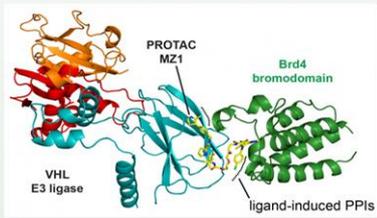


# Targeted Protein Degradation Platform

Expertise and Knowledge at **PROTAC** Technology

HD Biosciences, a WuXi AppTec company, with its industry-leading capabilities, experienced leadership and science-driven teams, has been recognized as a reliable global partner for preclinical drug development and integrated R&D services. Our reputable *in vitro* pharmacology platform synergized with WuXi AppTec chemistry provides comprehensive supports for **PROTAC** R&D with validated *in vitro* assays in good track record world-widely.

## PROTAC BIOLOGY & PHARMACOLOGY



### BINARY/TERNARY COMPLEX FORMATION

#### Biochemical & Biophysical Assays

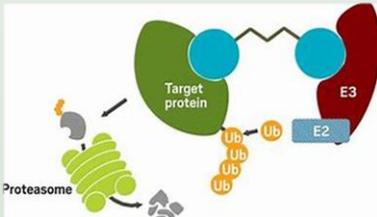
Biochemical binding assay (TR-FRET, AlphaScreen, FP, etc.)

Biophysical binding assay (SPR, TRIC/MST, DSF)

#### Cellular Assays

POI/E3 target engagement assay (NanoBRET)

POI-E3 ternary complex formation assay (NanoBiT, NanoBRET)



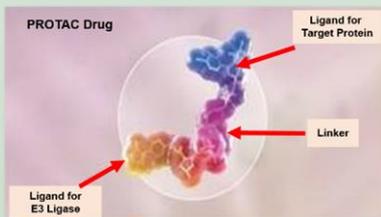
### TARGET UBIQUITINATION & DEGRADATION

#### *In vitro* Assays

- Target ubiquitination (IP-WB, NanoBRET or TR-FRET)

- Target degradation assay (HiBiT, ICW, ELISA, AlphaLISA, TR-FRET, WB)

#### PK/PD and Animal Disease Model Evaluation



## PROTAC CHEMISTRY

- PROTAC specific virtual library design

- Fast compound synthesis with in house collection of most common E3-ligase ligands, linkers, and some literature reported target-binding ligands

- Ligand and linker structure modification, conjugation and all type of custom syntheses from milligram to kilogram scale

- SAR follow up and lead optimization

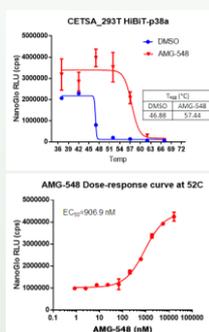
- Purification and analytical support on PROTAC featured compounds

# IN VITRO PHARMACOLOGY PLATFORM at HDB FOR PROTAC RESEARCH

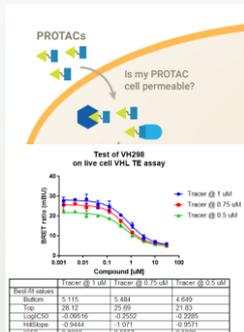
## Binary Binding Assay Platform

Binary binding assay works for warhead/linker optimization, cooperativity evaluation and PROTAC permeability evaluation

- Comprehensive solutions and multiple options for biochemical assays (TR-FRET, AlphaScreen, FP, radioactive, etc.), biophysical assays (SPR, TRIC/MST, DSF) and cellular assays (CETSA, NanoBRET)
- Scientific teams with experience >15 years
- Provide both customized assay development and ready-to-go assays upon request



HiBit-CETSA binary binding assay

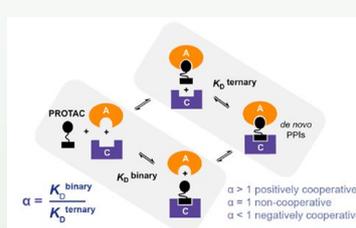


VHL target-engagement assay

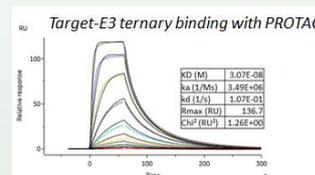
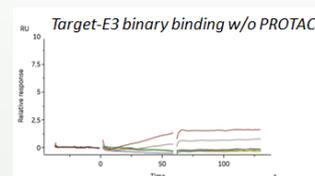
## SPR Assay Platform

SPR assay enables kinetic evaluation of binary/ternary complex formation and provides both affinity and kinetics parameters

- Biophysical approach to evaluate binary/ternary complex formation
- Provide affinity and kinetics parameters to truly characterize binding events
- Powdered by Biacore 8K/8K+ (first installation in China) offering both SAR and library screening



Graph excerpted from Michael J. Roy, et. al. SPR-Measured Dissociation Kinetics of PROTAC Ternary Complexes Influence Target Degradation Rate.

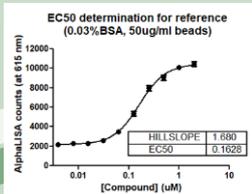
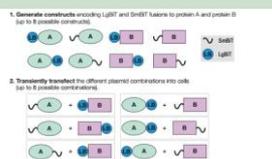
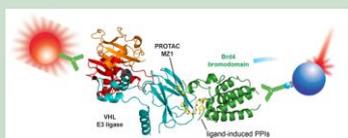


Binary/ternary binding SPR assay

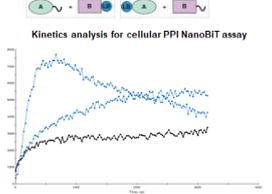
## Ternary Binding Assay Platform

Ternary binding assay is used to investigate ternary complex formation, and bridges between binary binding and degradation events

- Provide customized solutions to better address PROTAC R&D needs/challenges and understand binding/degradation connection
- Offer flexible options for cellular assay development (transient transfection/stable cell line generation; end-point/real-time kinetic analysis; 96/384/1536 well screening)



Ternary binding AlphaScreen assay

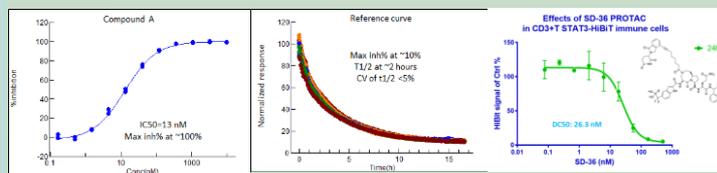
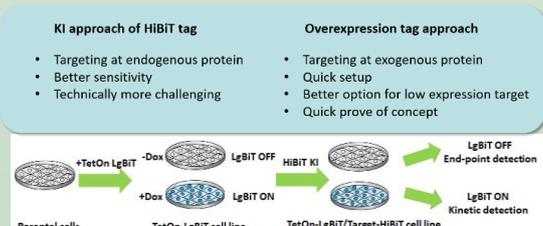


Ternary binding NanoBIT assay

## POI Degradation Platform

POI degradation was monitored at endogenous level and support both end-point and kinetic detection readout

- Available in diversified assay formats (HiBit, ICW, ELISA, AlphaLISA, TR-FRET, WB, etc.)
- HiBit knock-in cell line recommended for POI degradation evaluation with end-point and kinetic detection options



HiBIT cell line generation and assay development