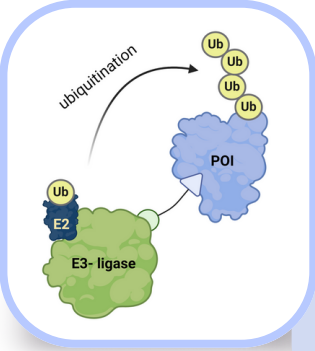
Targeted Protein Degraders (TPD)

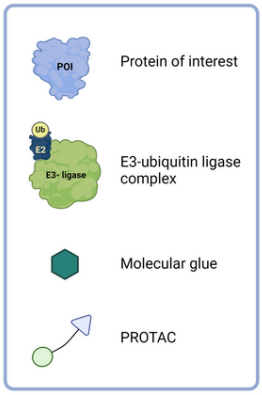
Targeted protein degradation is gaining interest in the drug discovery world as a novel therapeutic method for cancer and immune diseases. These novel small molecules have been shown to enable inactivation or elimination of disease-causing proteins previously thought to be "undruggable."

Model-Informed Decision-Making Enables You To Answer Key Questions

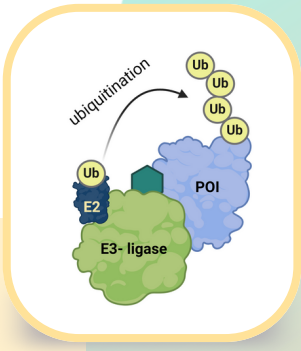
- **Target Feasibility:**
  - How druggable is this target given its expression levels and turnover rate?
  - Does the selected ligase provide adequate targeted degradation?
- **Lead Selection Criteria:** What binding affinities are expected to provide maximal protein degradation?
- **Selectivity:** What therapeutic properties are expected to help me avoid off-target activity?
- **Select Mechanism of Action** - Which MoA (PROTAC or MGD) is superior for our ligase/target pair and indication?
- **Preclinical to Clinical Translation:** How do preclinical safe/efficacious doses translate into projected human safe/efficacious doses?
- **Dose and Dosing Regimen:**
  - What dose and regimen is needed to maintain target levels below a particular threshold for the whole dosing interval?
  - For which doses/regimens does target degradation saturate (no sense in dosing higher for efficacy so could potentially dose lower and avoid unnecessary toxicity)?



PROTACs (PROteolysis TArgeting Chimeras) are bifunctional molecules where one part of the molecule targets binding sites on a protein and the other part can recruit an enzyme called the E3 ubiquitin ligase, enabling protein degradation by the ubiquitin-proteasome system.



Molecular glues are small molecules that facilitate interaction between the target protein and a cellular enzyme, such as Cyclophilin A or E3 ligases, to signal the recruitment of additional protein partners to degrade or deactivate it.



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Pre-built Pharmacology Protein Degrader Models to Inform Early-Stage Decision-Making

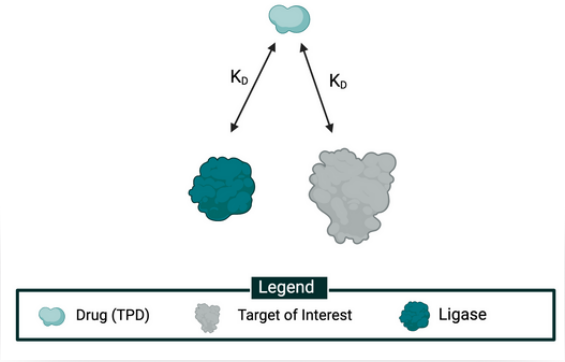
Applied BioMath Assess™ Protein Degrader Model Pack includes 4 models covering in vivo and in vitro models of PROTAC and Molecular Glue Degrader pharmacologies. Licensing this software enables the user to prioritize targets and leads that are expected to be the most developable early on. Parameters are defined and varied by the user to explore parameter impact on simulated MGD PK, target engagement, and MGD-facilitated target degradation.

PROTAC degrading an intracellular protein in vitro
An in vitro model of a PROTAC targeting and degrading intracellular proteins

PROTAC degrading an intracellular protein in vivo
An in vivo model of a PROTAC targeting and degrading intracellular proteins

MGD degrading an intracellular protein in vitro
An in vitro model of a molecular glue degrader targeting and degrading intracellular proteins

MGD degrading an intracellular protein in vivo
An in vivo model of a molecular glue degrader targeting and degrading intracellular proteins



PROTAC Mechanism of Action

Image created with BioRender.com

Each model includes target expression levels and turnover rates to yield a constant baseline amount of these proteins, binding reactions, and ubiquitination/degradation reactions which together will predict changes in drug concentration, ternary and binary complexes, and target degradation profiles over time.

Custom Models

You may request custom models to accommodate your particular program mechanism of action, including:

- Downstream biomarkers (in vivo studies)
- Ubiquitination reactions (unbinding/rebinding of Ub-target)
- Additional PPI characteristics (reduced affinity of Ub-target)
- Multiple cell types (vary target/ligase concentrations)

Trial for free or request a demo

Use **Applied BioMath Assess™** Pre-Built Models

Try a 7-Day Free Trial: Use the pre-built model - no modeling experience needed!

Request a Demo: Our support team can walk you through a demo.