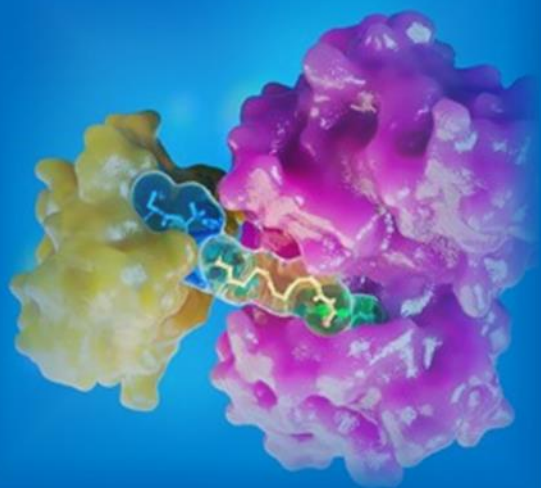




Integrated Solution to Target Protein Degradation Drug Discovery

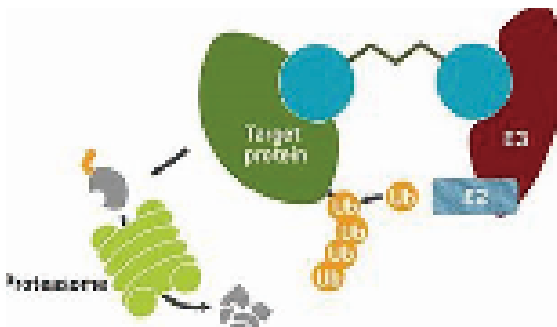
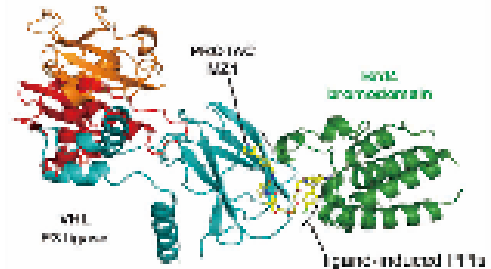
WuXi Biology's reputable *in vitro* pharmacology platform, synergized with WuXi Chemistry and WuXi Testing, is dedicated to providing comprehensive R&D supports on **Degraders**.



In Vitro Biology & Pharmacology

Binary/Ternary complex formation

- POI/E3 binary binding assay (TR-FRET, FP, SPR, SPS/TRIC)
- POI/E3 ternary binding assay (TR-FRET, AlphaScreen, SPR, SPS/TRIC)
- POI/E3 cellular engagement assay (NanoBRET)
- POI/E3 ternary complex formation cellular assay (NanoBiT, NanoBRET)

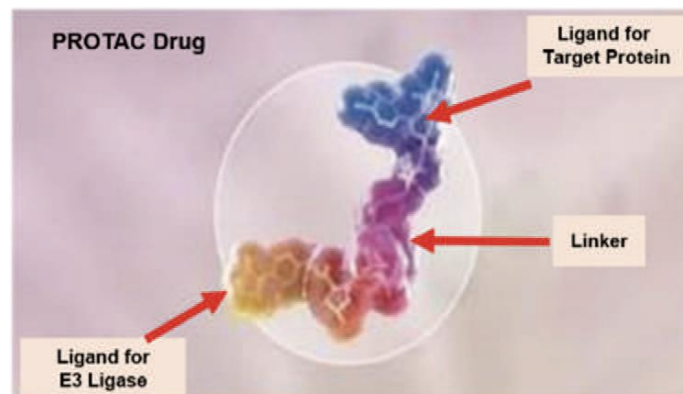


Target Ubiquitination & degradation

- POI ubiquitination assay (TR-FRET/ AlphaScreen, pulldown-WB/NanoBRET)
- POI degradation assay (HiBiT/ In-cell Western, ELISA, AlphaLISA, TR-FRET, WB/JESS)
- Other assays (POI functional assay, neo-substrate degradation profiling, degradation MOA study, global proteomics, etc.)

Chemistry

- Degradable specific virtual library design
- Fast compound synthesis within house toolbox of most common E3-ligase ligands, linkers, and some literature reported target-binding ligands
- Conventional and special DEL for ternary complex finding
- Ligand and linker structure modification, conjugation and all types of custom syntheses from milligram to kilogram scale
- SAR follow up and lead optimization
- Purification and analytical support on Hetero-bifunctional molecules



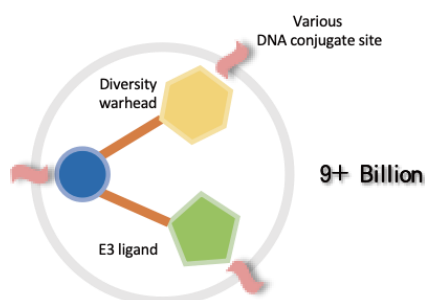
Hit Finding for Ternary Complex Formation

Novel library designs and screening methods enable the hit identification of ternary complex formation.

One stop screening for both POI and linker with bifunctional DEL



DNA Barcode



Diverse warhead:

liner & brancher scaffolds cover wide chemical space

Diverse linker:

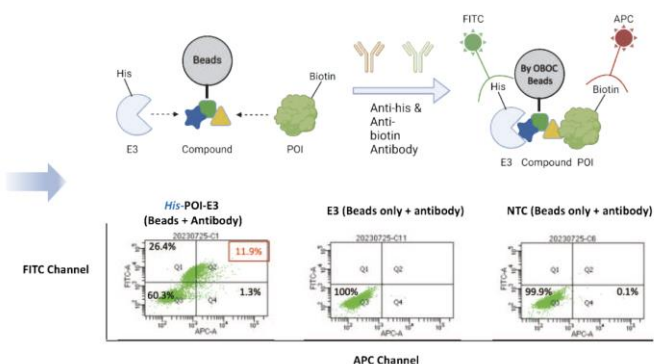
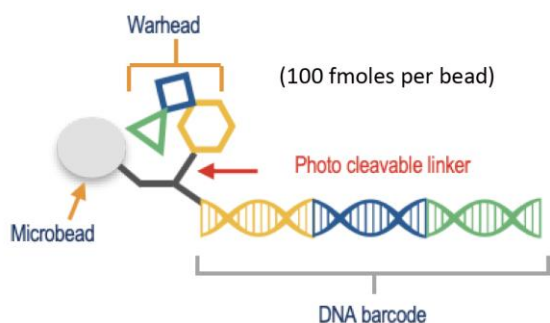
length and type (flexible and rigid) are selected based on statistics of reported PROTAC®

Various validated DNA conjugate site

Widely used & novel reported E3 ligands

Intermediate library with handle for fast customized design

Ternary complex screening with On-Bead DEL



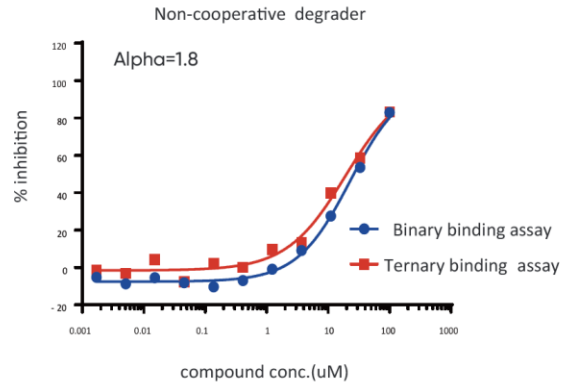
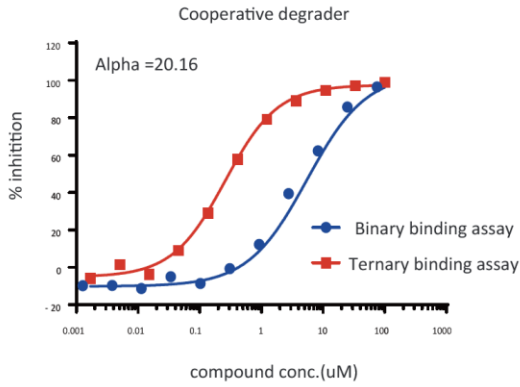
- On-Bead DEL is a hybrid of DEL and miniaturized HTS
- One bead : one type of molecule : one DNA tag
- It enables both affinity- and function-based selection of hits
- POI and E3 are stained by using corresponding fluorescence-labeled antibody
- Beads have both positive fluorescence signals can be sorted out using FACS

Efficient hit finding approach for TPD and MGD molecules from WuXi Biology's proprietary and customized libraries. Bi-functional DEL can achieve the screening for both POI binders and linkers simultaneously, and OBOC screen is able to sort out ternary complex directly based on the fluorescent signals.

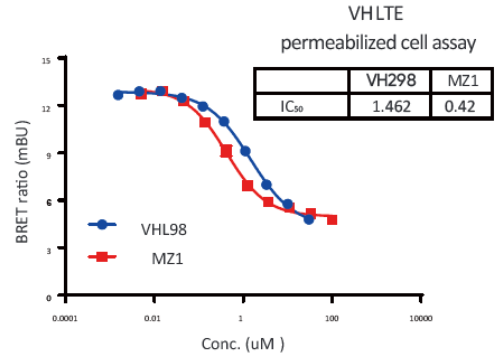
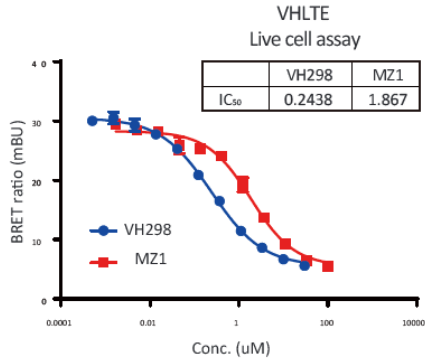
Binary Binding Assay Platform

Binary binding assays could be utilized to drive warhead/linker optimization, cooperativity, target engagement and cell permeability evaluation.

Evaluation of binding cooperativity



Evaluation of permeability

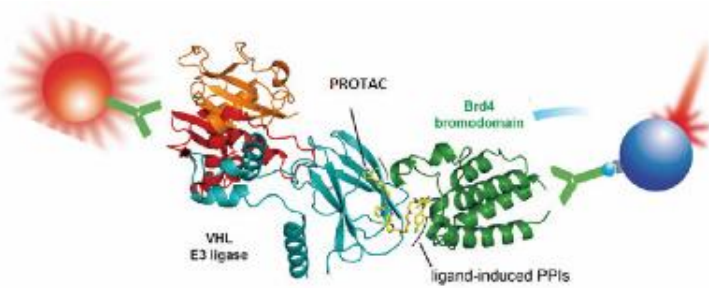


Compound		VH298	MZ1
IC ₅₀ (uM)	Live cell assay	0.2438	1.867
	Permeabilized cell assay	1.462	0.42
Potency shift		6.00	0.22
Relative binding affinity (RBA)		0.1668	4.4452
Availability index (AI)		1	26.6568

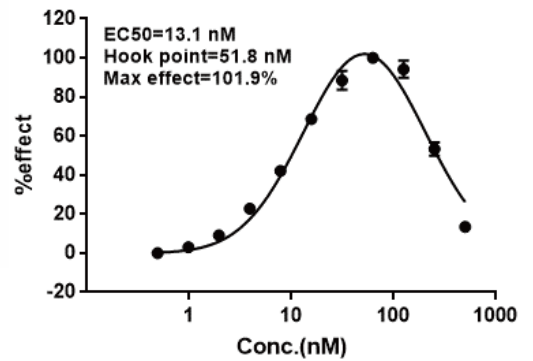
Ternary Binding Assay Platform

Ternary binding assays connect the binding events with ubiquitination/degradation and offer better data translation/prediction than binary binding assays.

Biochemical ternary binding assay

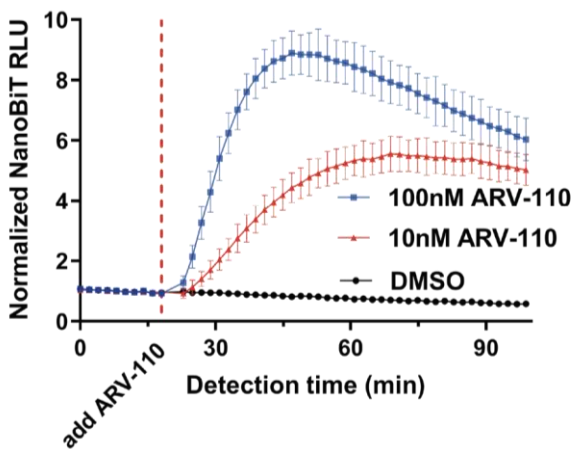


Test of reference in ternary complex assay

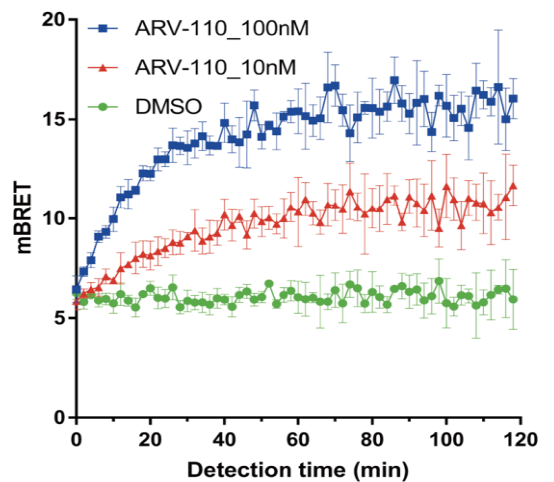


Cellular ternary binding assay

ARV-110 ternary complex formation_NanoBiT



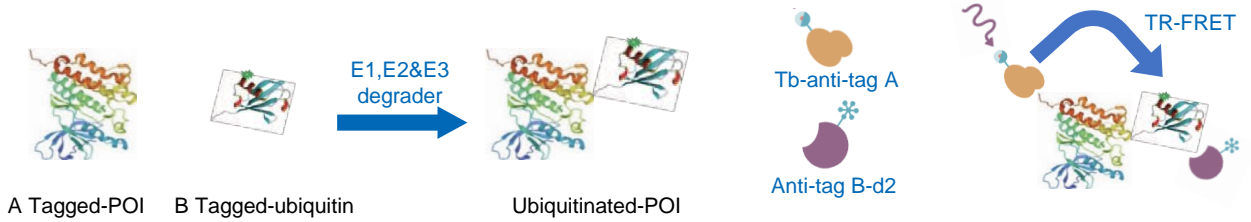
ARV-110 ternary complex formation NanoBRET_RFP-CRBN



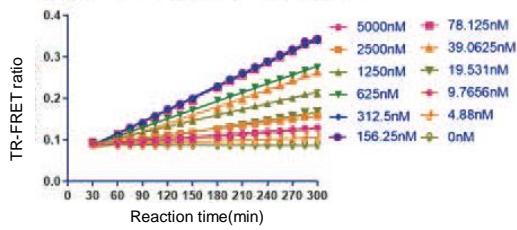
POI Ubiquitination Assay Platform

POI ubiquitination assays provide further insights and understanding on the degradation mechanism, help to drive SAR and support candidate nomination.

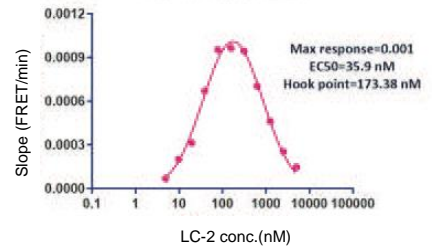
Biochemical POI Ub assay



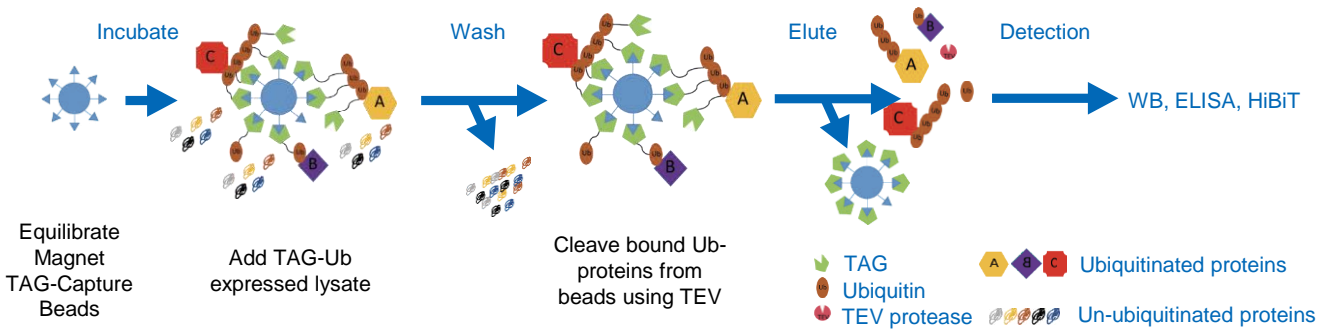
Progress curve for LC-2 induced VHL-dependent ubiquitination of KRAS G12C



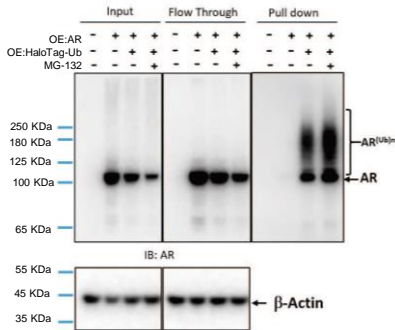
Curve fitting for LC-2



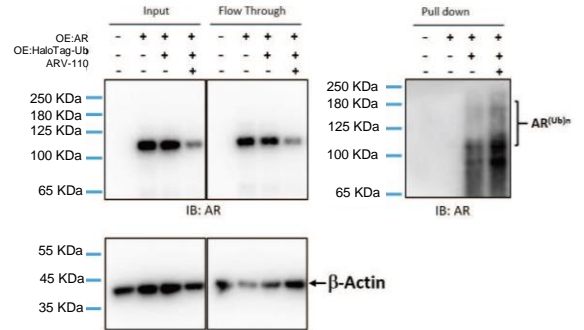
Cellular POI Ub pull-down assay



Validation of pull-down system



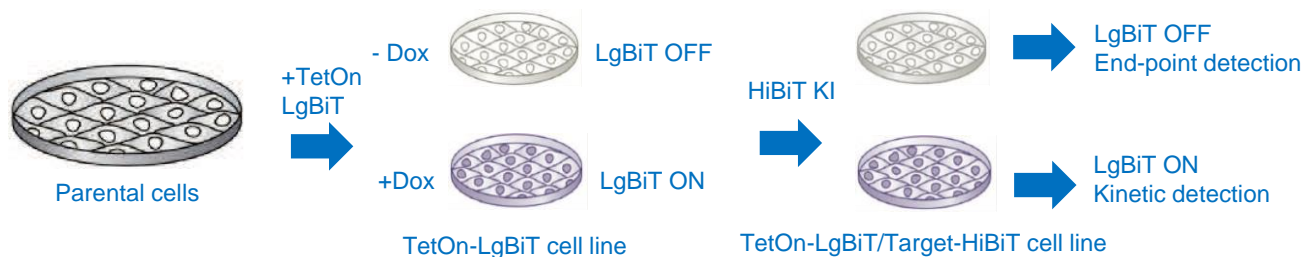
Validation using reference degrader



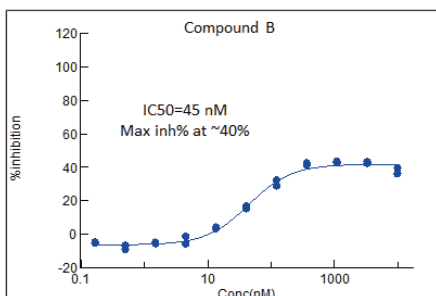
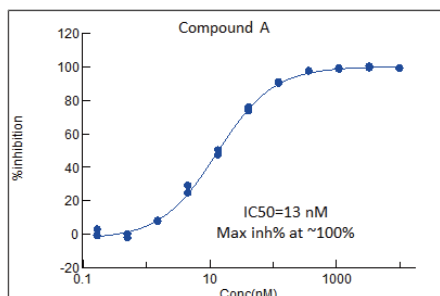
POI Degradation Assay Platform

Diversified formats (HiBiT, In-cell Western, ELISA, AlphaLISA, TR-FRET, WB/JESS) are offered for customizing the most suitable POI degradation evaluation at specific R&D stage.

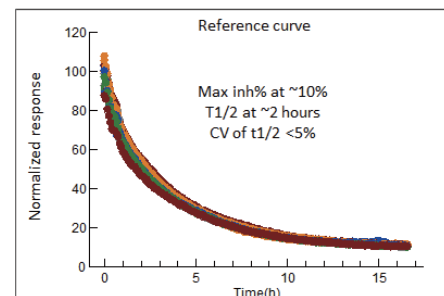
“ 2 in 1 ” POI degradation system



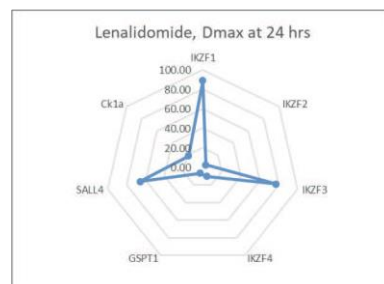
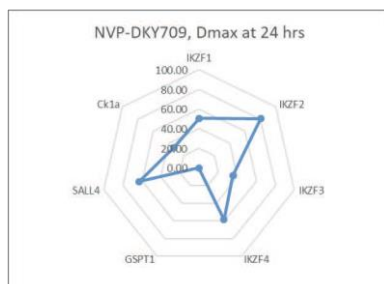
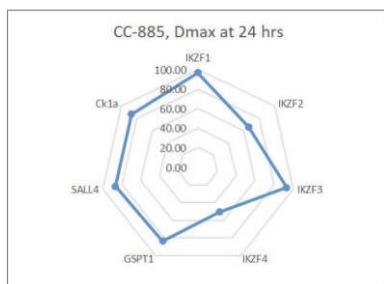
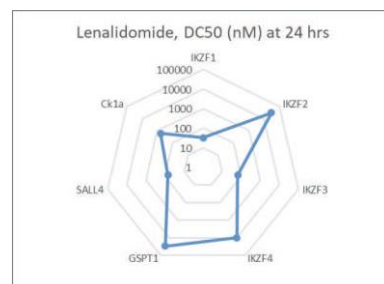
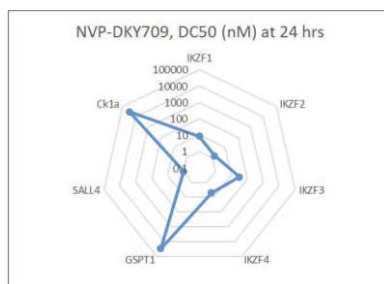
End-point assay



Kinetic assay

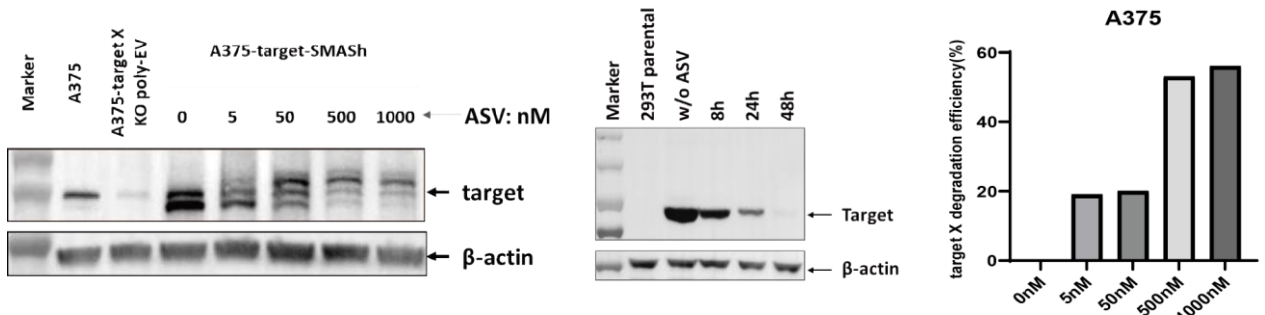
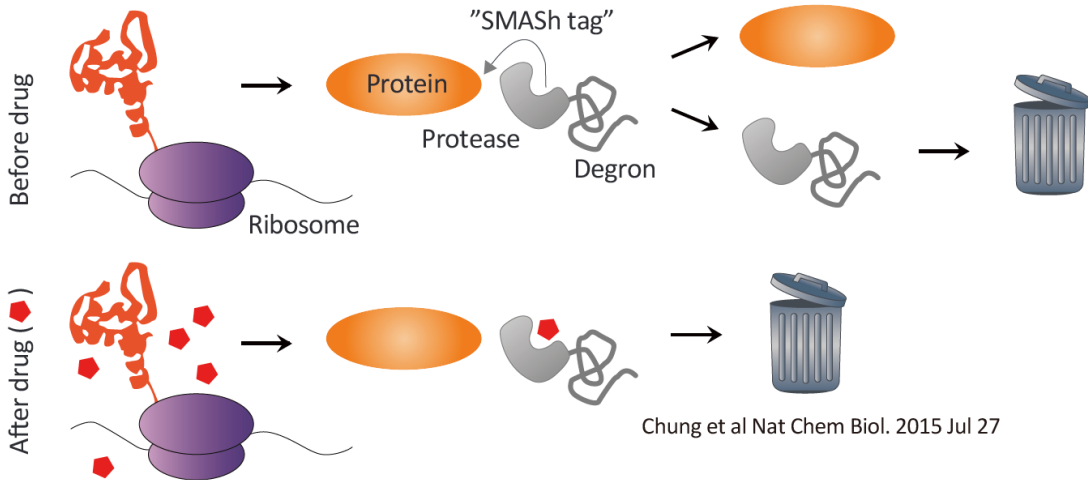


Degradation profiling against neo-substrates



Representative degradation bias profiling for 3 references

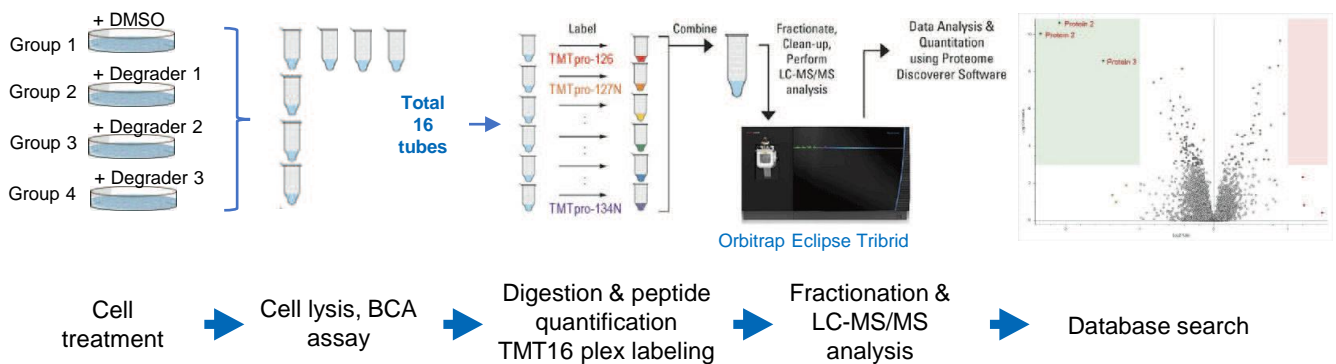
Target Validation and MoA Investigation



ASV triggered rapid target degradation in time- and dose-dependent manner, enabling target validation and MoA investigation.

Quantitative Protein Level Analysis

Quantitative Protein Level Analysis is the golden standard for unbiased /selectivity evaluation of TPD molecules and could be applied to drive the candidates away from potential toxicity issue.



WuXi Biology

A comprehensive spectrum of services and solutions, supporting stand-alone and integrated projects from early discovery to clinical development.

Comprehensive discovery and translational biology centers, with **~3,000** experienced scientists and global footprints in **9** sites

State-of-the-art early discovery screening platform, providing diverse hit finding solutions such as DEL/HTS/ASMS/FBDD* and virtual screening, supported by **cutting-edge** informatics and data sciences

Thousands of validated, 'ready to go', in vitro assays and in vivo models enabling discovery biology for comprehensive target classes, therapeutic areas and modalities

Extensive **Oncology, Immunology, Infectious Disease, Inflammation, Neuroscience and Metabolic Disease indication**, offering an end-to-end service from discovery, through optimization and into clinical development

AAALAC accredited and **BSL-2** certified small animal and large animal facilities on multiple sites

CAP-certified pathology and FACS capabilities supporting clinical biomarker services



Shanghai(Waigaoqiao), China



Munich, Germany



Boston, USA



Shanghai(Zhangjiang), China



Chengdu, China



San Diego, USA



Nantong, China



Suzhou, China



Cranbury, USA

Expertise and Knowledge on Degraders

- Build 20+ *in vitro* assays to investigate binary/ternary complex formation, POI ubiquitination and degradation
- Offer tailored research strategy consulting service based on the study phase and progress to organize efficient study structure.
- Provide integrated solutions covering Chemistry, Structural biology, Target validation and *In vitro* pharmacology, *In vivo* evaluation and Biomarker Analysis.

Hit Finding for Ternary Complex Formation

Binary Binding Assay

Ternary Binding Assay

POI Ubiquitination Assay

POI Degradation Assay

Degradation Mechanism & Selectivity

In vivo Efficacy and PK/PD



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