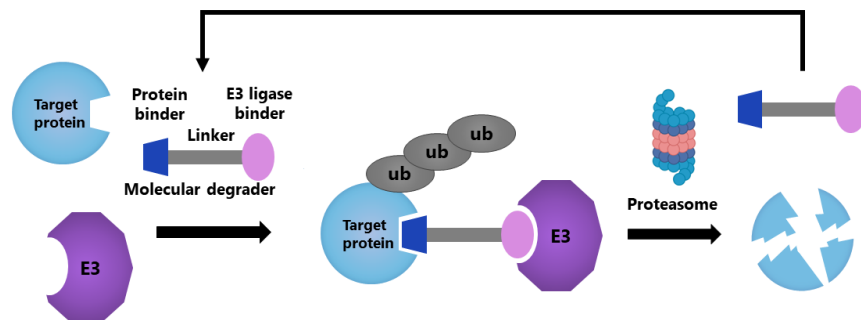


# Molecular Degraders And Ubiquitin-Mediated Degradation

Molecular degraders represent a new and promising approach to downregulate proteins of therapeutic interest using targeted degradation. This technology uses a bifunctional linker molecule that brings together the target protein and a ubiquitin E3 ligase, resulting in ubiquitination of the target protein and subsequent proteosomal degradation.

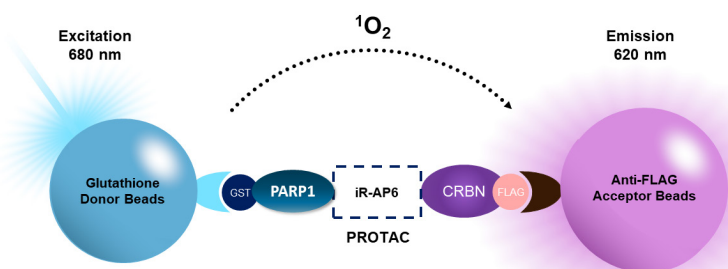
## Advantages

- Circumvent enzyme resistance against sustained inhibition
- Promiscuous ligands can still demonstrate high degradation efficiency
- Ineffectual ligands which do not alter enzymatic activity can mediate degradation
- It becomes possible to target proteins previously deemed "undruggable"

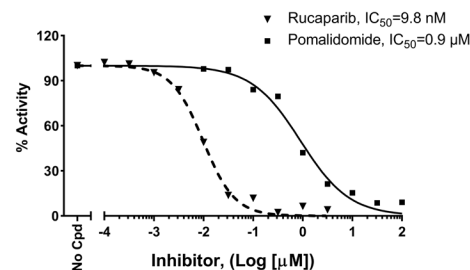


## PROTAC™ Optimization Kits

These assays were designed for the screening and profiling of molecular degraders and PROTACs against specific targets, engaging a select E3 ligase. A degrader of interest interacts with both PARP and CRBN, bringing them in close proximity. For example in the assay shown here, PARP-GST is recognized by the GSH donor bead, while CRBN-FLAG binds to anti-FLAG conjugated to the acceptor bead. Excitation of the donor bead results in excitation of the acceptor bead and light emission. This is a homogeneous AlphaLISA™ assay.



iRucaparib-AP6-mediated PARP1 binding to CEREBLON



*Inhibition of iRucaparib-AP6-mediated interaction of Cereblon with PARP1 by increasing concentrations of Rucaparib (PARP1 inhibitor) or Pomalidomide (CRBN inhibitor), measured using the PROTAC® Optimization Kit for PARP1-Cereblon Binding (BPS Bioscience #78441).*

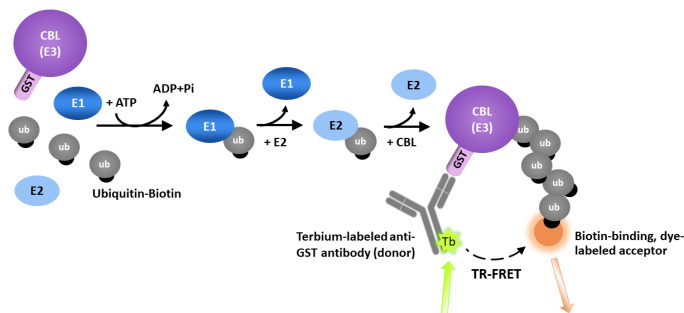
## Products and Services

BPS Bioscience is a leading product manufacturer and service provider in the Molecular Degradator space. We support assay design and optimization, and will perform screening & profiling of compounds using our homogeneous proximity assays to assess chemical adaptors.

# Molecular Degraders And Ubiquitin-Mediated Degradation

## Ubiquitination TR-FRET Assay Kits

CBL (Casitas B-lineage lymphoma proto-oncogene) is an E3 ligase that functions as a negative regulator of T cell activation. The protein is a promising therapeutic target in cancer. The CBL TR-FRET Assay Kits measure the auto-ubiquitination of c-CBL or CBL-B in a homogenous 384-well format.

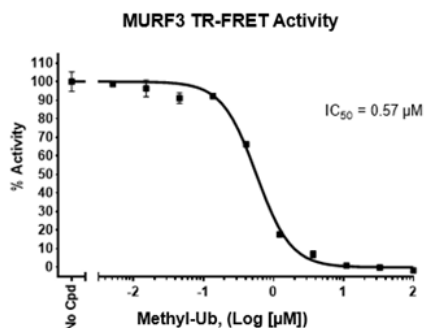


## CBL-driven Tyro3 Ubiquitination Intrachain TR-FRET Assay Kits

Based on the same principle as our Intrachain assay kits, these c-Cbl and CBL-B assays measure CBL-mediated poly-ubiquitination of tyrosine kinase and CBL target Tyro3 (BPS Bioscience [#79786](#) and [#79575](#)).

## Ubiquitin Intrachain TR-FRET Assay Kits

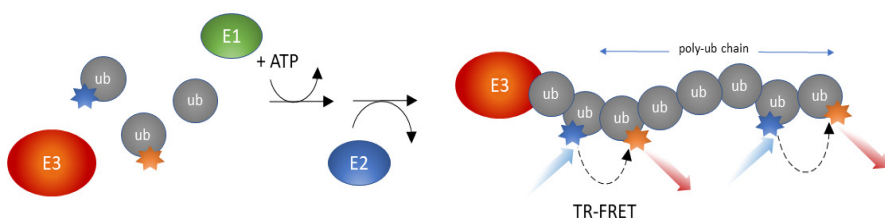
Our unique intrachain assay kits measure the auto-ubiquitination activity of various E3 ligases in a sensitive, homogeneous 384-well format. These assays use a Europium-labeled ubiquitin (donor) and a Cy5-labeled ubiquitin (acceptor) to complete the proximity pairing. These assay kits are ideal for high-throughput screening of small molecule inhibitors, determination of compound  $IC_{50}$  and real-time kinetic analyses.



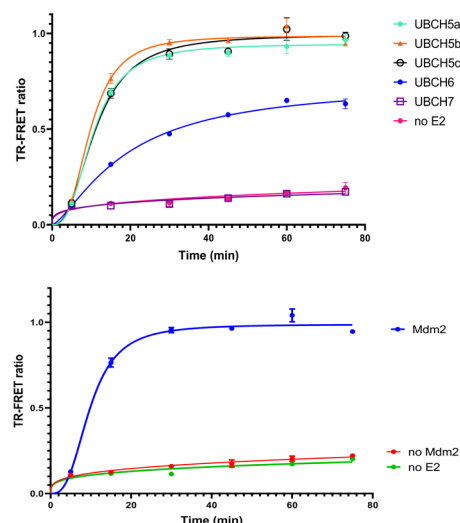
*Inhibition of MURF3 auto-ubiquitination measured in the presence of increasing concentrations of Methylated Ubiquitin.*

Available intrachain assay kits include Cereblon, MDM2, SMURF1 and SMURF2, VHL, XIAP, DCAF11 and DCAF15, WWP1, MURF3 (TRIM63), TRAF6, NEDD4, with more in development (Visit [Intrachain TR-FRET Assay Kits](#)).

## Choose E2 and E3 Intrachain Assay Kits



The **ChooseE2-Opti™ Intrachain TR-FRET Assay Kit** is a real-time, high-throughput screening assay designed to identify E2 enzyme(s) that are functional partners for a purified E3 ligase. The assay kit contains five E2 enzymes to be tested with the E3 ligase of interest, and two E3 ligases (SMURF1 and MDM2) to use as internal controls. On the other hand, the **ChooseE3-Freedom™ Intrachain TR-FRET Assay Kit** was designed to measure the auto-ubiquitination of *any* purified E3 ligase of interest. These homogeneous assays are especially amenable to real-time kinetic analyses and are ideal to optimize E2/E3 pairs.



*Upper panel: Real-time kinetics of MDM2 in the presence of a panel of E2 enzymes (ChooseE2-Opti™ Assay Kit [#78561](#)). Lower panel: Real-time analysis of MDM2 E3 ligase activity (ChooseE3™-Freedom Assay Kit [#78560](#)).*