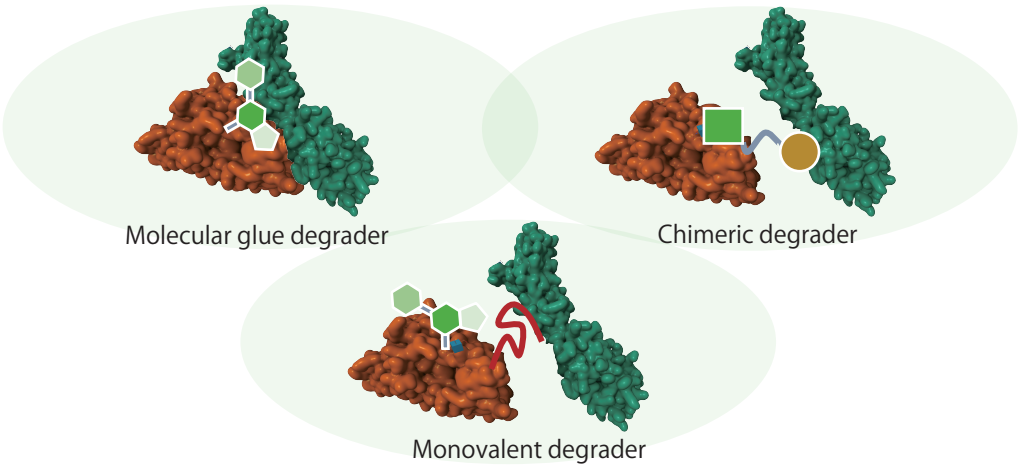
AXCELEAD
Drug Discovery Partners

Targeted Protein Degrader Integrated Solutions

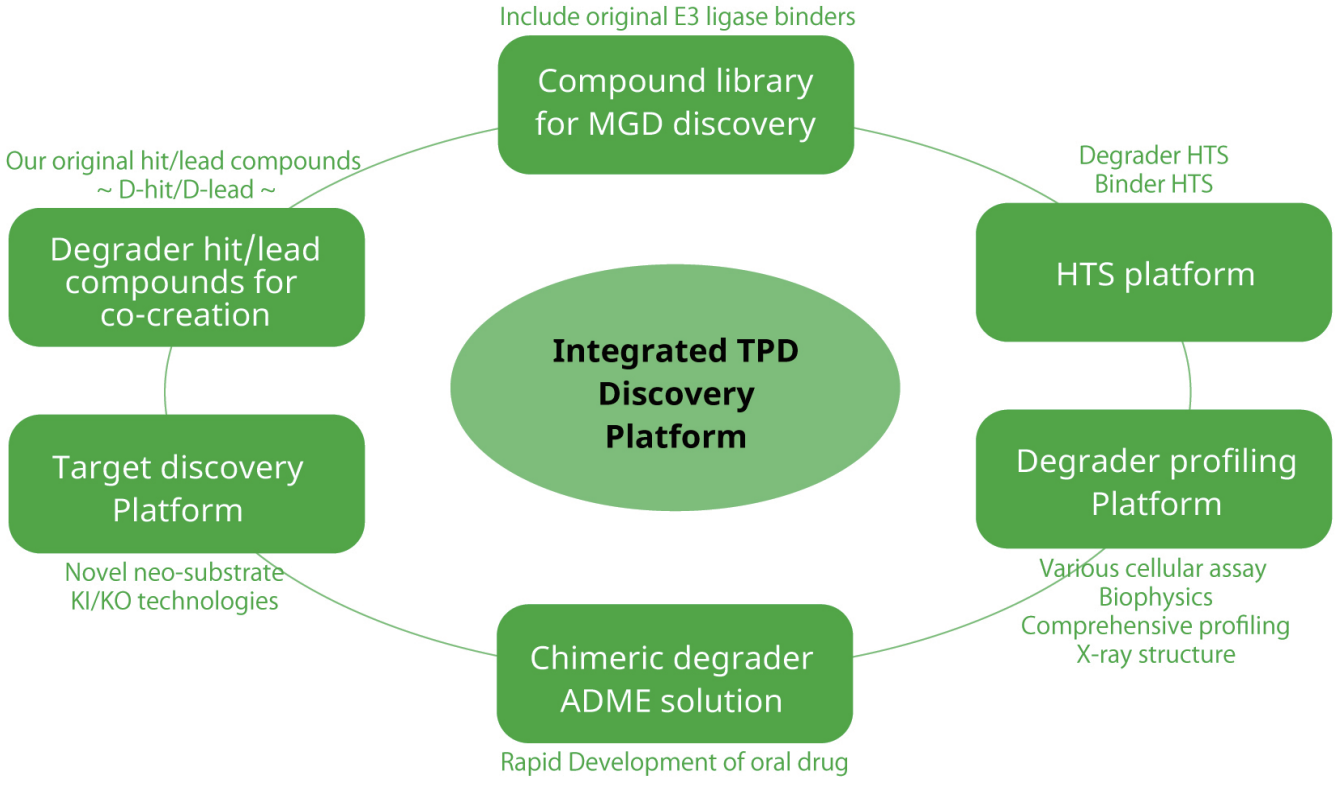
Unleash the Power of Targeted Protein Degrader Drug Discovery with AXCELEAD Diverse Array of Solutions!

In Targeted Protein Degrader (TPD) drug discovery, each type presents unique challenges and levels of difficulty, requiring advanced techniques, evaluation systems, diverse expertise across multiple fields, and specialized compound libraries. At Axcelead, we have built a platform that offers a variety of approaches. Our experienced researchers, well-versed in the characteristics of each TPD and familiar with the bottlenecks in drug discovery, will work closely with you to achieve innovative breakthroughs in drug discovery.

TPD that Axcelead can handle

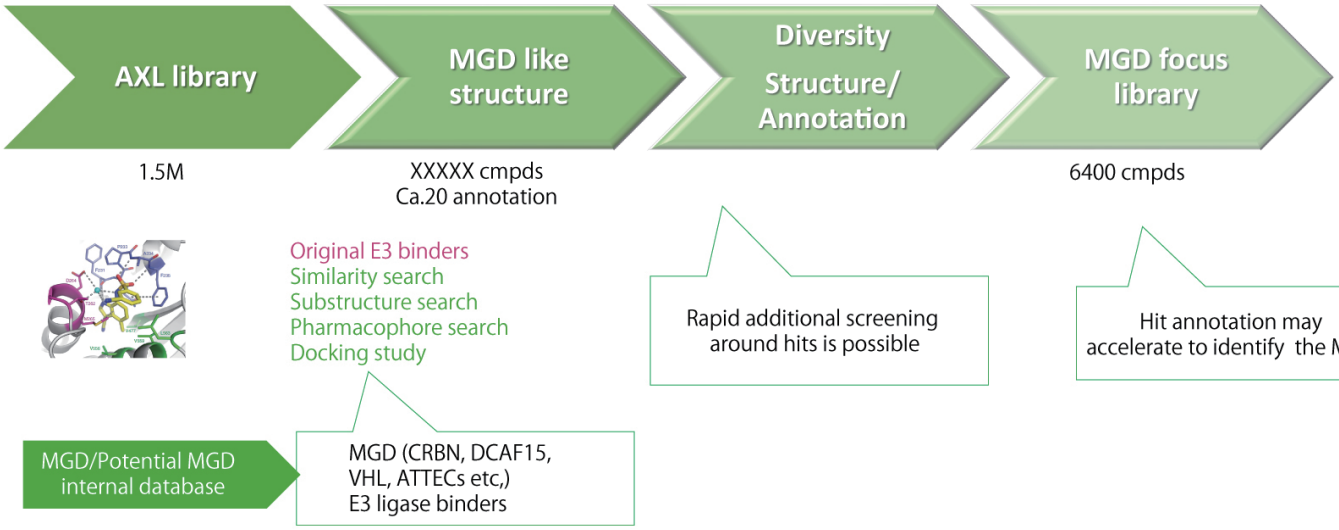


Axcelead offer an integrated evaluation system, compound library, and profiling techniques to realize TPD drug discovery. We provide tailored solutions based on your challenges and requirements. Even for challenges that cannot be solved by a single platform, consult Axcelead, where we can propose comprehensive solutions leveraging our collective expertise. Our team of experts from various fields collaborates to swiftly resolve project challenges.



Molecular Glue Degrader（MGD）Focused Library

- 6400 compounds selected from Axcelead 1.5M library, which would be suitable for various MGD discovery.
- Our original binders of several E3 ligases are included.
- Mainly, the library were selected by our multiple computational analysis of known MGDs and diverse potential MGD, followed by selection considering structural diversity in each annotation.



High-Throughput Screening (HTS) Platform

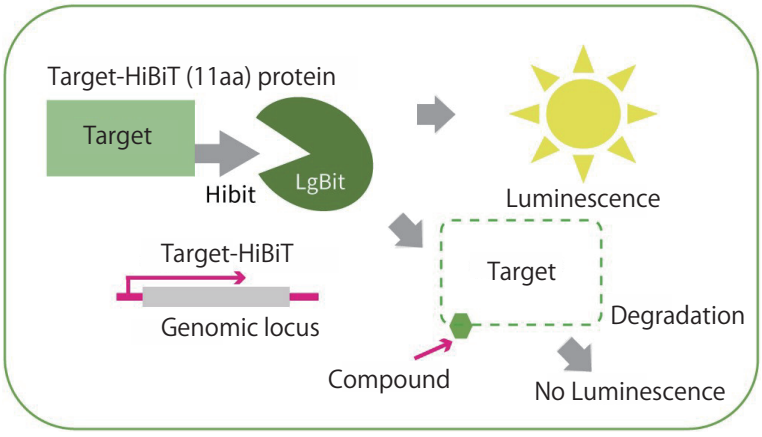
TPD drug discovery, dealing with several related proteins requires mastery of various assay systems. At Axcelead, we excel in a wide range of assay systems and offer tailored recommendations for the optimal assay system based on your specific targets.

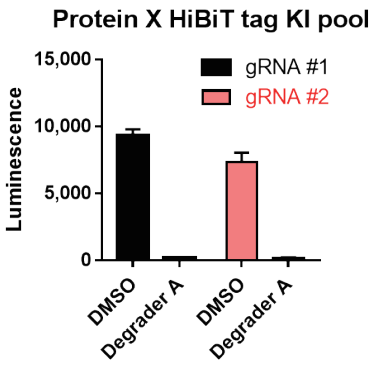
Cell-free HTS experience

- 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 HTS experience

- HiBiT tag knock-in cell line by CRISPR-Cas9
  Due to the limited number of cell lines available for purchase, the introduction of HiBiT tag into clinically relevant cells by CRISPR-Cas9 and the establishment of assay systems are important technologies.





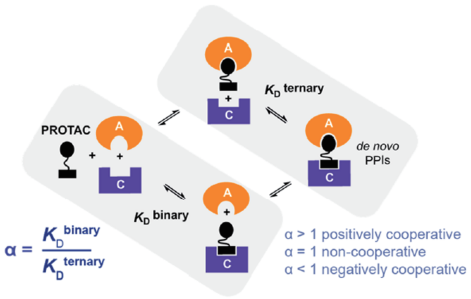
Established HiBiT-Protein X knock in cell line at Axcelead

Others

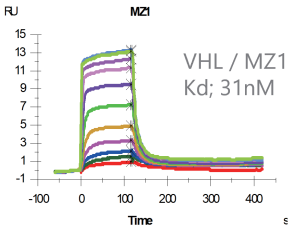
- HTS monitoring expression level of target of interest
  HiBiT knock-in cell line
  High content screening
- Cell-based ternary complex assay using NanoBRET system (in-progress)

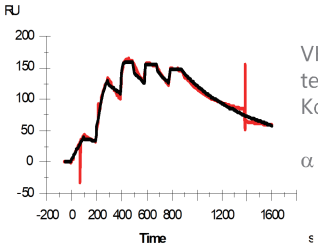
Degrader profiling assay

Biophysical ternary complex assay by SPR



In-house experiment:
Binary Kd and ternary Kd determination





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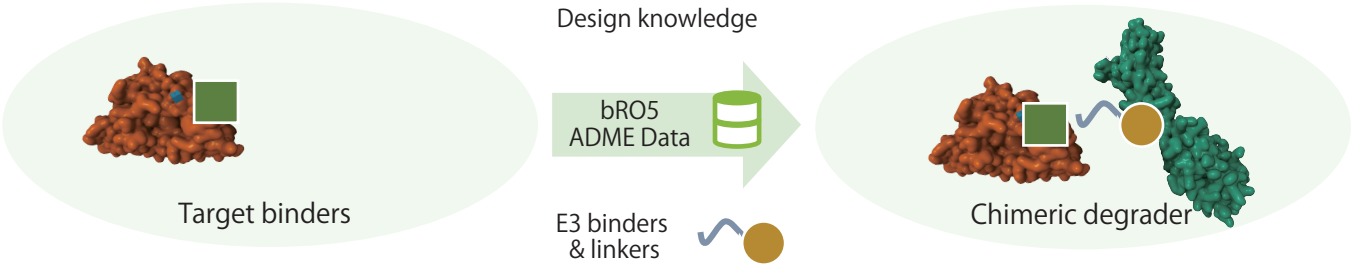
Others
- Cell-based ternary complex assay using NanoBRET system (in-progress)
- Crystal structure analysis capability (yet to be utilized for degrader project)

Various profiling assays

- Simple Western (Jess) system for high throughput and routine assay
- Proteomics: Global protein expression/interaction analysis

ADME Solution of Chimeric Degrader

We can rapidly discover chimeric degraders with favorable ADME properties !!



✓ Sweet range of good BA
✓ New correlation parameters

Track record (in house research)

Legacy target X binders → Synthesized ca. 60 compounds → compounds indicated oral absorption* >90%

Several compounds ; Oral BA>20%*
Acceptable in vitro ADME profile
MW range 700~830
Confirmed target X degradation

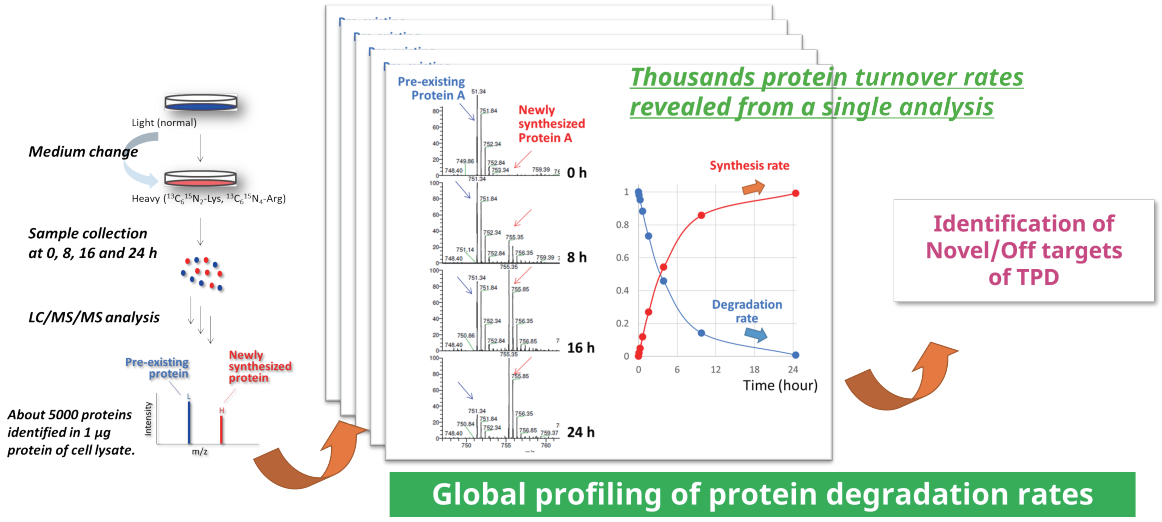
*Mouse PK, Cassette dosing

At Axcelead, our ADME and chemistry experts work together to advance your project. We provide one-stop-solution for discovery your chimeric degraders with good ADME properties.

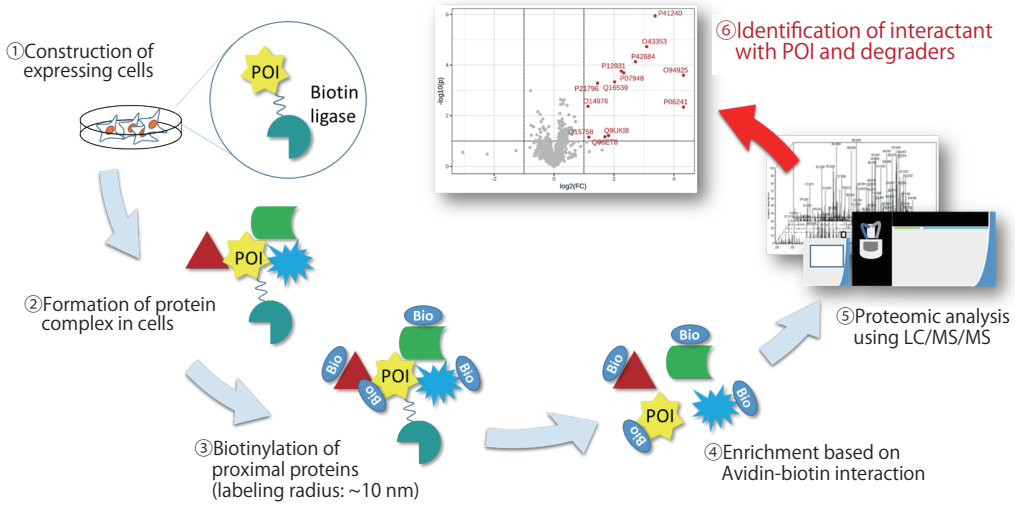
Target Discovery Platform

In TPD drug discovery, Omics is considered a vital capability. However, relying solely on Proteomics alone does not provide a clear distinction between actual degradation and accidental reduction. At Axcelead, we complement Proteomics with Proximity labeling, enabling us to thoroughly examine the potential for direct degradation.

[Application#1] Pulsed SILAC



[Application#2] Proximity labeling proteomics



Discover of Protein Degraders for "Co-creation"

We leverage the TPD drug discovery seeds created at Axcelead and collaborate with you to pursue candidate generation.

Track record of in-house research

- In-house research to explore chimeric degraders identified multiple compounds with favorable ADME profiles.
- Discovery of monovalent and chimeric degraders from our legacy binders of an undruggable target

Meet our experts if:

- You have challenging targets that you want to degrade.
- You aim to achieve efficient drug discovery by leveraging our seeds.
- You want to discover promising seeds using phenotypic screening.

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