LifeSensors <u>TUBEs</u>: TANDEM <u>UBIQUITIN BINDING ENTITIES</u>

POLYUBIQUITIN BINDING DOMAINS

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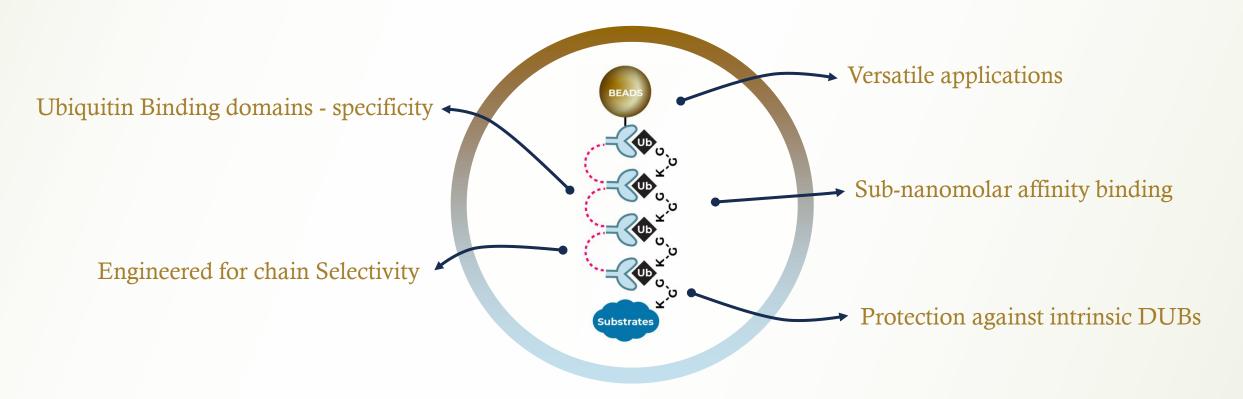
LifeSensors Inc. Mission

- Leadership in UPS, <u>PROTACs</u>, <u>DUBTACs</u>, and <u>Molecular Glues</u>
- Drug Discovery, <u>UPS Enzymes</u>, <u>DUBs</u>, <u>PROTAC Screening Services</u>
- Biomarker Development and Collaborative Research
- ~500 Products, <u>DUBs</u>, <u>E3 ligases</u>, <u>Ubiquitin Affinity Matrices (TUBEs</u>), <u>Assay Kits</u> and Proprietary <u>Protein Expression Systems (SUMO)</u>
- Profiling Compounds Against <u>Ubiquitin Ligases</u> and <u>DUBs</u>



TUBEs:

TANDEM UBIQUITIN BINDING ENTITIES







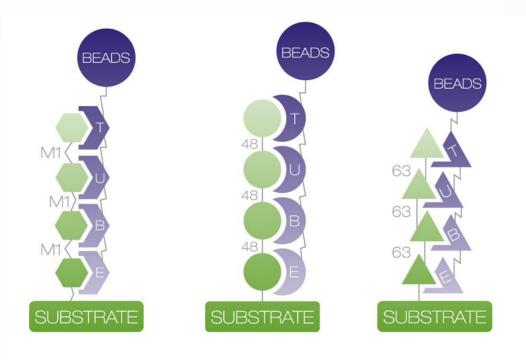
Novel Application of TUBES, in addition to Ubiquitination Studies

- ✓ Superior to antibodies, <u>detection by Western blot</u>
- ✓ Versatile tool for monitoring <u>PROTAC and molecular glue function</u>
- ✓ Isolation of ubiquitylated substrates from cell lysates
- ✓ Linkage specific isolation of ubiquitinated species
- ✓ Ubiquitin mass spec proteomics bypassing SILAC
- ✓ HTS of <u>in vivo ubiquitylated proteins</u>
- ✓ Perform E3 ligase assays using <u>TR-FRET assays</u>
- ✓ Imaging tools for In situ detection with fluorescence



What are TUBEs?

TUBEs are high affinity 'ubiquitin traps' that capture poly-ubiquitinated proteins with subnanomolar affinity.

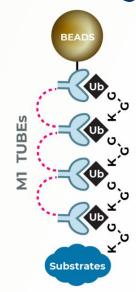


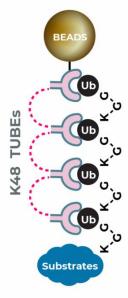
TUBEs can be used for capture or detection of total polyubiquitin or enrichment of linkage specific proteins K63-linked polyubiquitin, K48-linked polyubiquitin, and M1-linear polyubiquitin.

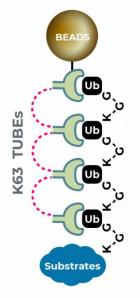


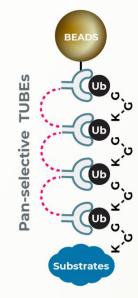
from genomics to proteom

TANDEM UBIQUITIN BINDING ENTITIES (TUBEs)

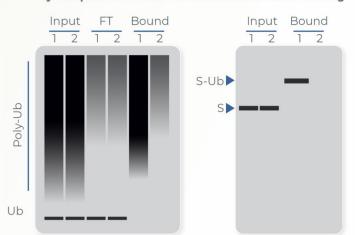




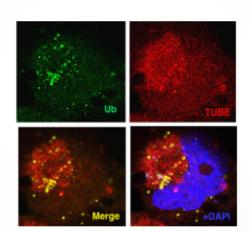




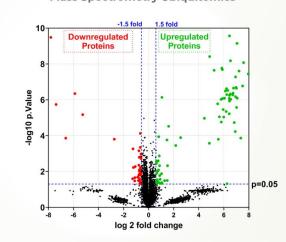
Poly-Ubiquitin Substrate Enrichment & Western Blotting



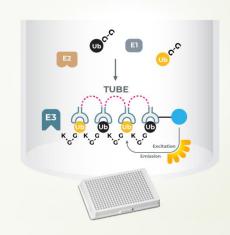
Fluorescent Microscopy



Mass Spectrometry Ubiquitomics



High-Throughput Screening







TUBEs for Research

- ✓ Follow dynamics of UPS by purification and detection of ubiquitinated proteins
- ✓ Follow PROTAC mechanism by analyzing Ub^{MAX} (maximum ubiquitination)
- ✓ Analyze chain selective ubiquitination of target proteins
- ✓ Pulldown studies with TUBEs to perform ubiquitin mass spec proteomics (ubiquitome)
- ✓ TUBE embedded microtiter plates to study diagnostic biomarker from blood
- ✓ TUBE microtiter plates to analyze overall up or down regulation of global ubiquitome/proteome
- ✓ Application of pan, K48, K63, M1 (linear) TUBE microtiter plates to analyze chain selective ubiquitination of POI
- ✓ Variety TUBE-based E3 ligase assays and HTS



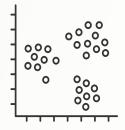
TUBEs address critical TPD challenges



Ternary complex not sufficient to induce ubiquitination



Inherent rigidity hinders the formation of the ternary complex, affecting the overall degradation efficiency of the target protein



TUBEs, a flexible platform for comprehensive analysis of liganddependent ubiquitination

The Power of TUBE Applications

Magnetic TUBEs

Pull-down of polyubiquitinated proteins

Biotin TUBEs

Biochemistry
Ubiquitin Detection
TR-FRET
'Far Western' Blot
Histochemistry

TAMRA-TUBEs

Fluorescein TUBEs Histochemistry Cytochemistry Flow cytometry TR-FRET

Agarose TUBEs

GST

TUBEs

Mass Spec & Proteomics



Biomarkers

NEW!

Phospho
-TUBEs

Neurodegeneration,
Mitophagy,
Autophagy
Biomarkers

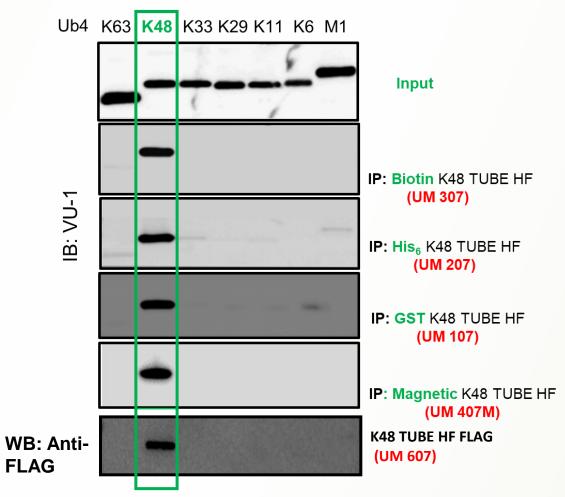


TUBEs for Drug Development

- ✓ Monitor drug mediated <u>changes in ubiquitination in cells or tissues</u>
- ✓ Analyze <u>inhibitors or activators of E3s</u>
- ✓ Assess <u>DUB inhibitor or DUBTAC activity</u> in cells or tissues
- ✓ Examine activation or inhibition of proteasome function in diseases
- ✓ <u>Neurodegenerative diseases profiling</u> from poly-ubiquitinated proteins from neurons
- ✓ Heart Failure and Cushing disease



Lysine 48 Poly-ubiquitin TUBES are Highly Selective

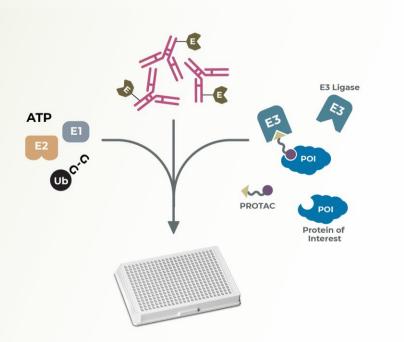


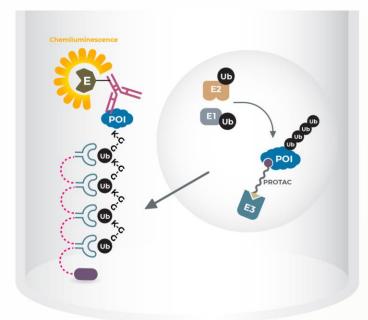
K48 TUBE HF FLAG detects only K48-linked ubiquitin chains in Western Blots

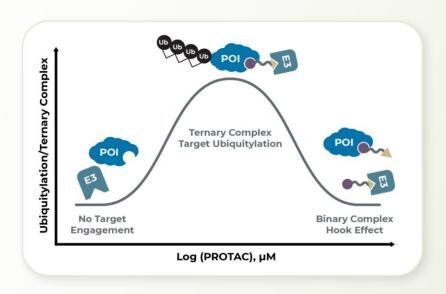


TUBE Application for HTS- In Vitro Biochemical Assay

To study functional ternary complex and 'PROTACability'



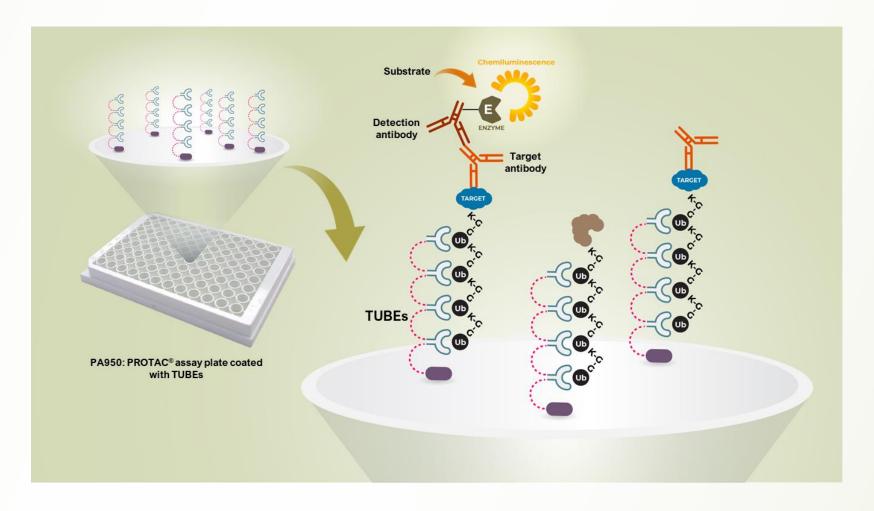




TUBE Capture & PROTAC Mediated Ubiquitination of POI Detection

Cell-Based PROTAC Assay using TUBE-coated plate

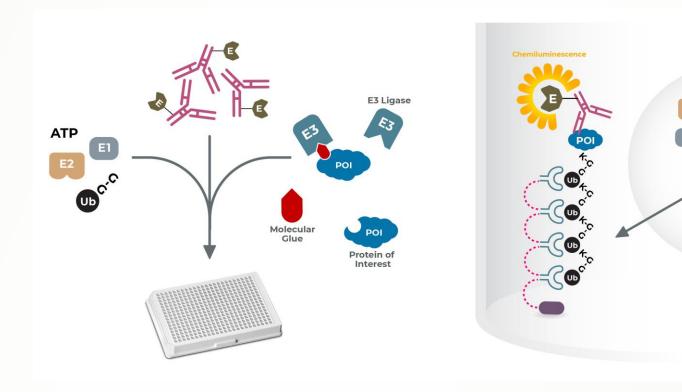
Directly monitor PROTAC-mediated ubiquitination and degradation of target protein





TUBEs' Role in Molecular Glue Discovery

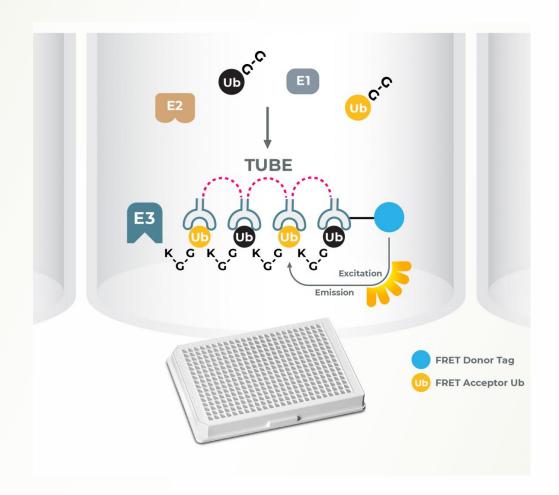
Study Molecular Glue mediated ubiquitination and degradation simultaneously





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TUBEs Facilitate Discovery of Novel E3 Ligase for KRAS



- ✓ High throughput screening for E3 ligase activators
- ✓ Homogenous assay for library screening
- ✓ Identification of novel E3 ligands
- ✓ SPR / TSA based confirmation and PROTACability

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Novel Application of TUBES, in addition to Ubiquitination Studies

- ✓ Remarkable tools for monitoring PROTAC and molecular glue function
- ✓ HTS of in vivo ubiquitinated proteins
- ✓ Isolation of PROTAC/Mol Glue mediated ubiquitinated substrates from cell lysates
- ✓ Ubiquitin mass spec proteomics bypassing SILAC
- ✓ Perform E3 ligase assays using TR-FRET assays
- ✓ Superior to antibodies for pulldowns, and detection by Western blot
- ✓ Imaging tools for In situ detection with fluorescence



Thank You

We are your partner in UPS, TUBEs, DUBs, E3s, PROTAC, Mol Glue, Protein Expression, CAR-T/Gene therapy and vaccine development

Contact Us!

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