AXCELEAD
Drug Discovery Partners

AXCELEAD

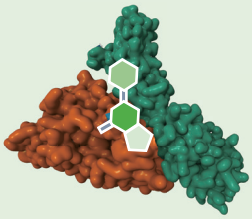
Targeted Protein Degradation (TPD) Integrated Solutions

Unleash the Power of Targeted Protein Degradation Drug Discovery with Axcelead's Comprehensive Range of Solutions!

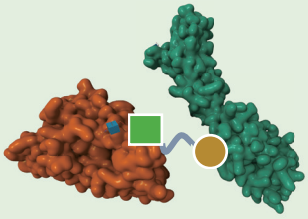
In Targeted Protein Degradation (TPD) drug discovery, each degrader type presents unique challenges and varying levels of difficulty, requiring advanced techniques, robust evaluation systems, diverse expertise across multiple fields, and specialized compound libraries.

Targeted Protein Degrader Types

Molecular Glue Degrader



Chimeric Degrader



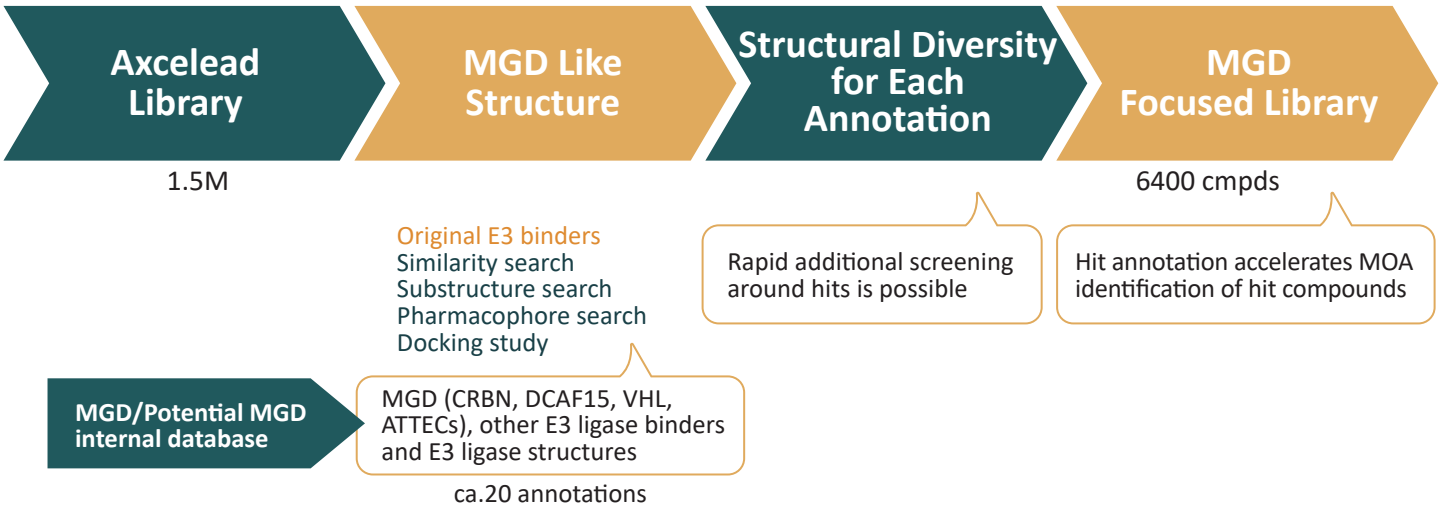
We have built an integrated platform to help you achieve innovative breakthroughs in TPD drug discovery. Moreover, our experienced researchers provide tailored solutions based on your specific challenges and requirements.

Integrated TPD Platform

- Molecular Glue Degrader (MGD) Focused Library
  - Includes original E3 ligase binders
- High-throughput Screeing (HTS) Platform
  - Degrader HTS
  - Binder HTS
- Degrader Profiling Platform
  - Various cellular assays
  - Biophysics
  - Comprehensive profiling
  - Degradation mechanism
- Target Discovery Platform
  - Novel neo-substrate
  - KI/KO technologies
- High-throughput Chimeric Degrader Synthesis
  - Fast access of diverse chemical space
- ADME Solution for Chimeric Degrader
  - Rapid development of oral drug

Molecular Glue Degrader (MGD) Focused Library

6400 compounds selected from Axcelead 1.5M library, including our original binders of E3 ligases



High-throughput Screening (HTS) Platform

TPD drug discovery requires mastery of various assay systems. We specialize in providing the most suitable assay systems, offering customized recommendations to ensure you get the perfect fit for your unique targets.

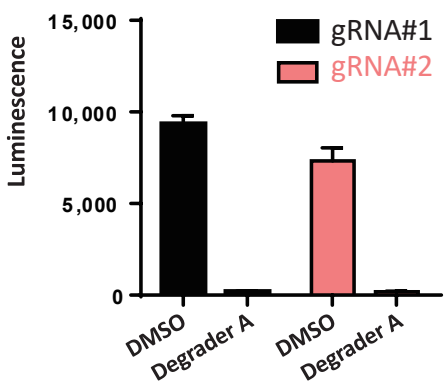
Cell-free platform

- E3 binder screening using fluorescent probes (e.g. CRBN) • Ternary complex formation assay （TR-FRET, AlphaScreen）
- Direct binding screening by ASMS (in-progress against multiple E3 ligases) • Ubiquitination enzyme assay HTS

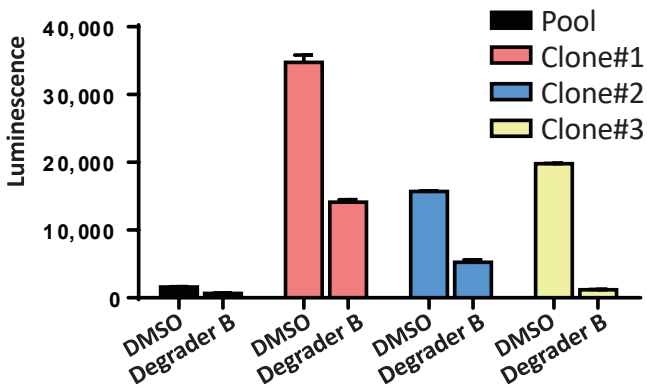
Cell-based platform

- HiBiT® tag knock-in cell line by CRISPR-Cas9 & HTS
- Cell-based imaging screening
- Cell-based ternary complex assay using NanoBRET® system

Protein X, HiBiT® tag KI pool

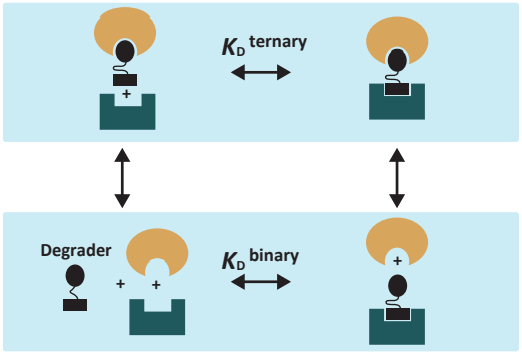


Protein Y, HiBiT® KI single cell cloning



Degrader Profiling Platform

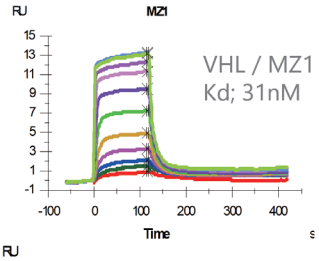
Biophysical ternary complex assay by SPR

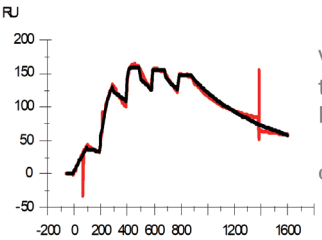


$$\alpha = \frac{K_D^{\text{binary}}}{K_D^{\text{ternary}}}$$

α > 1 positively cooperative
α = 1 non-cooperative
α > 1 negatively cooperative

In-house experiment:
Binary Kd and ternary Kd determination





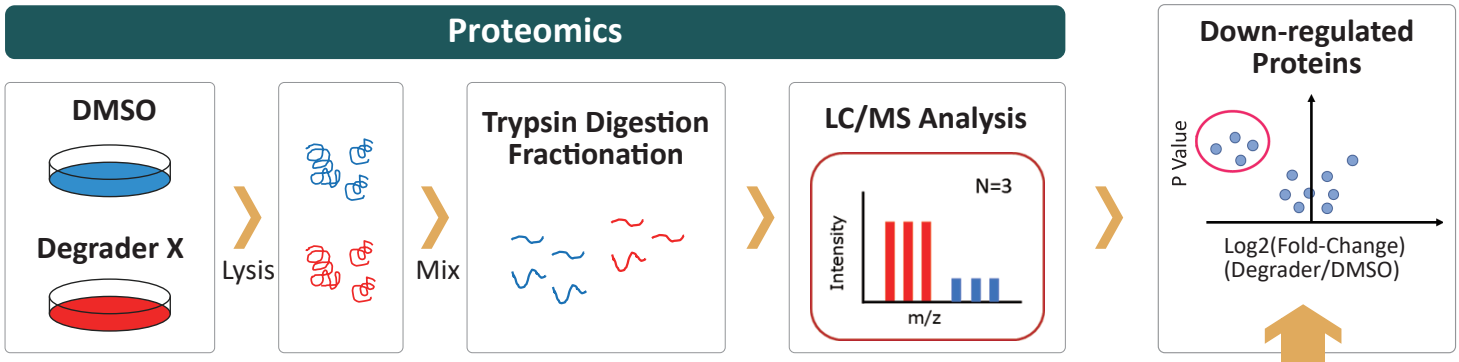
Others

- Simple Western (Jess) system for high throughput and routine assay
- Comprehensive analysis of degrader selectivity using proteomics
- Capabilities to identify the degradation pathway and mechanism

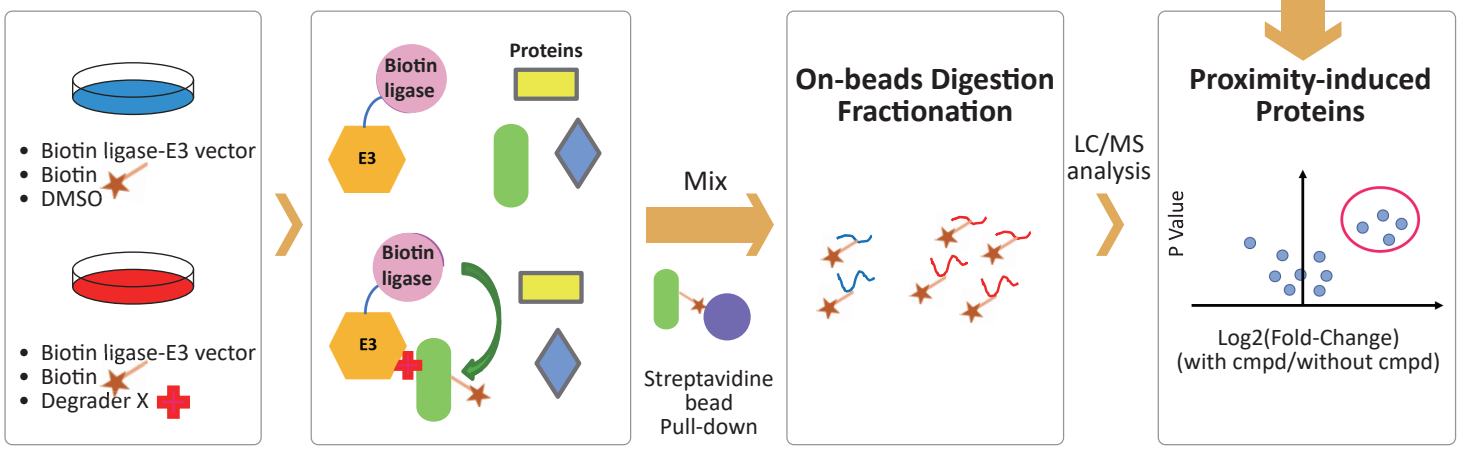
Target Discovery Platform

In TPD drug discovery, omics is considered a vital capability. At Axcelead, the combination of proteomics and proximity labeling allows for the thorough and efficient identification of neo-substrates that are directly degraded by the compound.

Proteomics



Proximity labeling



Consensus proteins
= Neo-substrate candidates

High-throughput Chimeric Degrader Synthesis

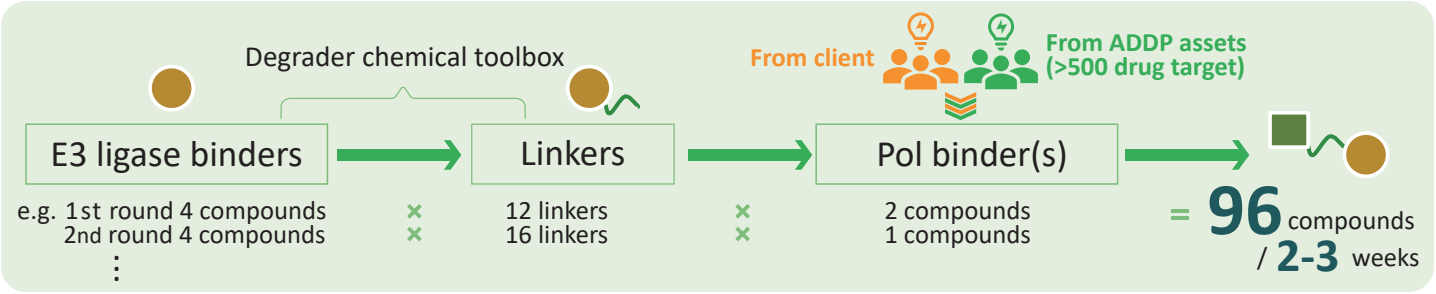
Degrader chemical toolbox + **Multi-step high-throughput synthesis**

Fast accessible E3 binders + Linkers

> 50 E3 ligase binders　　Several thousands linker

E3 binder + Linker + PoI binder

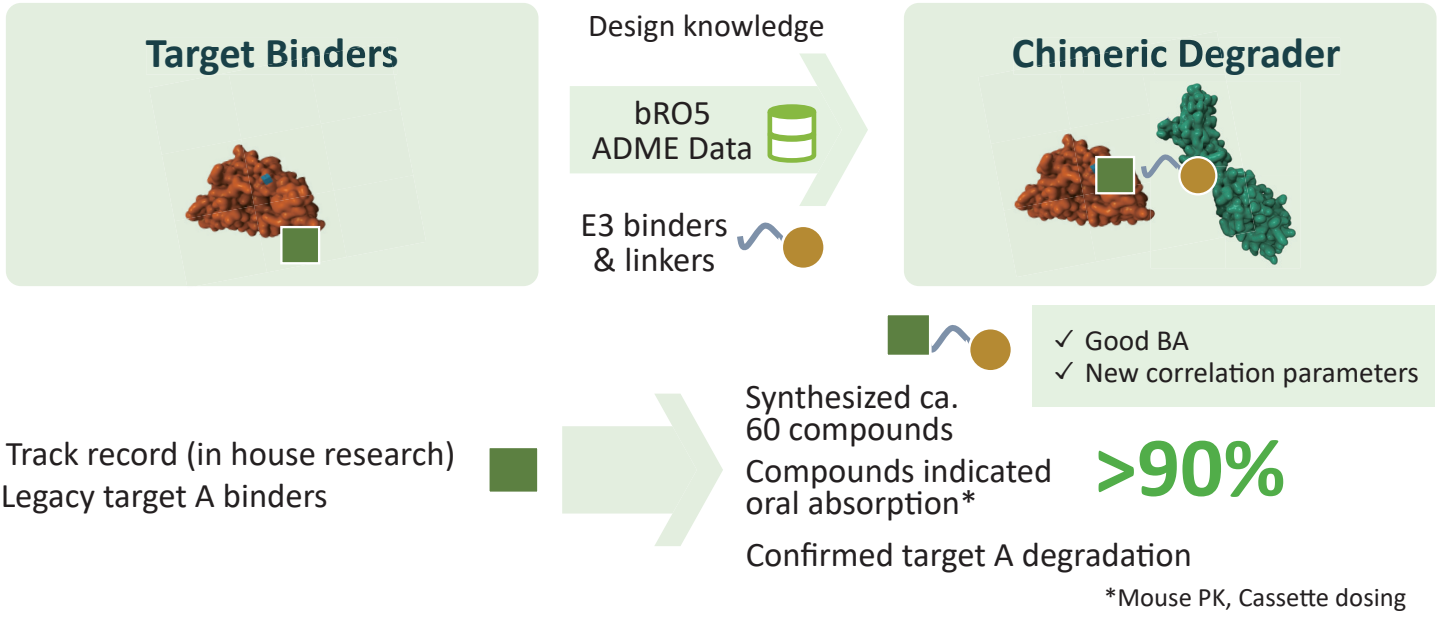
3-5 steps, 96 compounds/1 batch per 2-3 weeks



Flexible combination and fast access of diverse chemical space
Accelerate hit generation, lead generation and optimization

ADME Solution for Chimeric Degrader

We can rapidly discover chimeric degraders with favorable ADME properties !



*Mouse PK, Cassette dosing

Co-Creation with Axcelead in Protein Degrader Candidate Discovery

We are eager to collaborate with you to help achieve your goals and deliver success in TPD drug discovery by leveraging our integrated platform, advanced techniques, and specialized compound libraries.

Impressive track records

- Discovery of chimeric degraders with high potency, high efficacy and favorable ADME profiles
- Discovery of monovalent and chimeric degraders from our original binders for an undruggable target

Axcelead Drug Discovery Partners, Inc.
https://www.axcelead-us.com/

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