



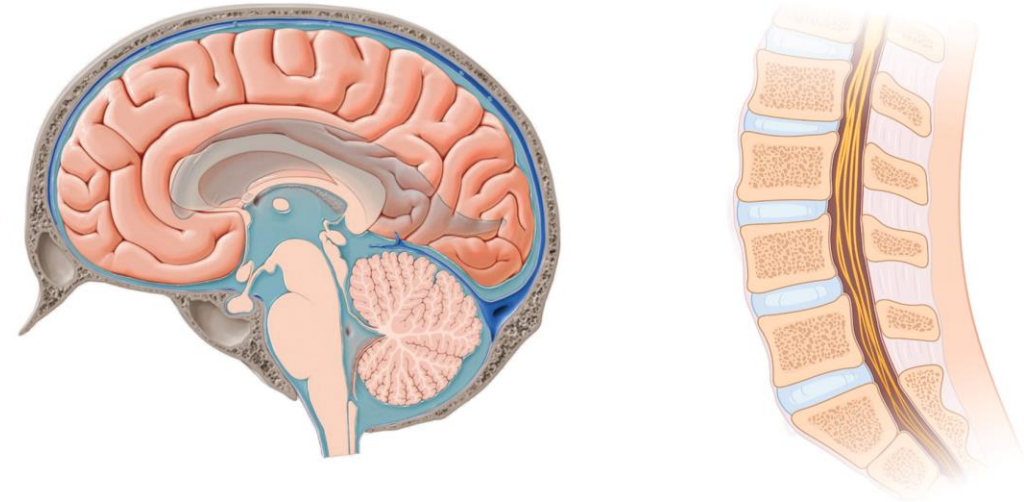
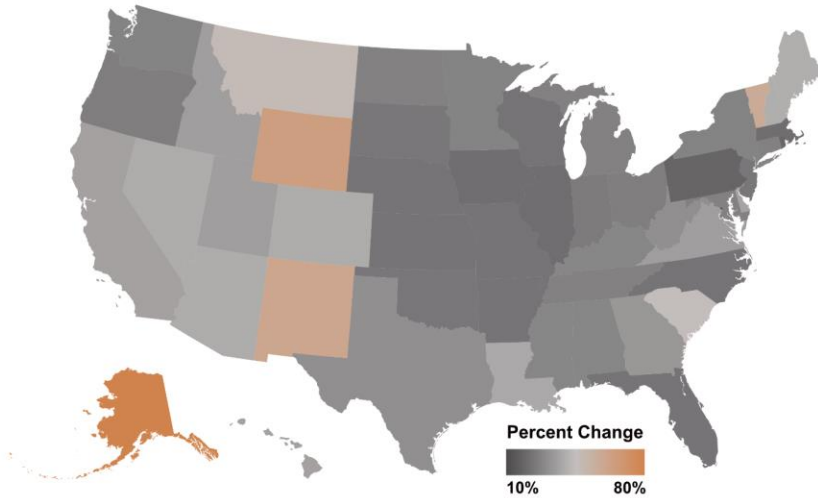
# Sample Agnostic Spectral Libraries: An Open Framework for Enhanced Data Independent Analysis Profiling Depth

Graham Delafield\*, Xiaofang Zhong\*, Qinying Yu, Chris Sauer, Henrik Zetterberg, Lingjun Li

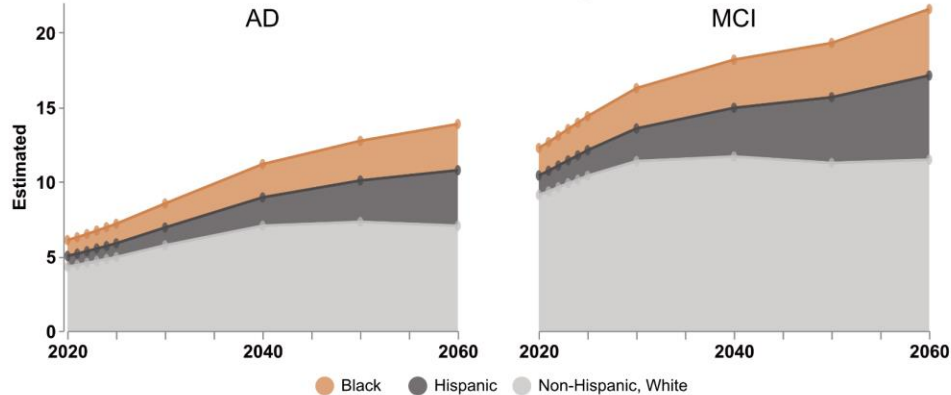
University of Wisconsin-Madison

# Current Approach Alzheimer's Disease Research

Rise in AD Diagnoses, 2010-2022



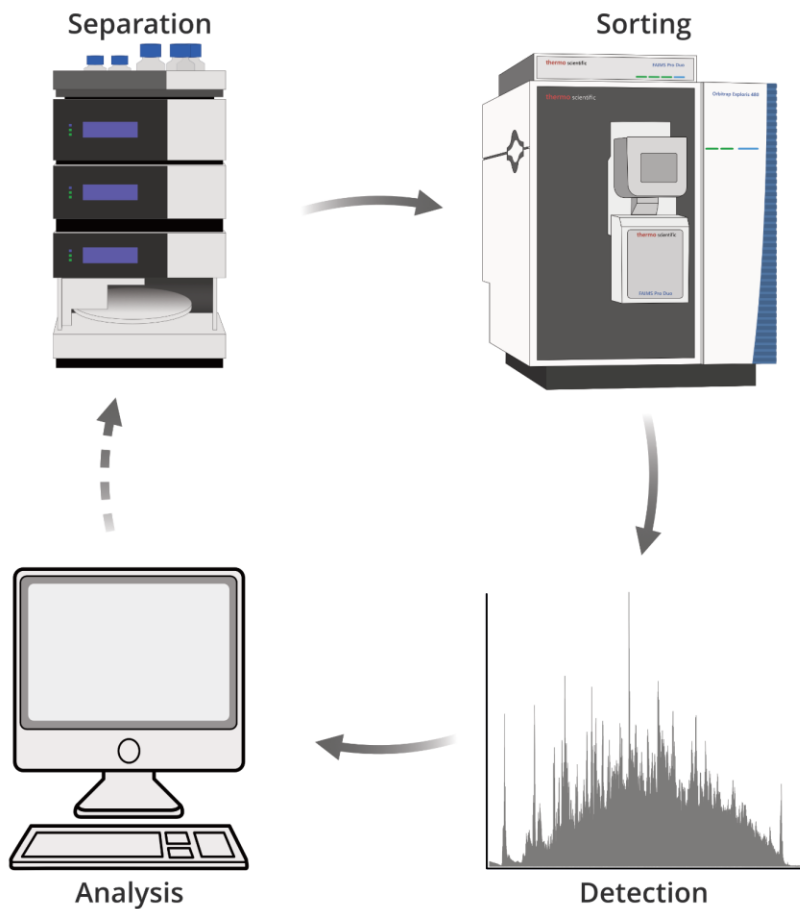
Estimated Rate of Incidence, 2020-2060



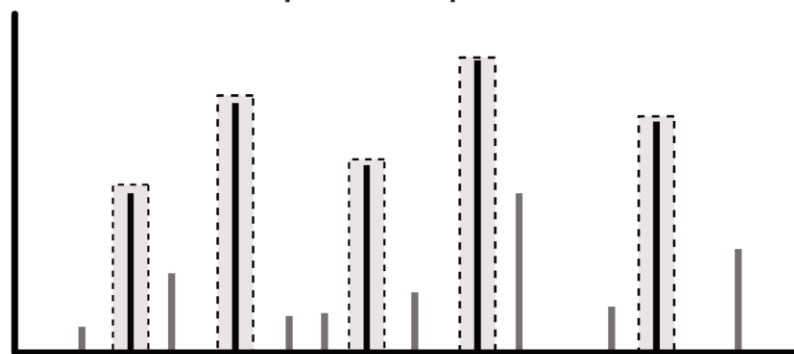
- Persistent increase in neurological disorders promotes need for early detection
- Biofluids are preferred matrix for analysis
- Invasive sampling and low availability requires dutiful handling and use



# MS-Based Biomarker Screening

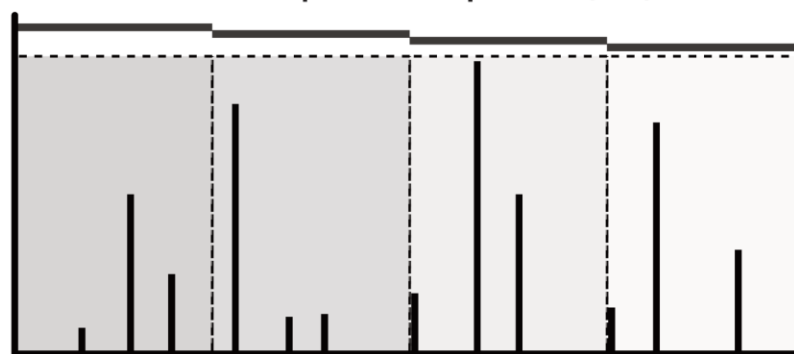


Data-Dependent Acquisition (DDA)



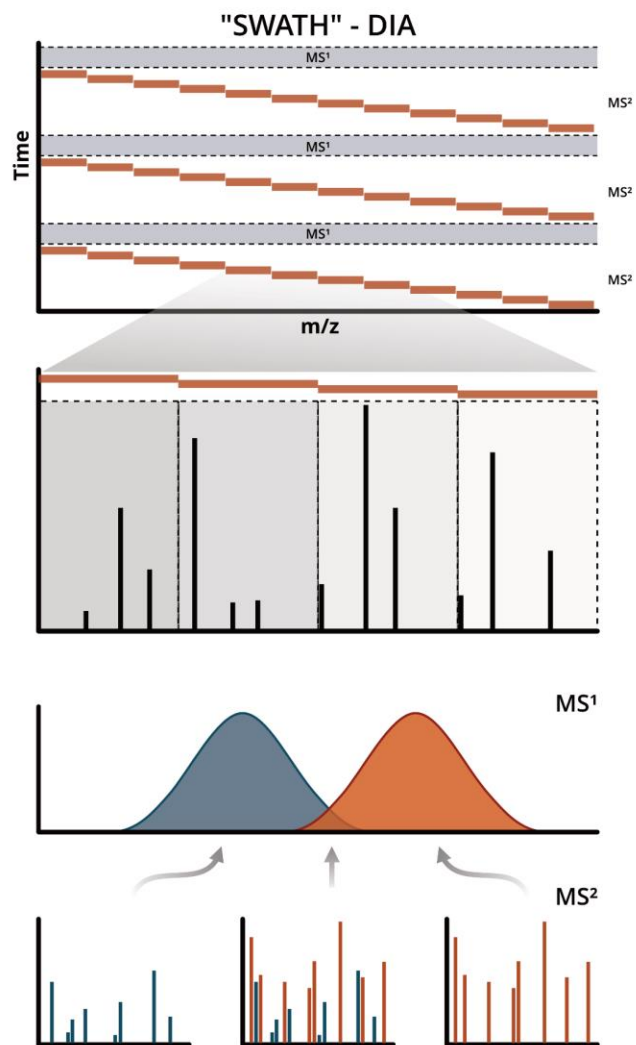
Biased ✗  
Confidence ✓  
"Cleanliness" ✓

Data-Independent Acquisition (DIA)



Unbiased ✓  
Throughput ✓  
Complex ✗

# DIA and Spectral Libraries

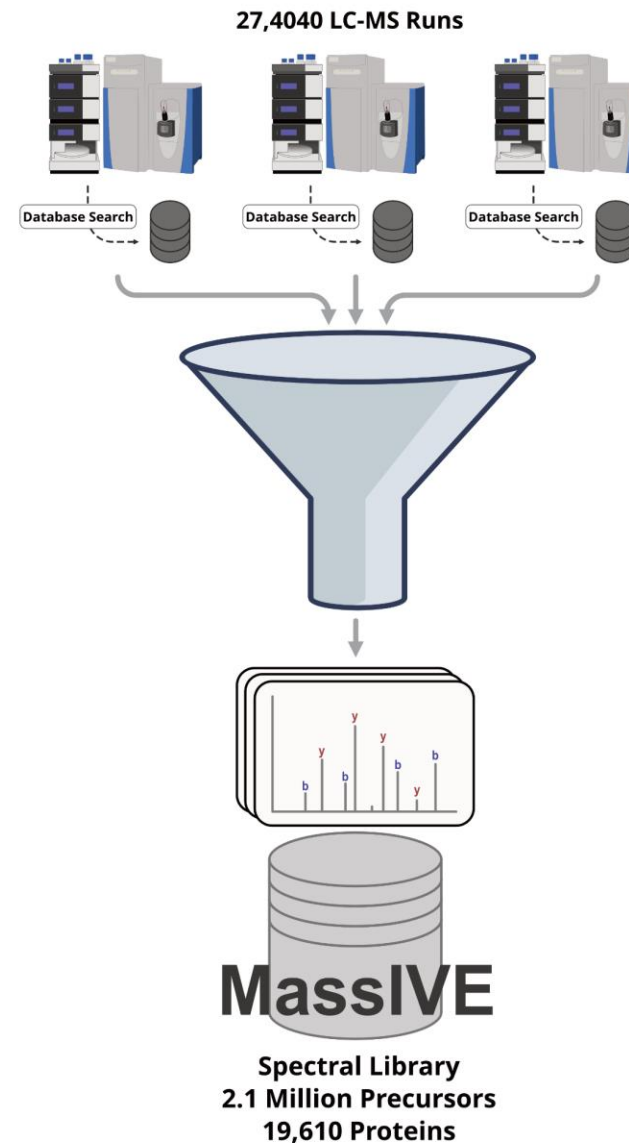


## Spectral Libraries

Retention Time	MS <sup>2</sup> Spectrum	Mass	Sequence	Protein
		800.36	PEPTIDE	RNAS1

Is there a way to 'calibrate' a spectral library to an individual experiment?

Can these sample agnostic libraries enhance our profiling depth?

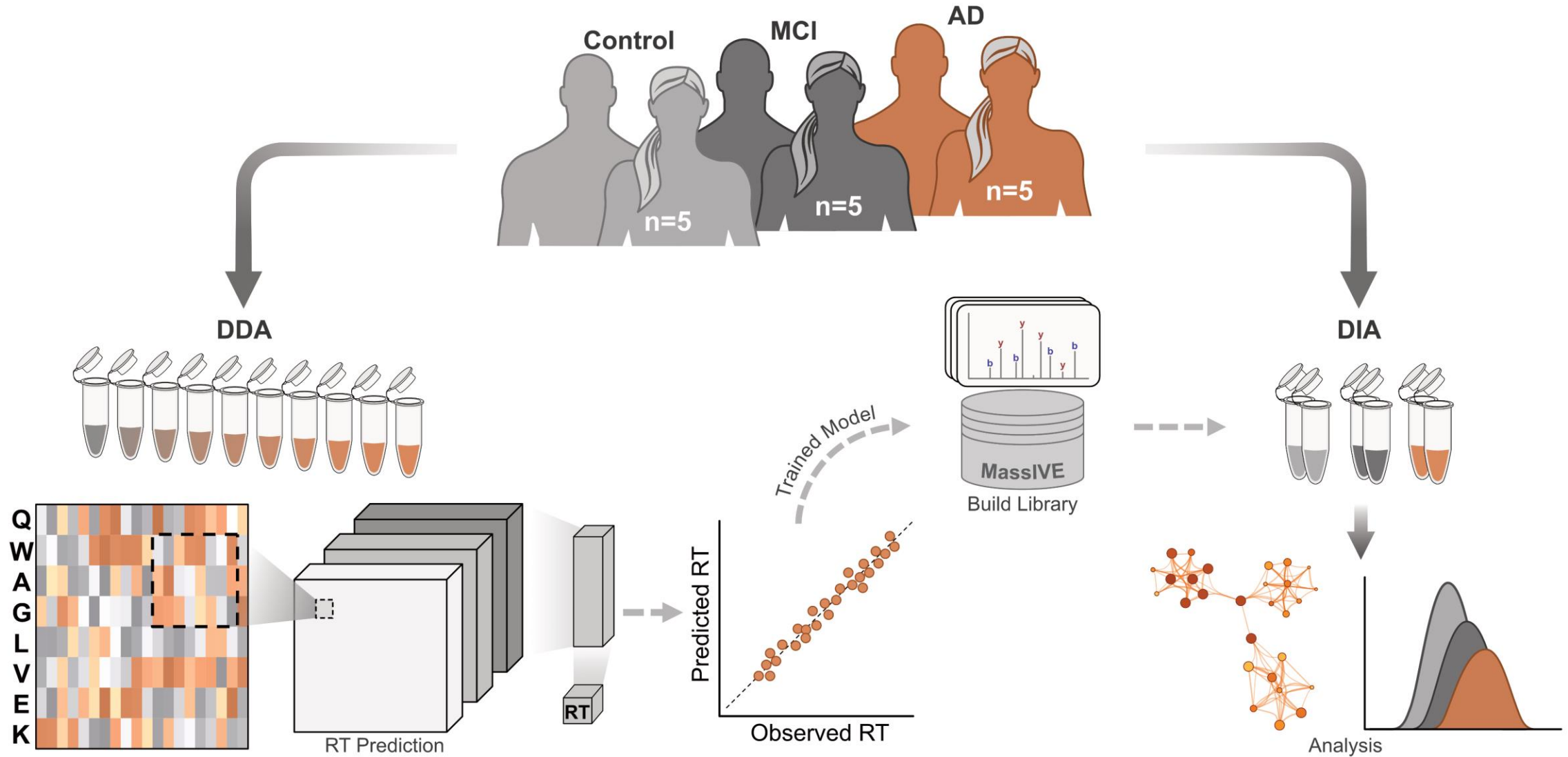




# Experimental Objectives

- 1) Validate an extensible, machine learning approach for library generation
- 2) Benchmark agnostic libraries against a typical DIA workflow
- 3) Evaluate the proteomic and quantitative depth

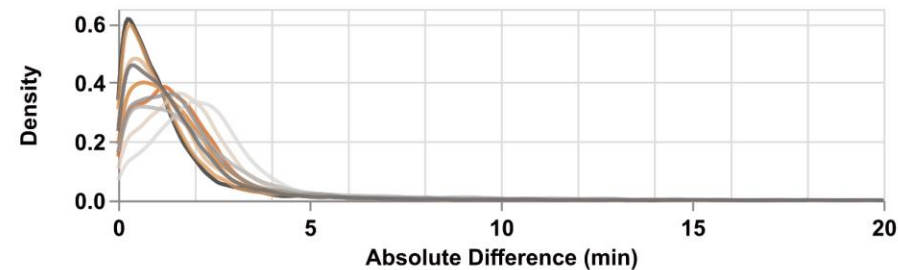
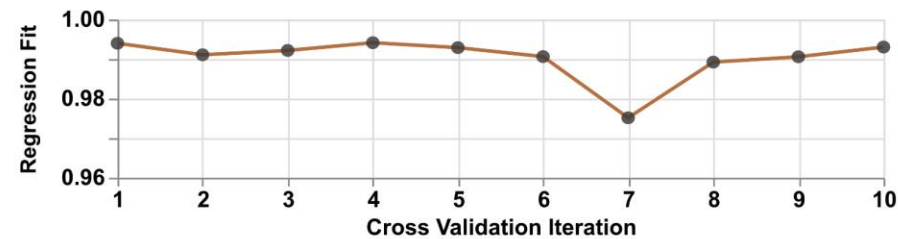
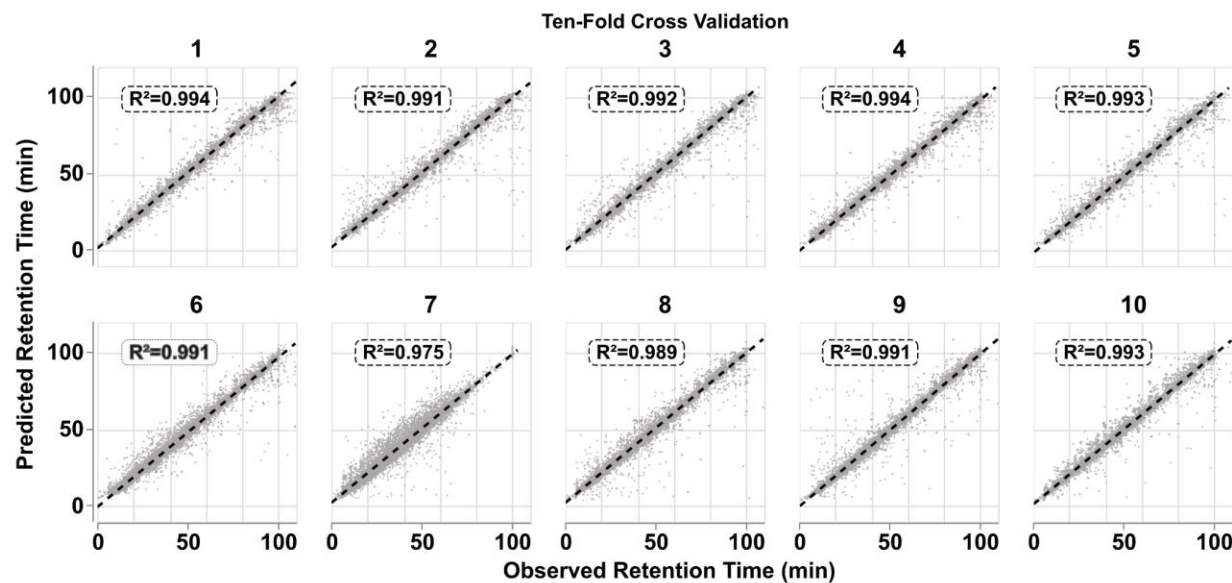
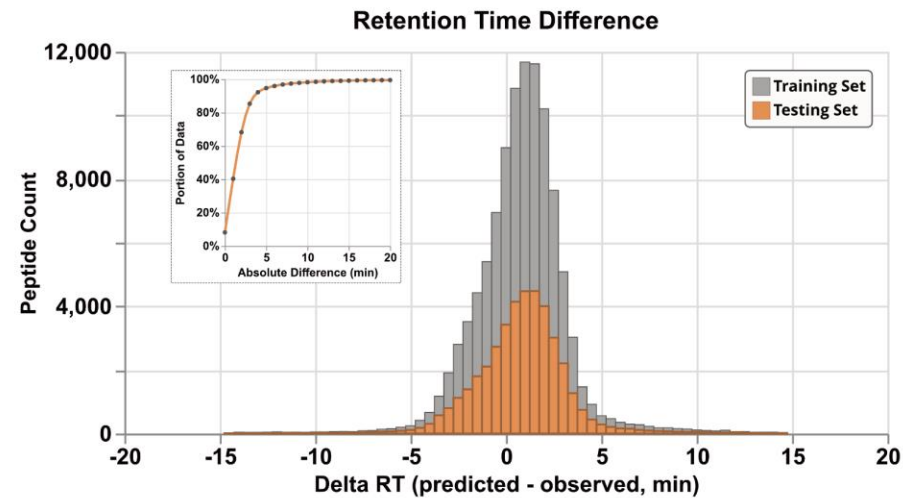
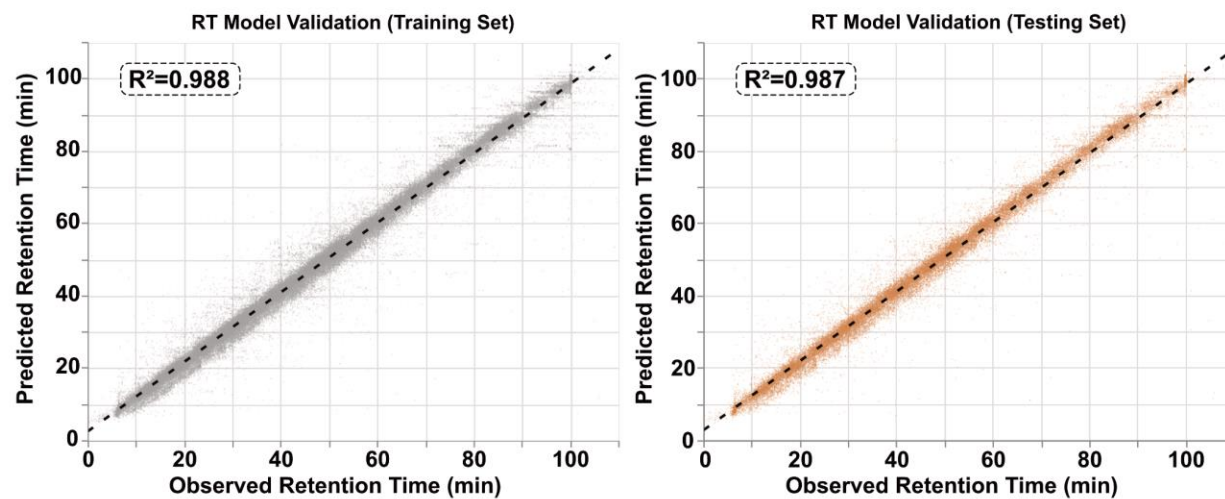
# Parallel Workflow





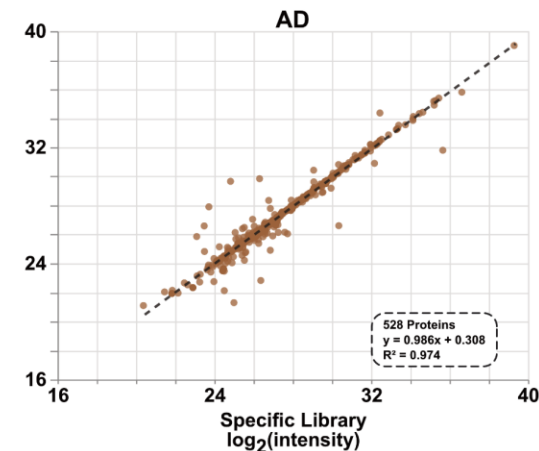
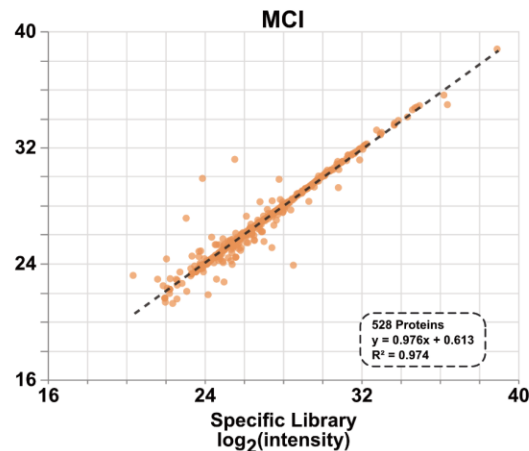
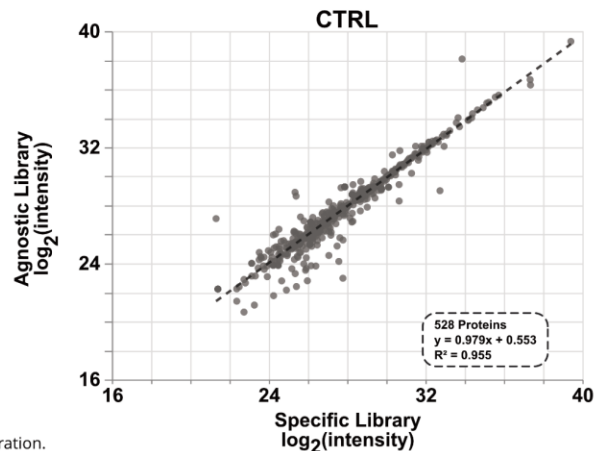
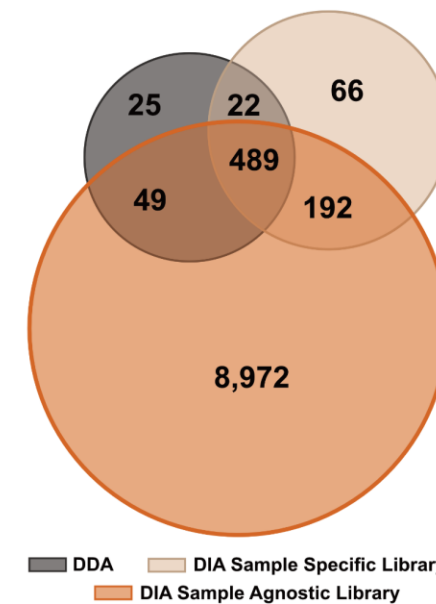
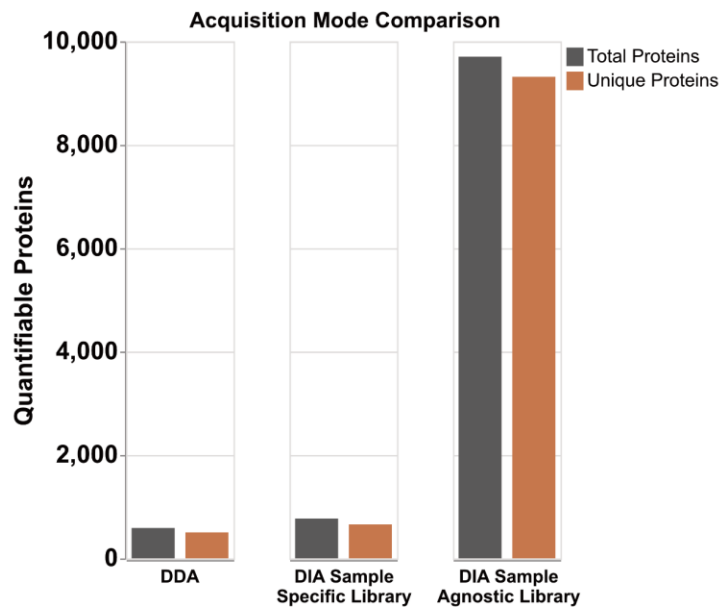
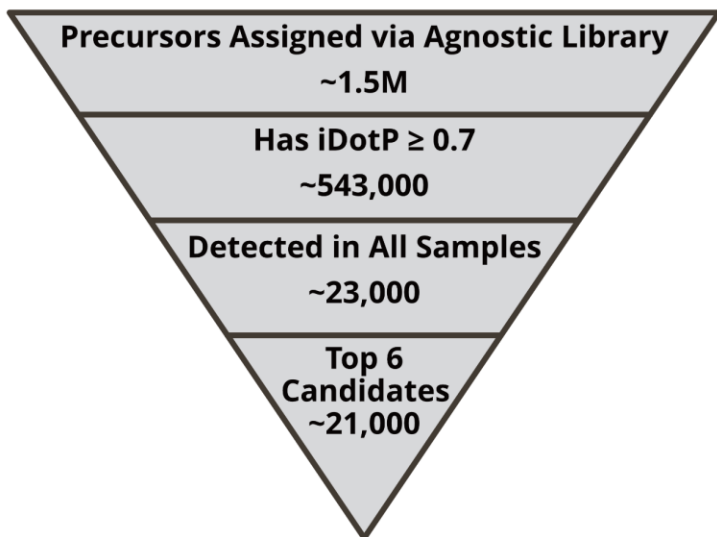


# Model Validation



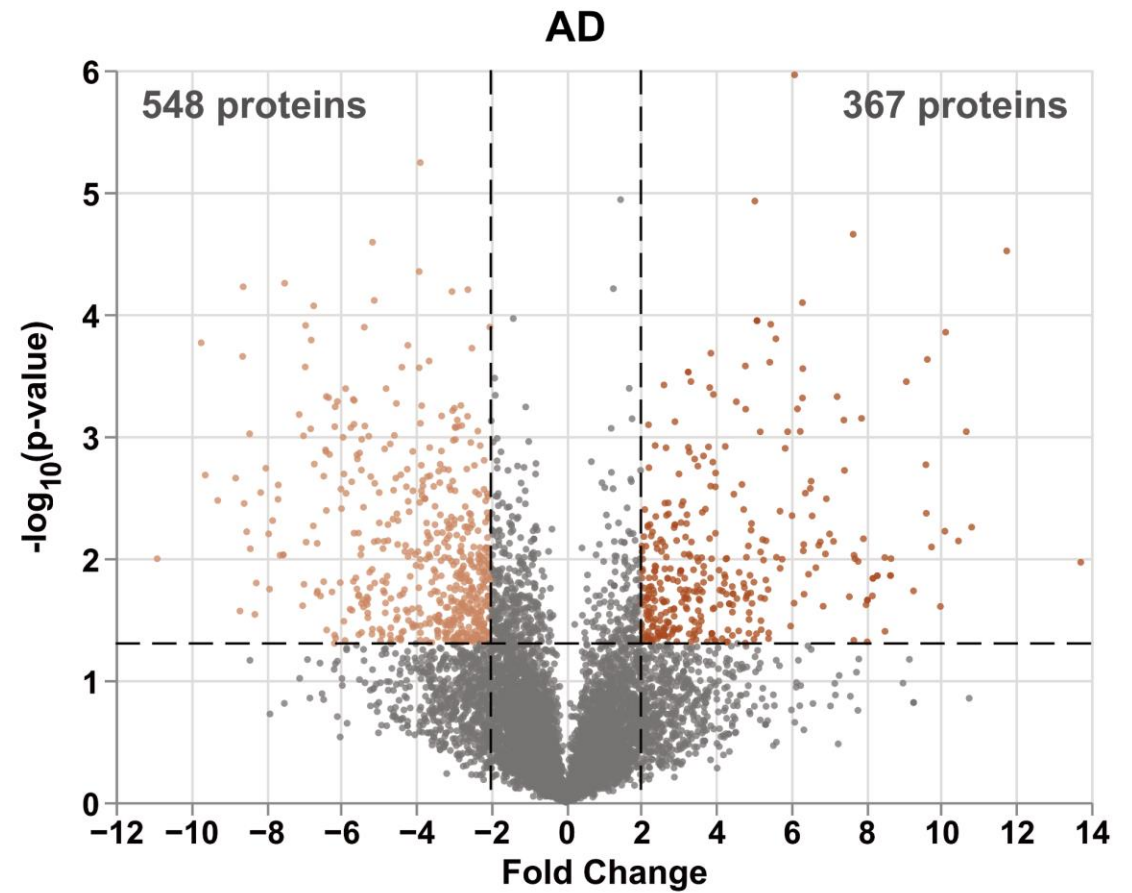
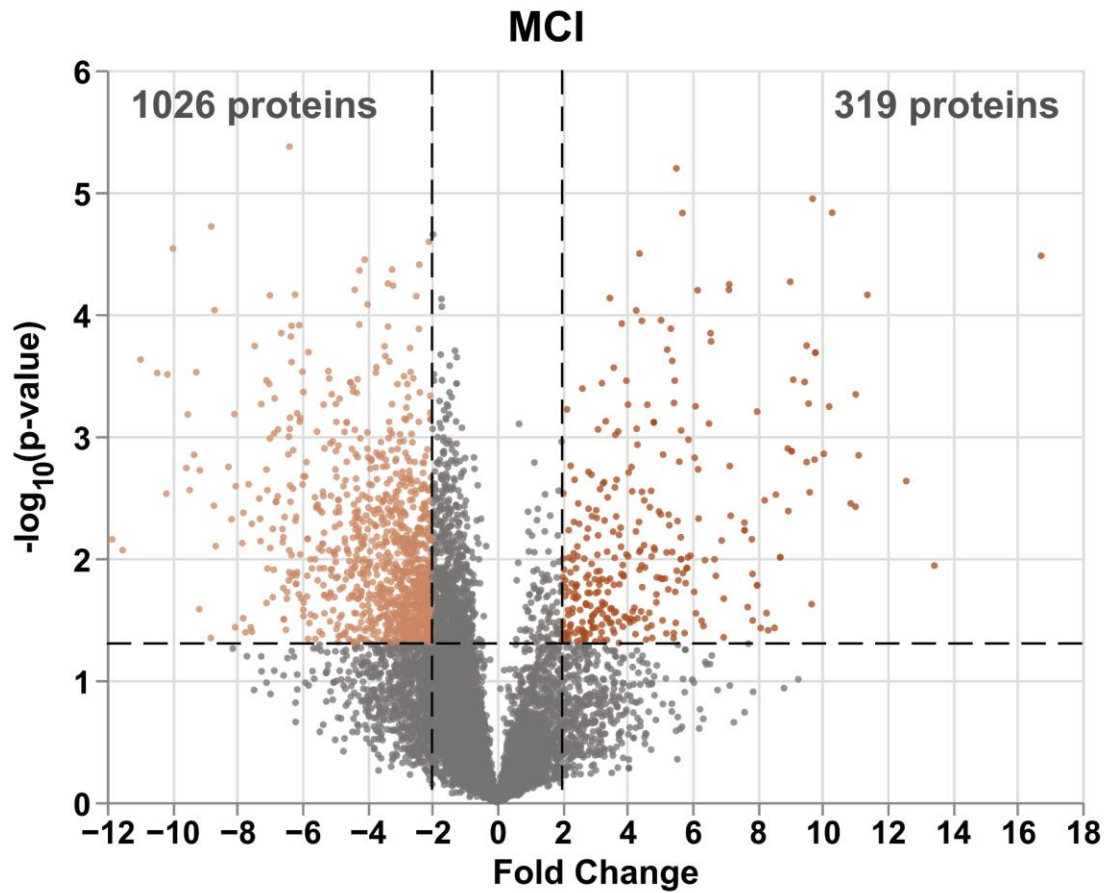


# Quantitative Comparison





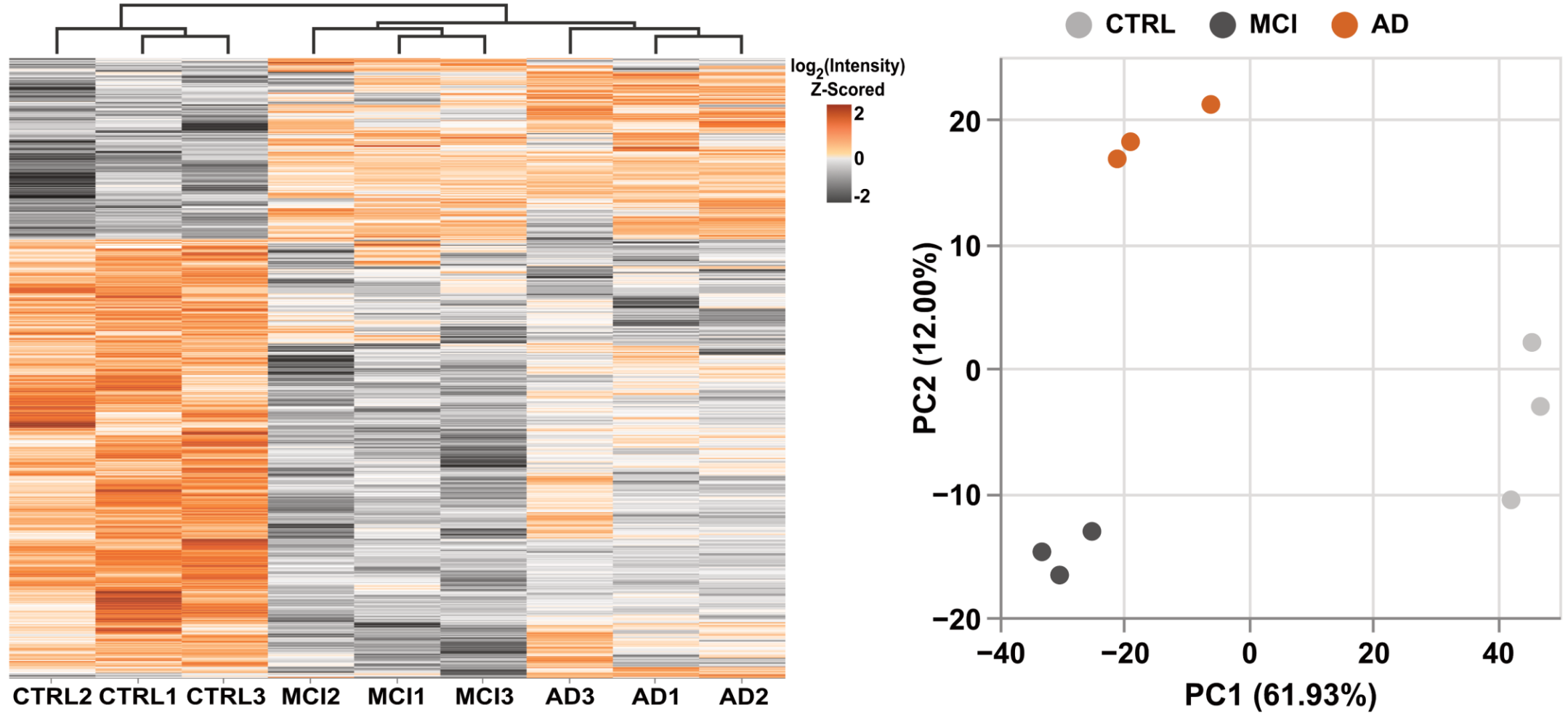
# Proteomic Perturbations in CSF



● Downregulated ● Normal ● Upregulated

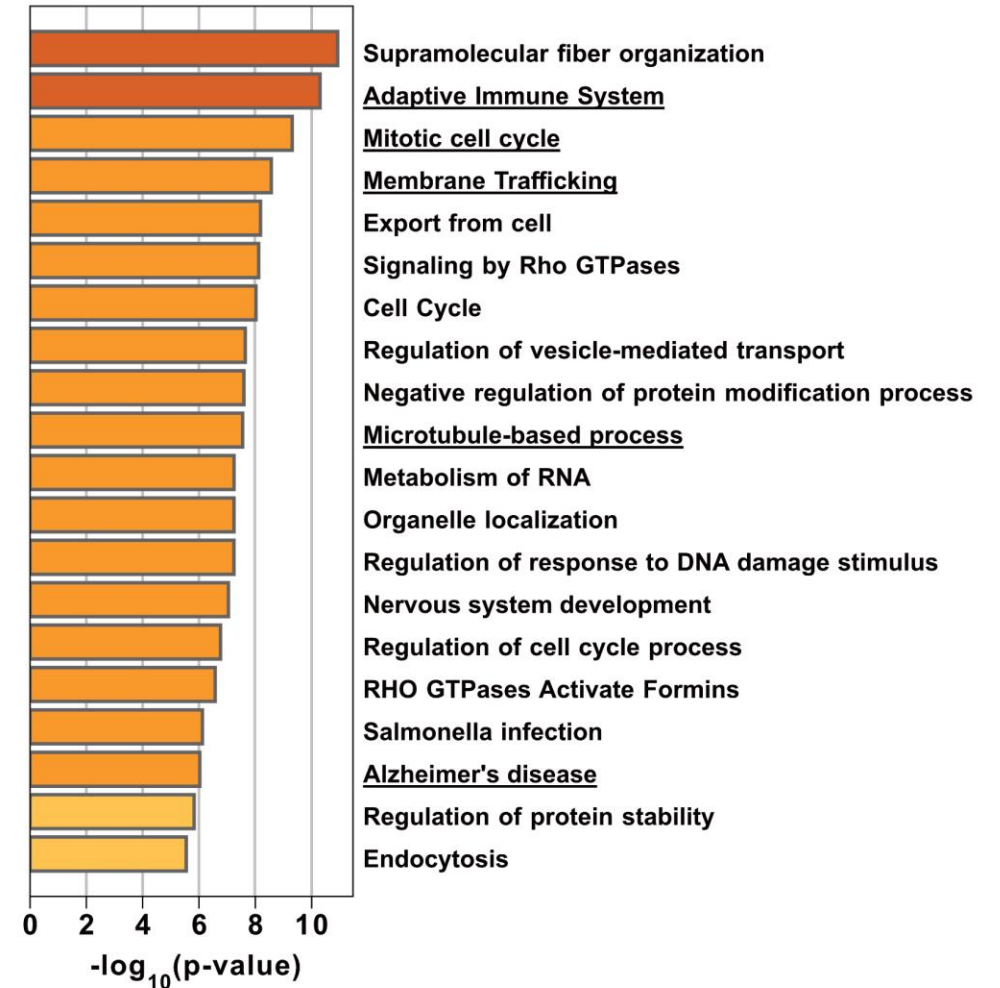
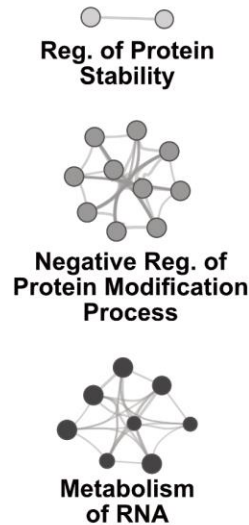
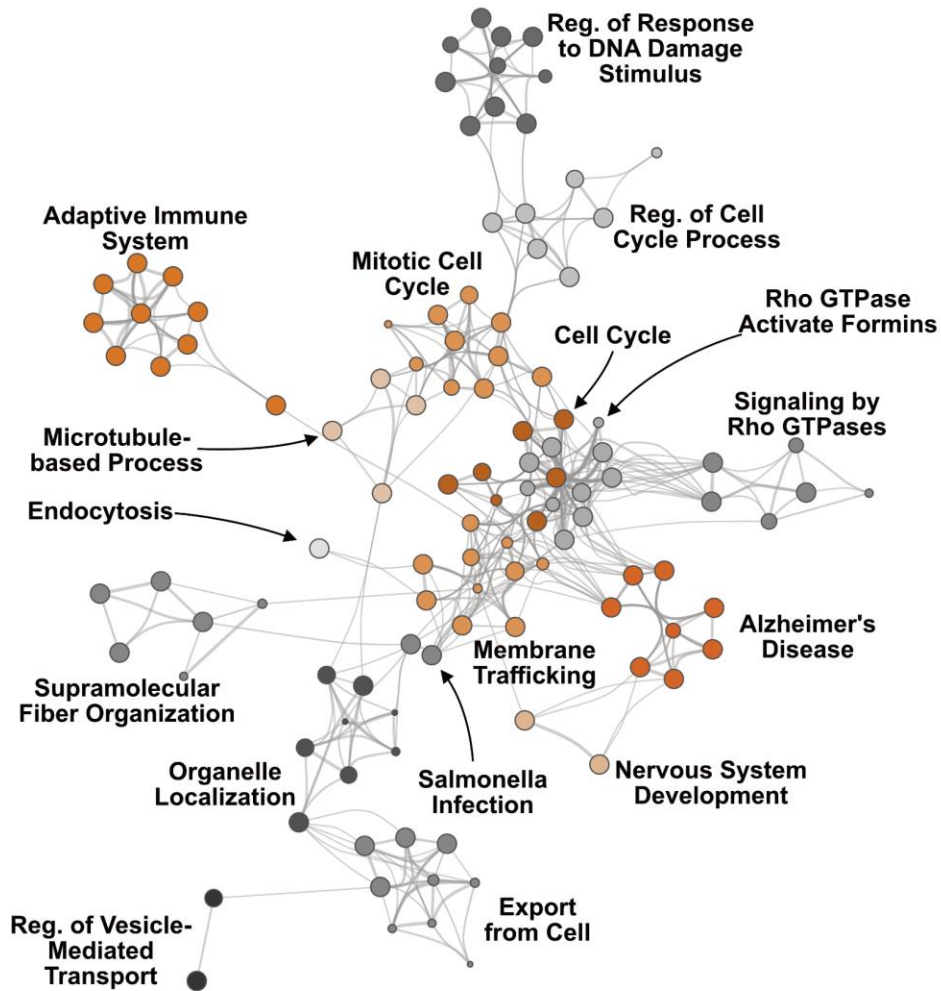


# Cohort Discrimination



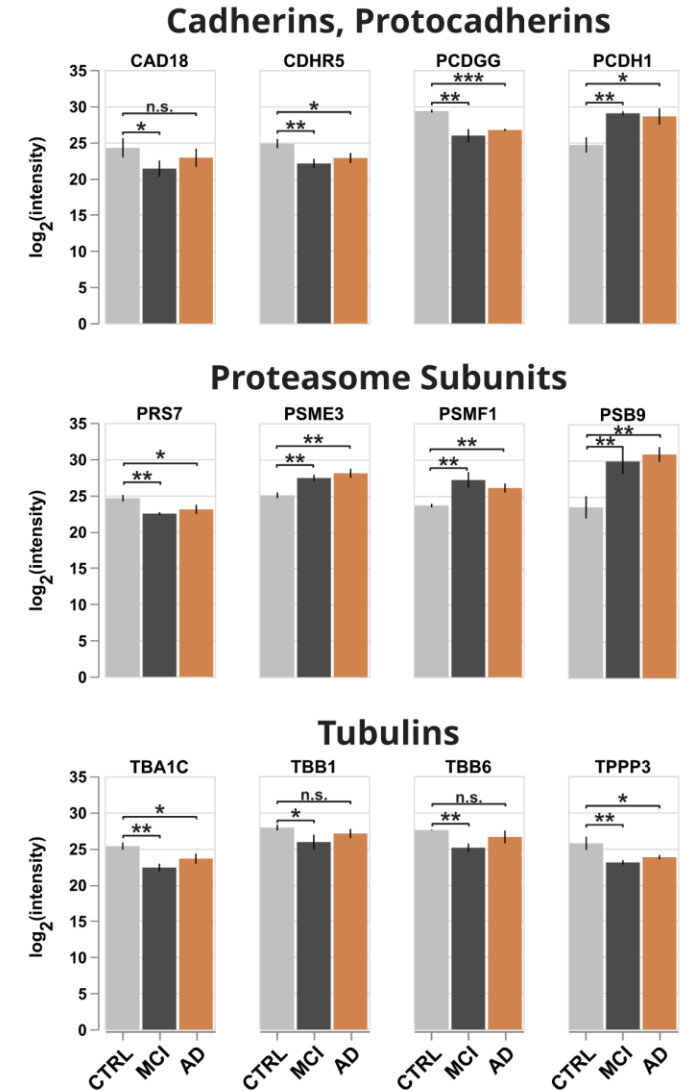
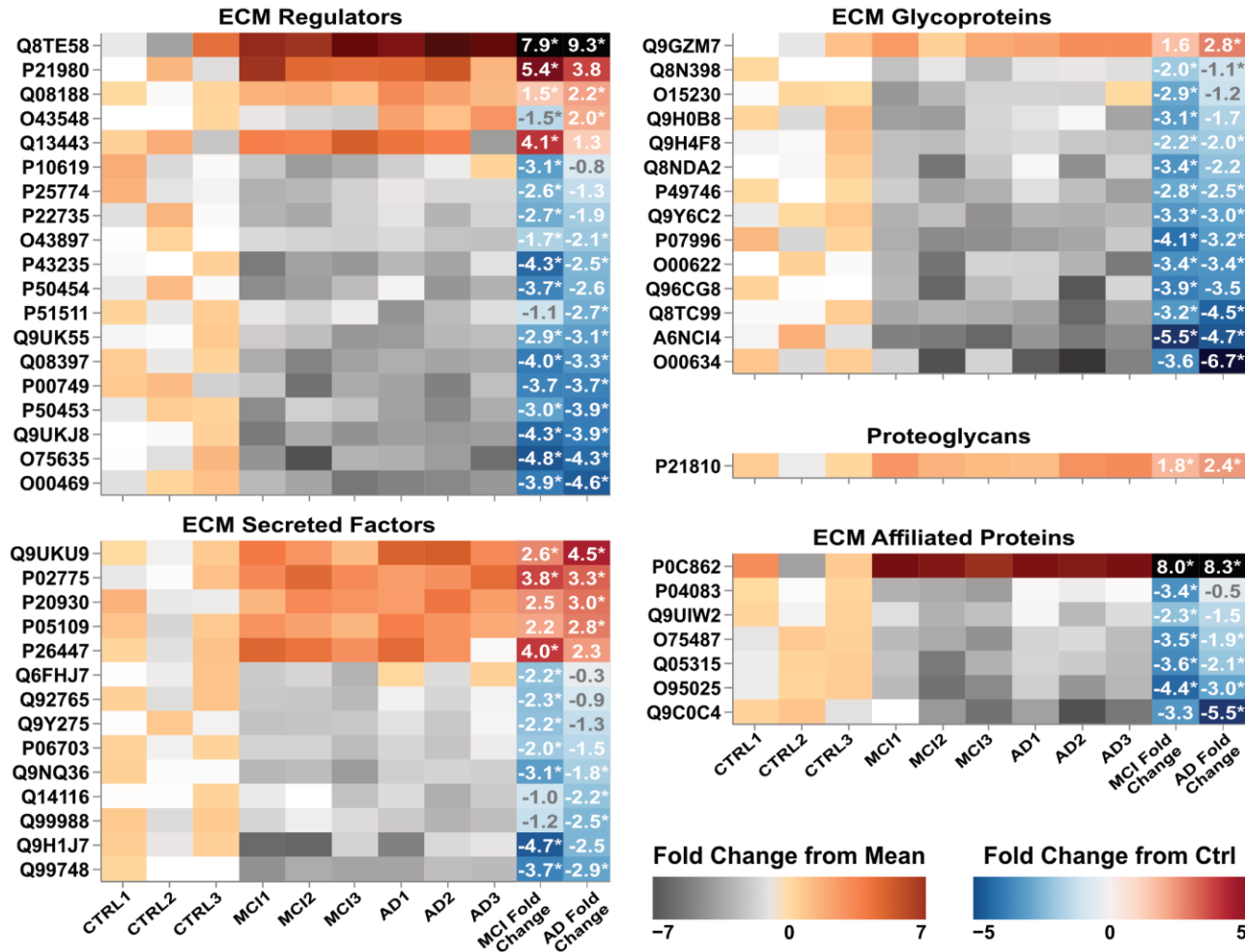


# Dysregulated Pathways





# ECM and Proteome Reorganization





## Conclusion

Using machine learning, spectral libraries can be effectively calibrated to a new experiment.

Agnostic libraries provide significantly improved profiling depth.

We advocate for a stronger community-driven approach to translate proteomic analyses to clinical application.



# Acknowledgments



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