Riley Hughes

Sterchi Award

Ph.D. Candidate, Chemistry

First Year ARCS Scholar

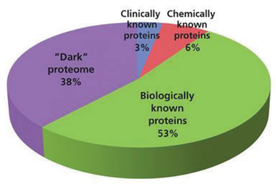
EMORY UNIVERSITY

Targeted Enrichment of the Alzheimer's Disease Ubiquitinome Using Novel Chemical Probes

This research has developed a novel chemical method to detect subtle changes in brain proteins that may signal the onset of Alzheimer's Disease, years before symptoms appear, with the potential to improve patient outcomes and accelerate the development of more effective treatments.

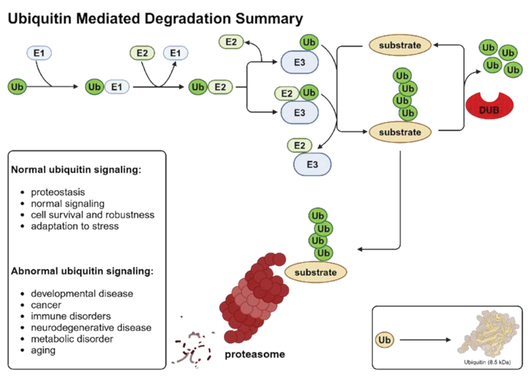
Using the Proteome to Understand Disease States

Type	Molecular Target	Data Type	Estimated Unique Entities
Genomics	Genome (DNA)	Sequence variants, mutations	~20,000 genes
Transcriptomics	Transcriptome (RNA)	Expression levels, splicing	~200,000 transcripts
Proteomics	**Proteome (Proteins)**	**Abundance, modifications, activity**	**>1,000,000 proteoforms**
Metabolomics	Metabolome (Metabolites)	Concentrations, flux	~5,000 metabolites

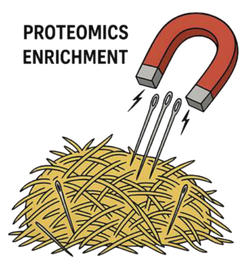


Goal: Map the "Dark Proteome" to expand the scope of known biomarkers and potentially therapeutic targets

Key Post-Translational Modification: Ubiquitin

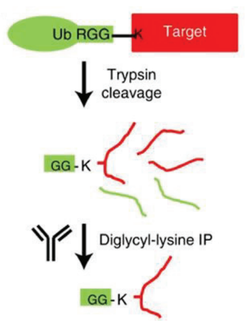


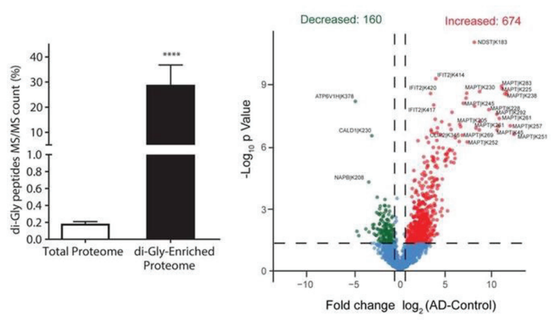
How can we detect such low-abundant species?



Typically done with antibodies, magnetic beads, etc…

Changes in Ubiquitin Levels are Linked to Alzheimer's Disease

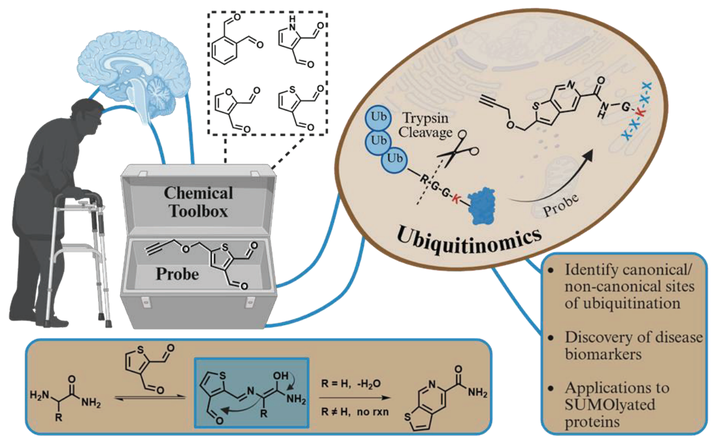




Weakness:

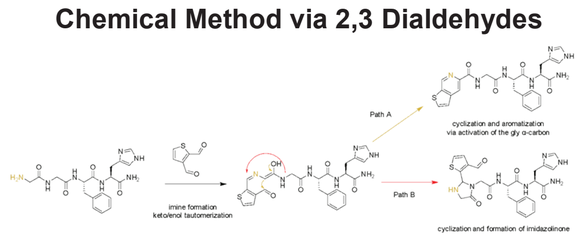
Fails to account for non-canonical ubiquitination!

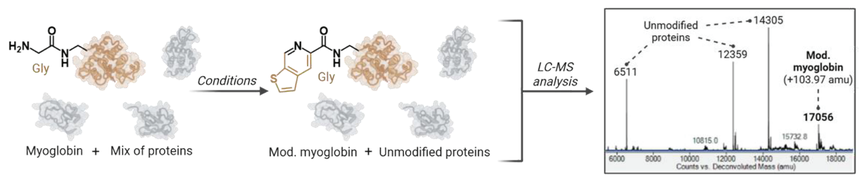
Our Approach: Selectively Tagging N-Terminal Glycine to Detect AD



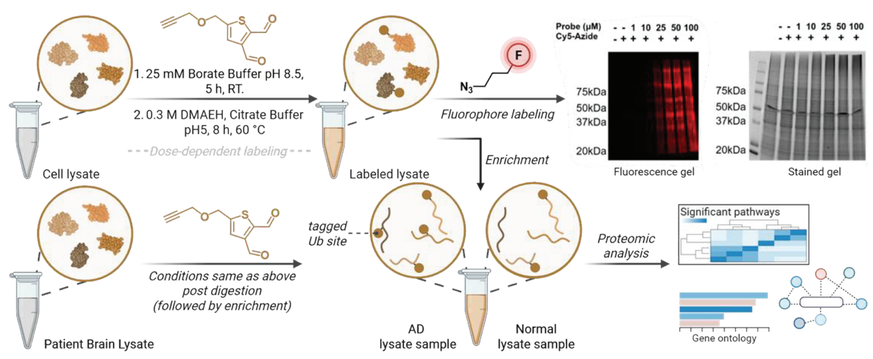
- Identify canonical/ non-canonical sites of ubiquitination
- Discovery of disease biomarkers
- Applications to SUMOlyated proteins

Chemical Method via 2,3 Dialdehydes





Preliminary Data



Scholar Awards Celebration

November 12, 2025

SCHOLAR AWARDS CELEBRATION ARCS FOUNDATION ATLANTA

Igniting Innovation in Georgia