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Sterchi Award

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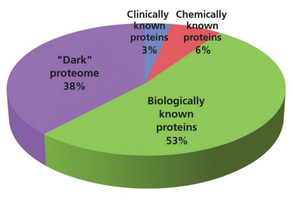
Targeted Enrichment of the Alzheimer's Disease Ubiquitinome Using Novel Chemical Probes

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.

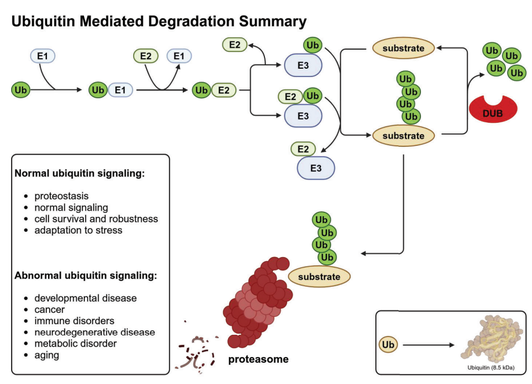
Using the Proteome to Understand Disease States

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

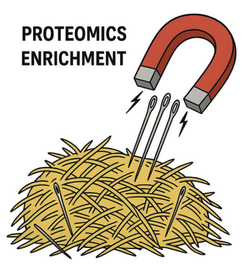


Goal: Map the "Dark Proteome" to expand the scope of known biomarkers and potentially therapeutic targets

Key Post-Translational Modification: Ubiquitin

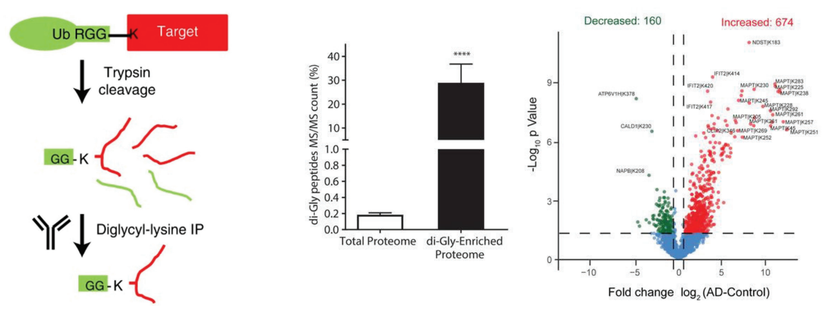


How can we detect such low-abundant species?



Typically done with antibodies, magnetic beads, etc...

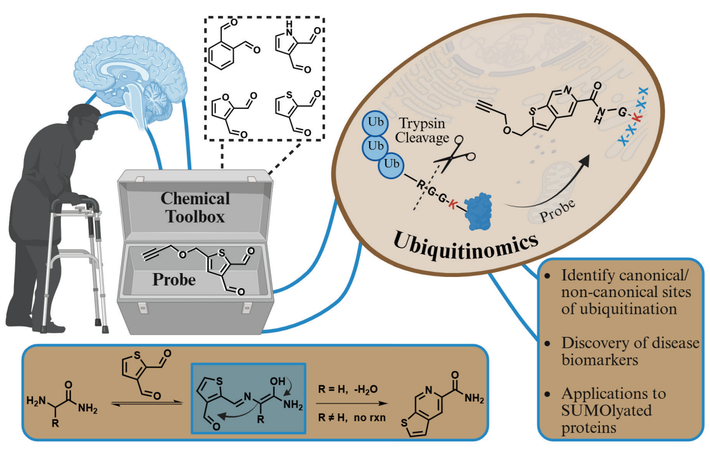
Changes in Ubiquitin Levels are Linked to Alzheimer's Disease



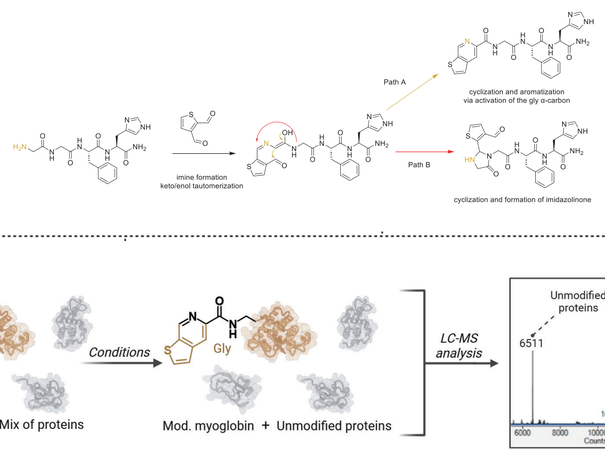
Weakness:

Fails to account for non-canonical ubiquitination!

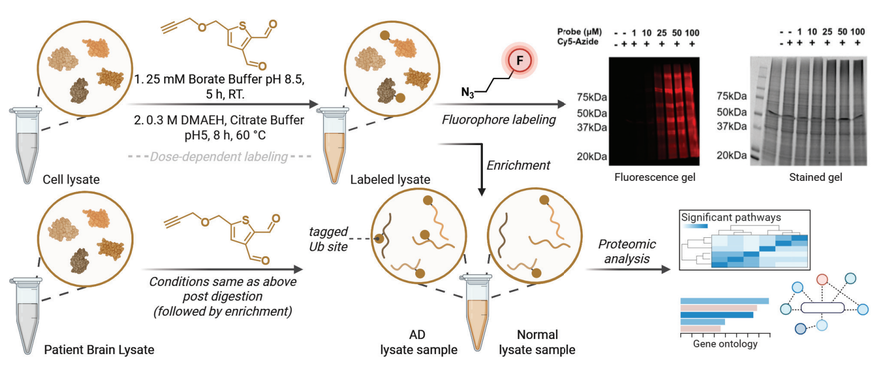
Our Approach: Selectively Tagging N-Terminal Glycine to Detect AD



Chemical Method via 2,3 Dialdehydes



Preliminary Data



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