X-CHEM
TAKE THE LEAD. DRIVE DISCOVERY.

Targeted Protein Degradation

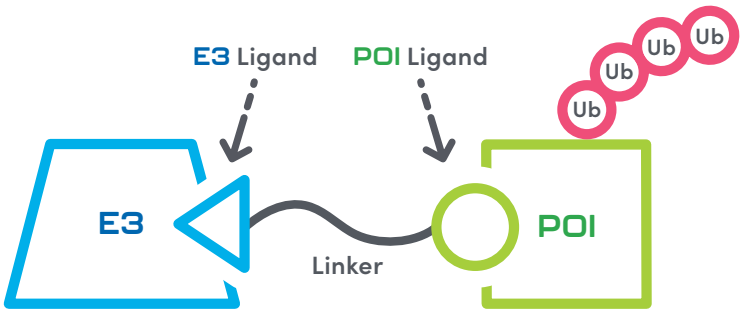
Looking for the best ligands for difficult-to-drug targets? Partner with X-Chem and let the pioneers of DEL technology help you accelerate your discovery.

DNA-Encoded Libraries and Protein Degradation: A Winning Combination for Targeted Drug Discovery

What Is Targeted Protein Degradation?

Targeted protein degradation (TPD) is one of the most exciting concepts in drug discovery to come along in the last 25 years. It holds the promise of not just inhibiting targeted proteins, but of wiping them out altogether. The power of TPD comes from harnessing the cell's mechanisms for protein housekeeping and repurposing them to target a protein implicated in disease.

A bispecific molecule (often called a chimera) is used to degrade the target proteins. A degrader has two binding elements: one targeting the protein to be degraded (often called the "protein of interest" or POI), and one targeting a protein known as an E3 ligase. The E3 ligases are a class of proteins that facilitate the degradation of cellular proteins by labeling them with ubiquitin. The strategy here is to use the dual-binding chimera to bring the E3 ligase and the POI into proximity, thereby inducing the E3 to ubiquitinylate the POI.



X-Chem's DNA-Encoded Library Platform Offers Greater Advantage for TPD Discovery

X-Chem's DNA-encoded library (DEL) platform is an ideal approach to discover both E3 ligase and POI binders for TPD. The DEL affinity-mediated selection experiment is, at its heart, a binding experiment. For TPD, binding alone, rather than functional modulation, suffices to bring the proteins into proximity and trigger ubiquitin-mediated degradation. Furthermore, since the DEL compounds are attached to DNA during the selection experiment, linker tolerance and positioning is easy to assess. This knowledge

X-CHEM
TAKE THE LEAD. DRIVE DISCOVERY.

DNA-ENCODED LIBRARY: A VERSATILE MODALITY FOR TARGETED PROTEIN DEGRADATION

- DNA linker data aids in the optimization of linker length and positioning
- Combine the power of DEL technology and TPD to select the best candidate degraders
- Expertise in the design of effective bispecific protein degraders
- DEL technology can expedite your next targeted protein degradation project
- Industry leaders of DEL technology with an unwavering focus on quality

is especially useful when it comes time to combine the POI and E3 ligase binders together via a chemical linker to generate a candidate degrader.

At X-Chem we have extensive experience in applying our DEL platform to the TPD space. We have screened many E3 ligases, both those known to support TPD as well as novel E3 ligases. We also have successfully taken POI ligands uncovered through DEL screening and incorporated them into functional degraders. One recently published example of our work demonstrates the effective degradation of the estrogen receptor α using DEL technology and exemplifies the advantage of this technology. X-Chem is proud to have built an extensive toolkit of reagents to allow us to rapidly assess E3 ligase and linker length preferences by making synthetic arrays of candidate degraders.

Whether you are looking for quality ligands to difficult-to-drug targets or want to demonstrate the use of a novel E3 ligase for TPD, X-Chem is the right partner. We have the experience, toolkit and high-quality libraries to maximize your chances of success.

How Can X-Chem's DEL Technology Facilitate Your TPD Drug Discovery?

- High-quality ligands for challenging targets
- Rational design of bispecific protein degraders
- Easily identify and assemble the binders, linkers and E3 ligands for your TPD projects
- An informed strategy to optimize linker length and positioning
- Extensive experience in applying the DEL platform to TPD projects
- Successfully screened several known and novel E3 ligases
- Incorporated new POI ligands discovered through DEL platform
- A versatile platform to validate novel E3 ligases and POI ligands
- Comprehensive toolkit to accelerate your drug discovery

X-Chem is the partner you need to unlock exponential possibilities in your targeted protein degradation drug discovery.

Find Your Next Drug Molecule With X-Chem

ABOUT X-CHEM

X-Chem, Inc. is the leader in small molecule discovery science, providing pharmaceutical and biotech companies a complete, seamless solution for screening, hit validation and lead optimization. As pioneers of DNA-encoded chemical library (DEL) technology, the company leverages its market-leading DEL platform to discover novel small molecule leads against challenging, high-value therapeutic targets. In-house lead optimization services enable clients to progress their compounds directly for even higher quality outputs. Our expertise in medicinal chemistry, custom synthesis and scale-up process chemistry enables us to support all aspects of drug discovery, supporting lead optimization through candidate identification.

781.419.6900 | info@x-chemrx.com

x-chemrx.com