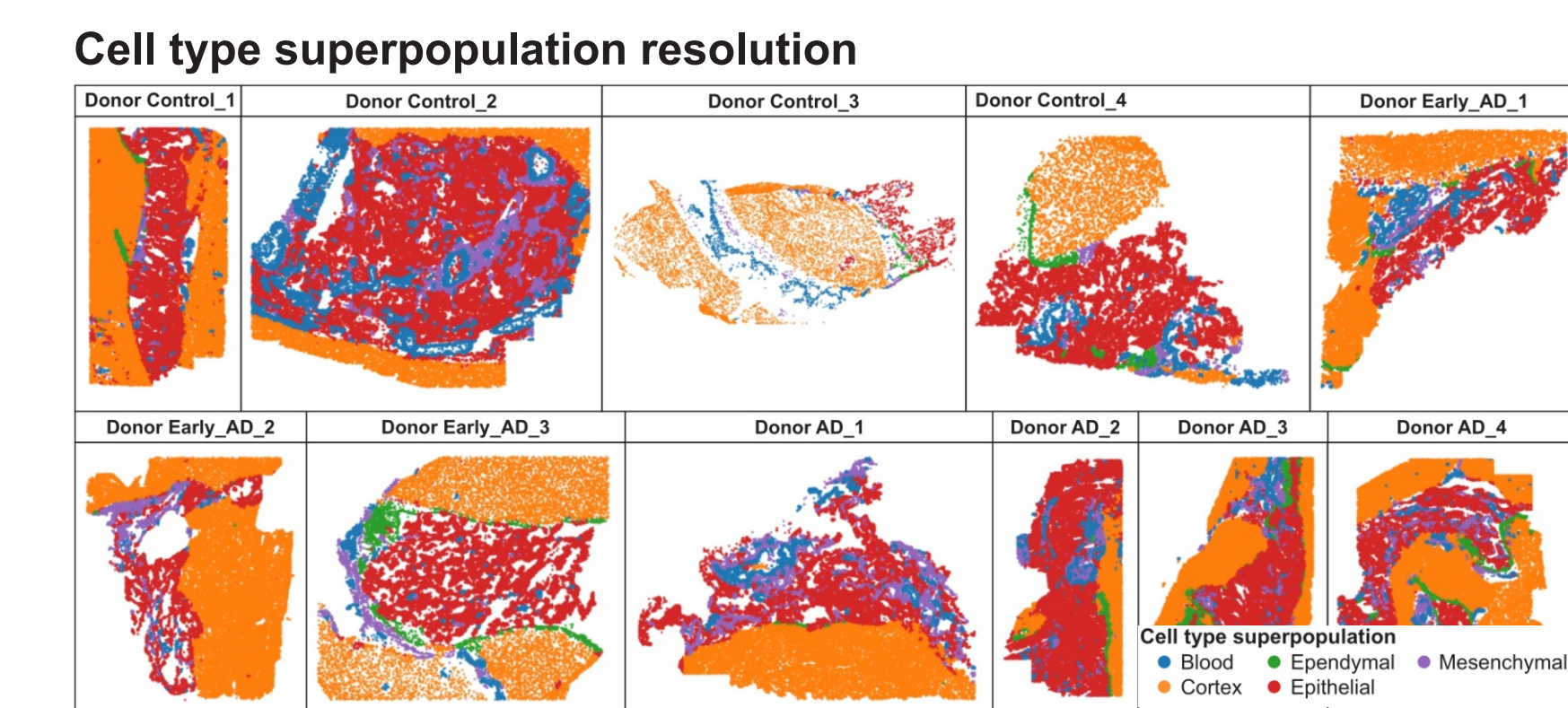
- Size: 160 postmortem human donors (AD case/control) 936,447 nuclei



Spatial transcriptomics dataset

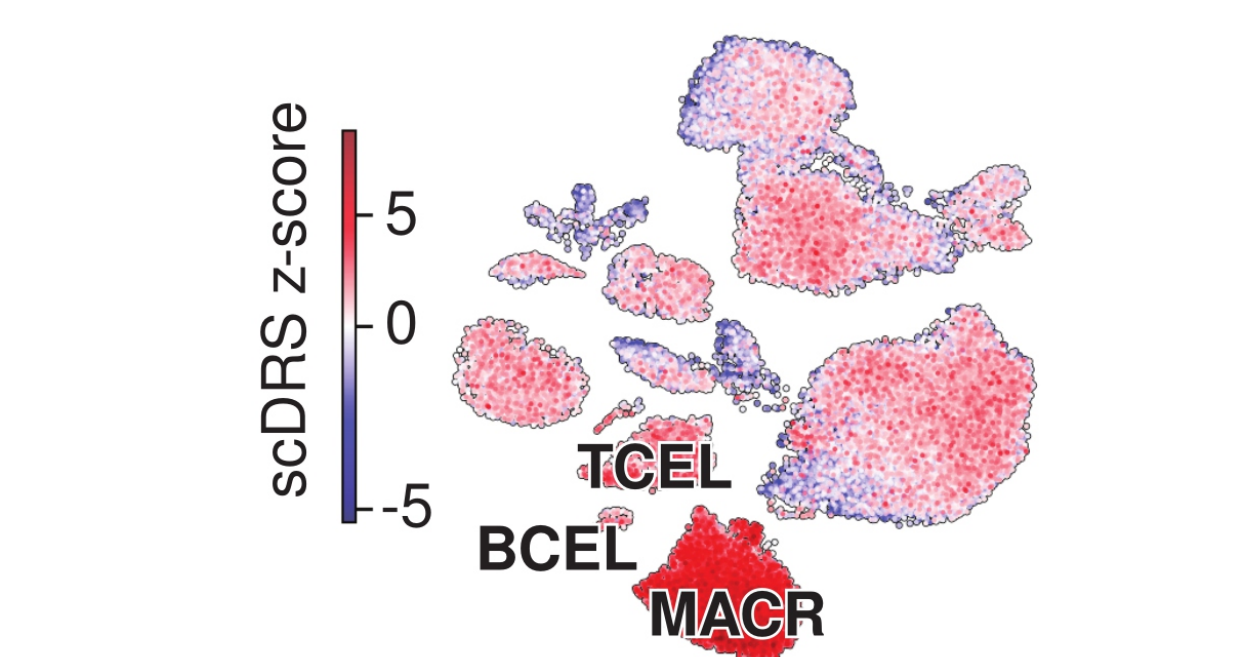
“Validation” cohort

- Size: 11 postmortem human donors (AD case/control) 872,358 nuclei



Genetic risk enrichment

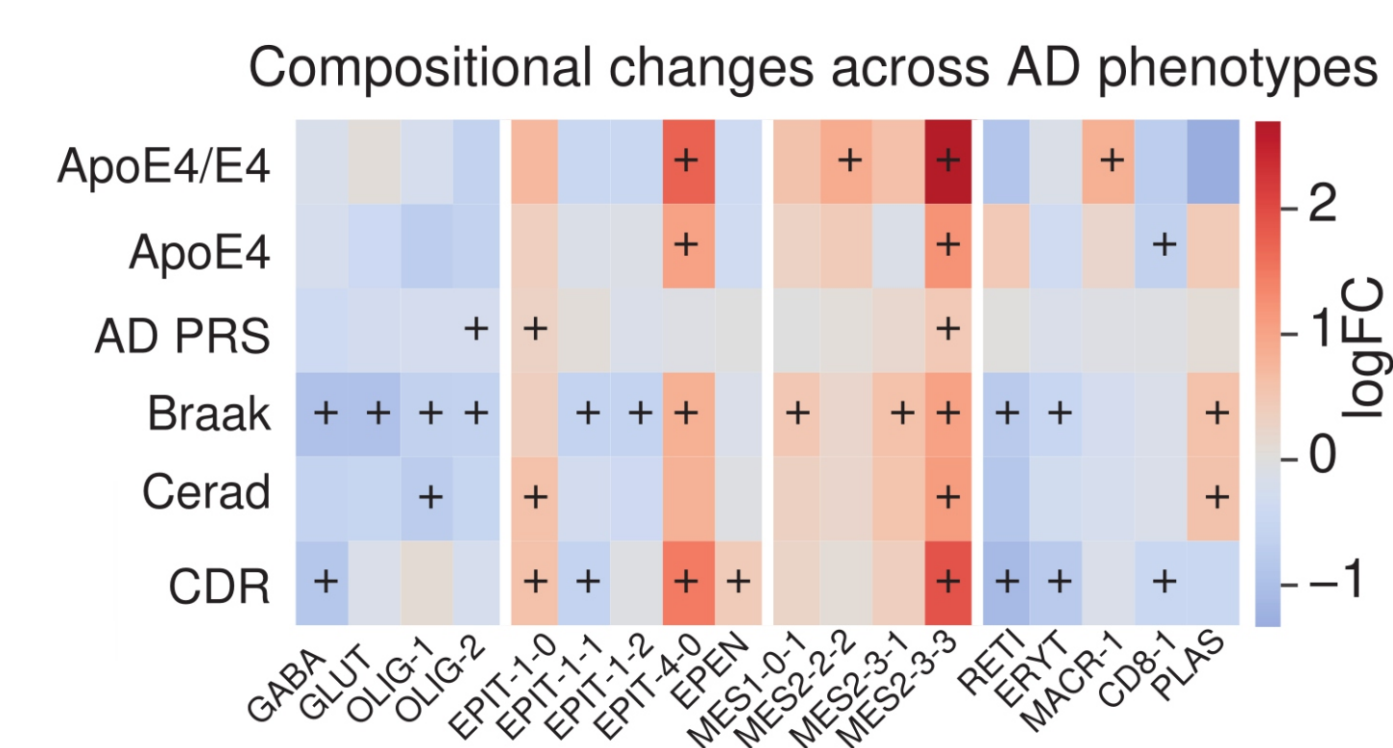
AD GWAS enrichment converges on macrophage cell population



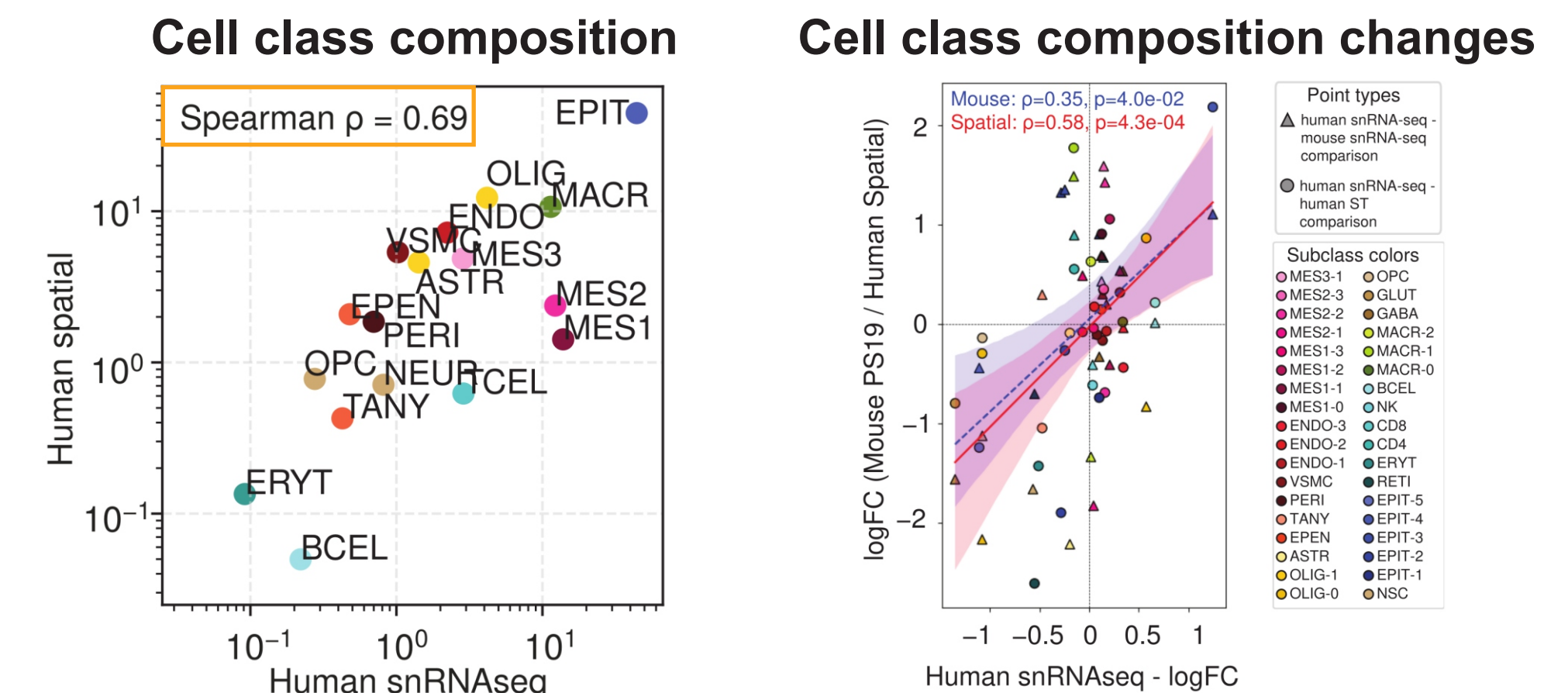
Cell type proportion changes

Multiple AD phenotypes

- 3x Genetic (one or two ApoE4 alleles; polygenic risk score)
- 2x Pathology (Braak and CERAD)
- 1x Cognition (Clinical Dementia Rating)

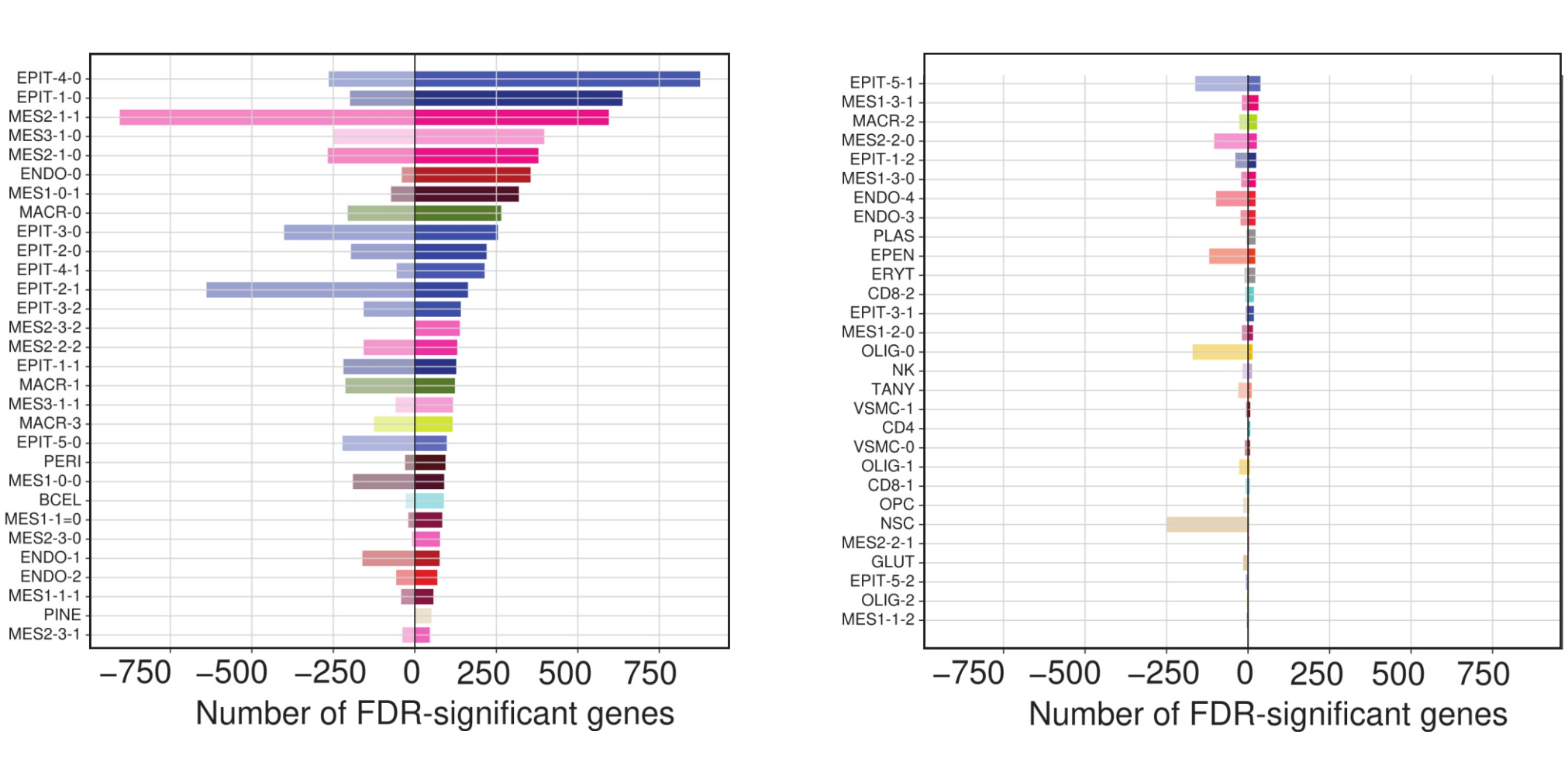


Concordance between our datasets



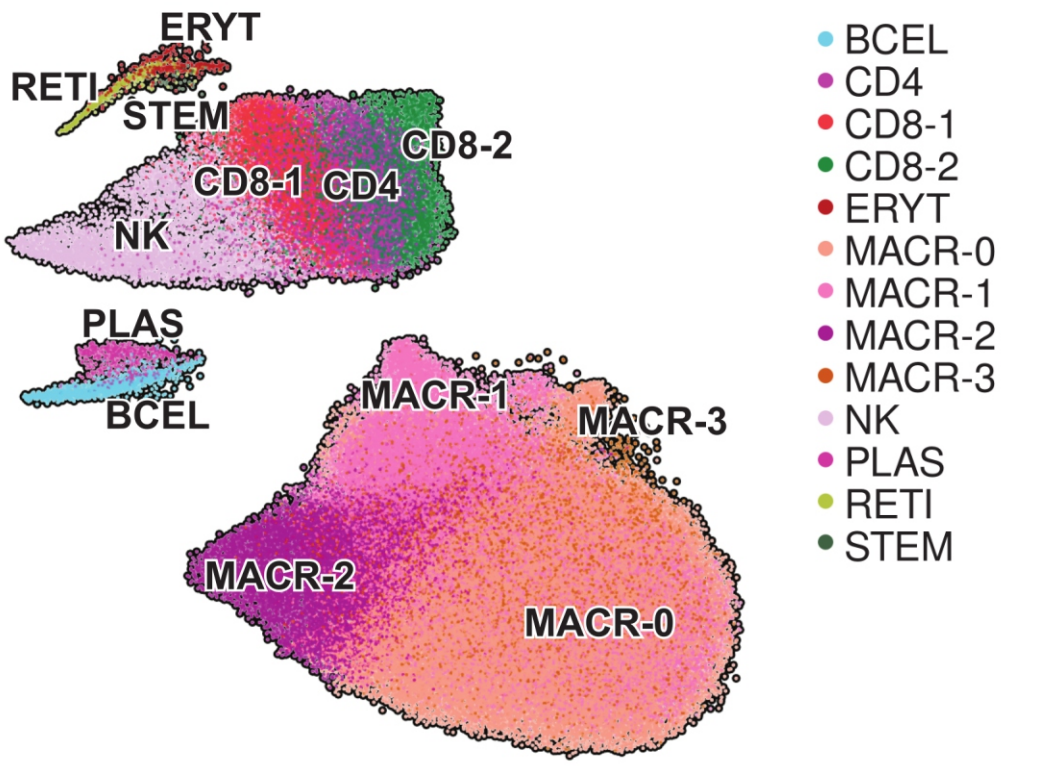
Differential gene expression (DEG)

DEG are concentrated in epithelial and mesenchymal cells

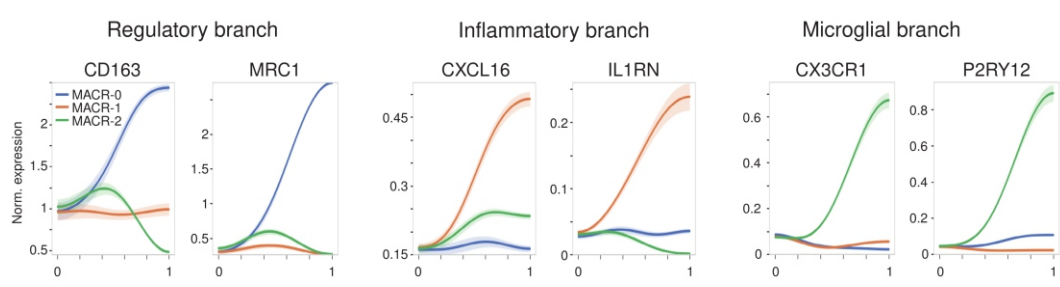


Deep dive: Immune cells

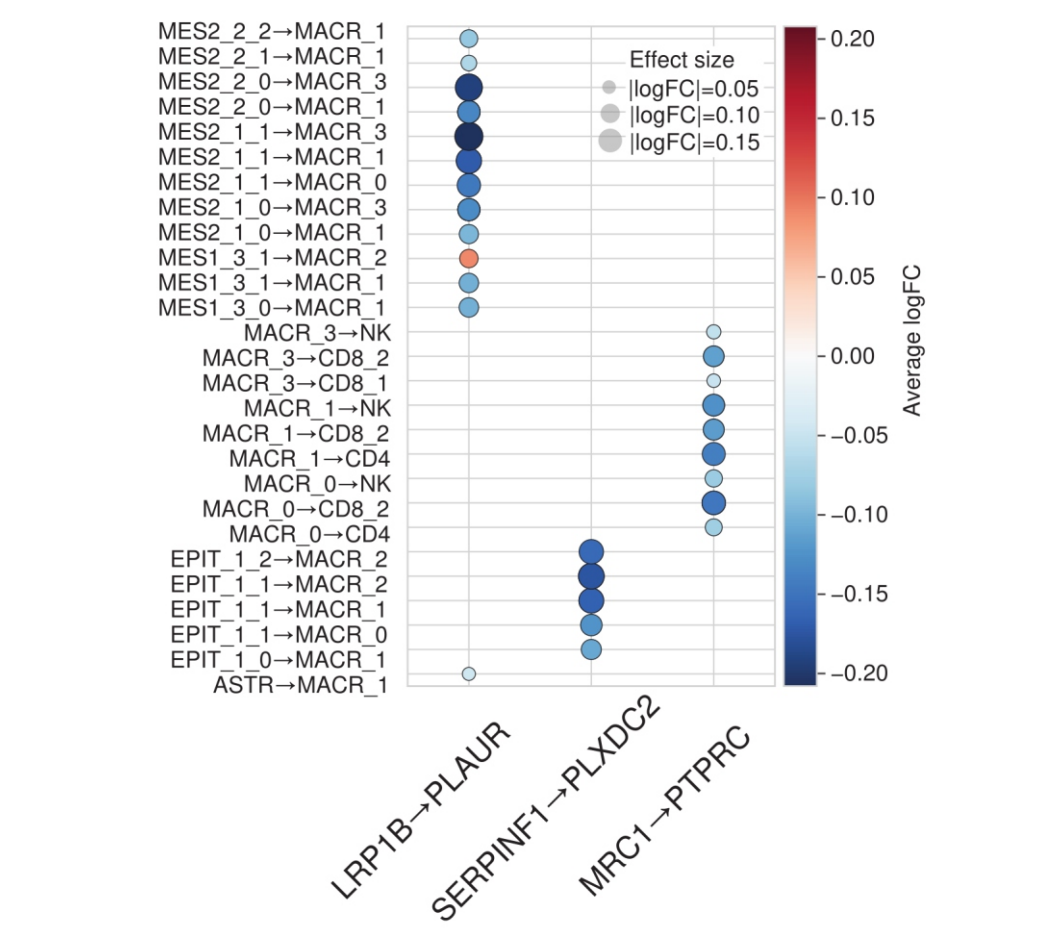
13 cell subtypes; 136,418 nuclei



3 distinct macrophage regulatory programs

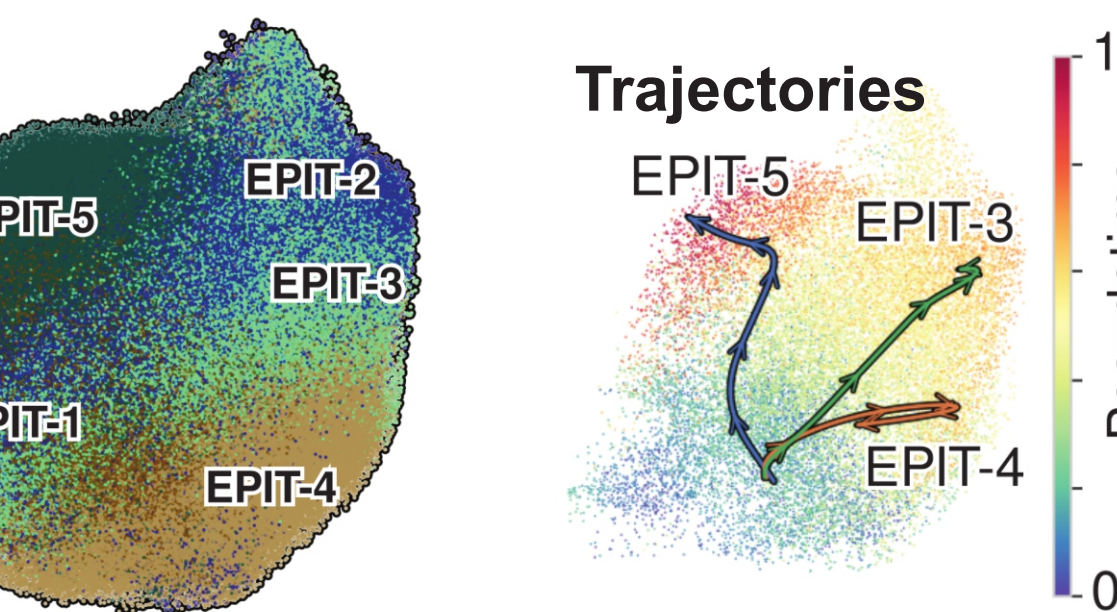


AD-perturbed ligand-receptor pairs

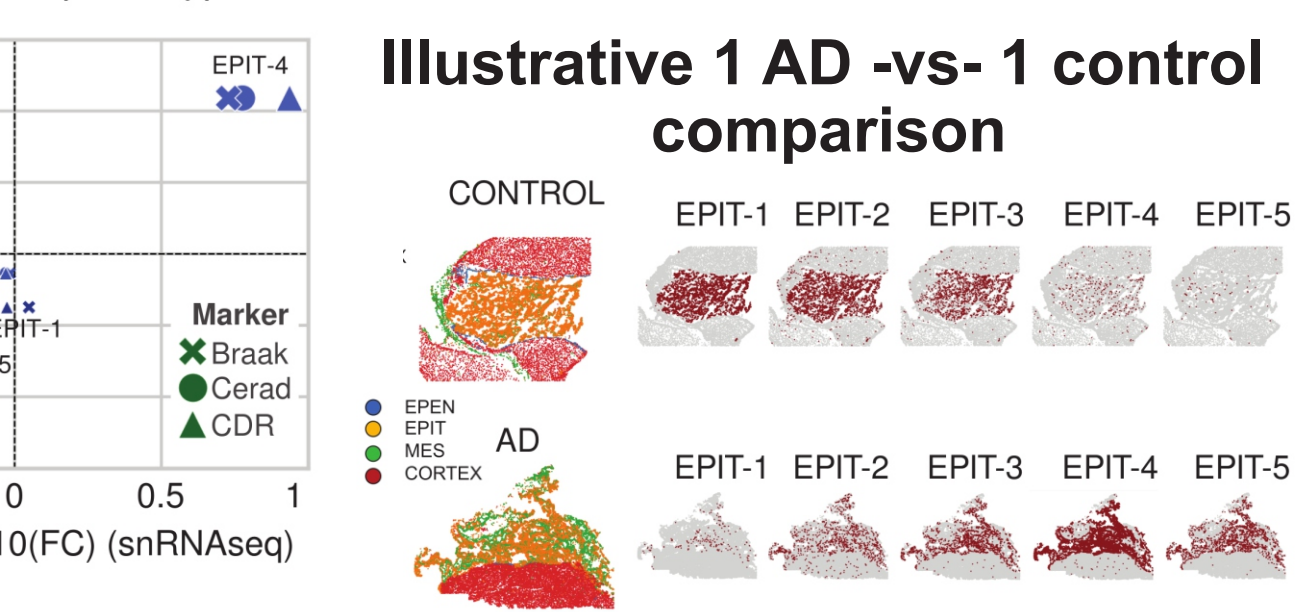


Deep dive: Epithelial cells

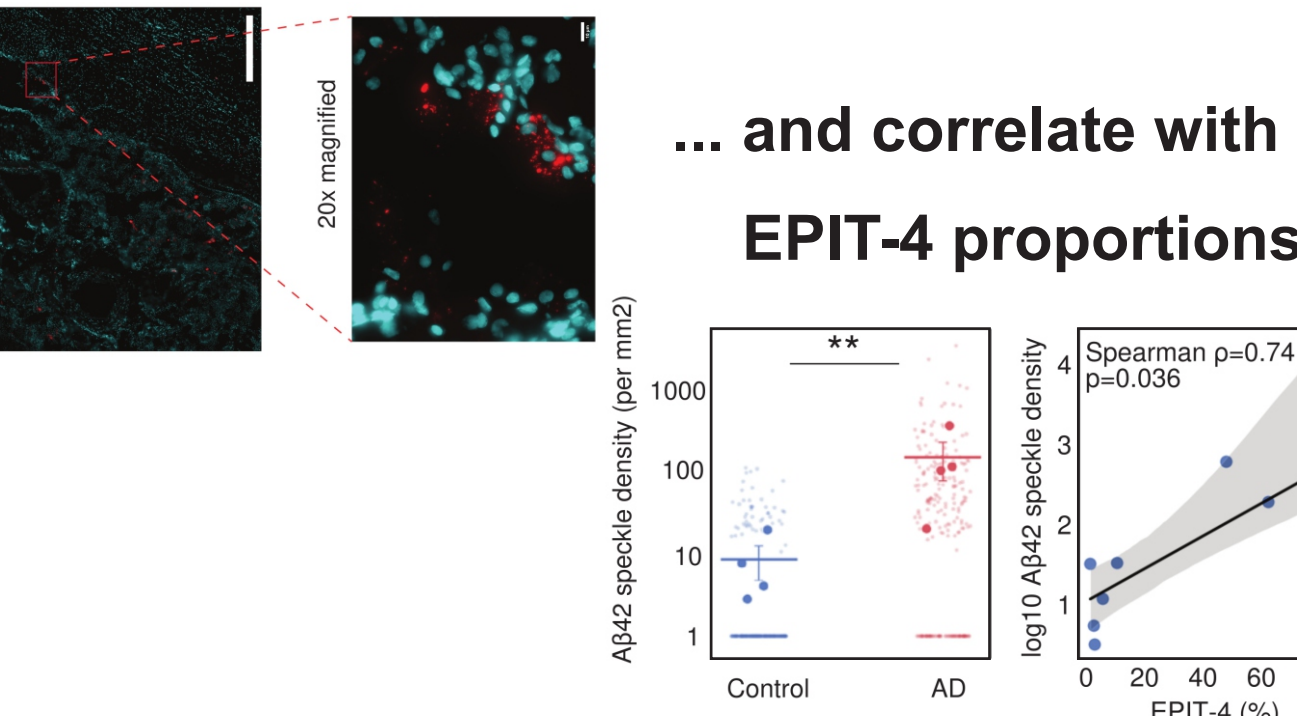
13 cell subclasses; 414,366 nuclei



EPIT-4 increased in AD in both discovery and validation cohorts



A β -42 deposits are increased in AD cases



Acknowledgement

NIH: R01AG067025, R01AG082185, R01AG065582, U24AG087563, R01AG050986, R01AG095776, R01NS143073

Status

Submitted for review
Preprint will be released by fall 2026