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The Eurofins Discovery PRODUCTS COMPANY

TARGETED PROTEIN DEGRADATION ASSAYS

Fast Cell-Based Assays for the Detection of Protein Turnover

SPRINTer ASSAY PLATFORM

Rapidly Screen Therapeutics and Quantify Changes in Protein Levels

Utilizing the cell's own protein destruction machinery (ubiquitin/proteasome-mediated system) for targeted protein degradation has opened up a new and emerging area of drug discovery. This new approach has expanded the druggable target space by allowing drugs to modulate protein turnover, or the depletion of over-abundant proteins; which have been associated with disease-states such as cancer (oncoproteins) or Alzheimer's Disease (TAU protein).

Implement SPRINTer™ Protein Turnover Biosensor Assays for rapid screening of small molecule therapeutics, and quantification of changes in endogenous protein levels in disease-relevant cell models. Easily detect protein turnover induced by targeted degrader molecules, such as PROTACs (Proteolysis Targeting Chimeras), with higher sensitivity and more rapid kinetics than phenotypic endpoint assays (e.g. cell proliferation).

- Robust & Highly Sensitive – Accurately detect target protein turnover at micro/nanomolar sensitivities
- Fast Results – Obtain results in as little as 5 hours to select the right candidate and accelerate development programs
- Easy-to-Run & Scalable – Simple, homogeneous protocol amenable to high-throughput formats for increased efficiency

SPRINTer PROTEIN TURNOVER ASSAY PRINCIPLE

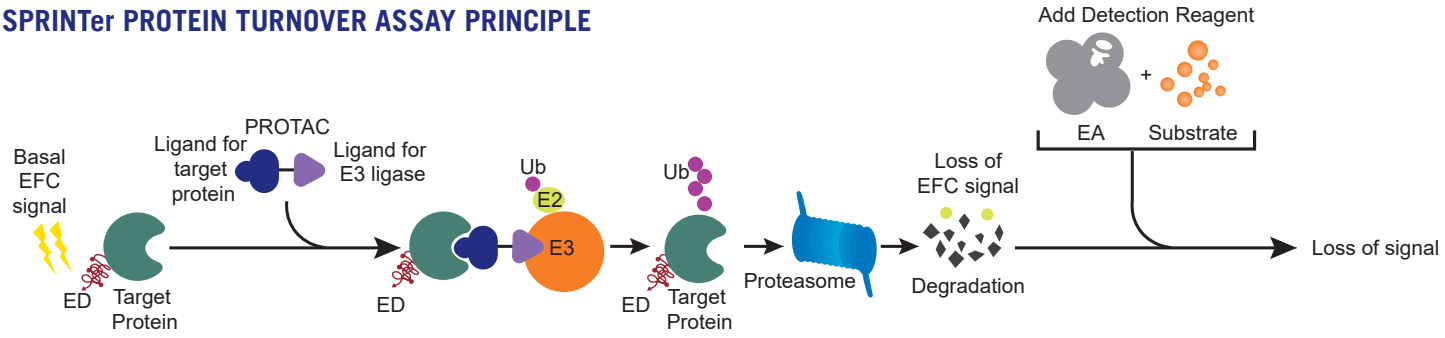

Figure 1. SPRINTer protein turnover, cell-based assays involve Enzyme Fragment Complementation detection of PROTACs-induced target protein degradation. PROTAC is a trademark of Arvinas.

Visit discoverx.com/turnover to learn more about these targeted protein degradation assay.

Contact us at NA_CAD@discoverx.com to discuss development of specific targets in desired cell models for your programs.

TARGETED PROTEIN DEGRADATION ASSAYS

RANK ORDER POTENCIES OF BET INHIBITORS AND PROTACS

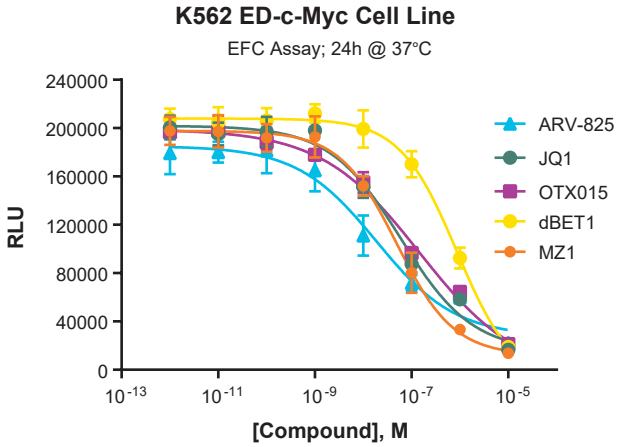

Figure 2. Rank order of BET inhibitors and PROTACs. The SPRINTer™ K562 c-Myc Protein Turnover Cell Line was used to rank order BET inhibitors (OTX15 and JQ1) and PROTACs (dBET1, MZ1 and ARV-825) with differential kinetics. Results show ARV825 > JQ1 = OTX015 > dBET, which have similar rank order of potencies to previously published ELISA data.

DIFFERENTIATE PROTAC EFFICACIES USING DIFFERENT CELL LINES THAT REPRESENT DISEASE-RELEVANT CELL MODELS

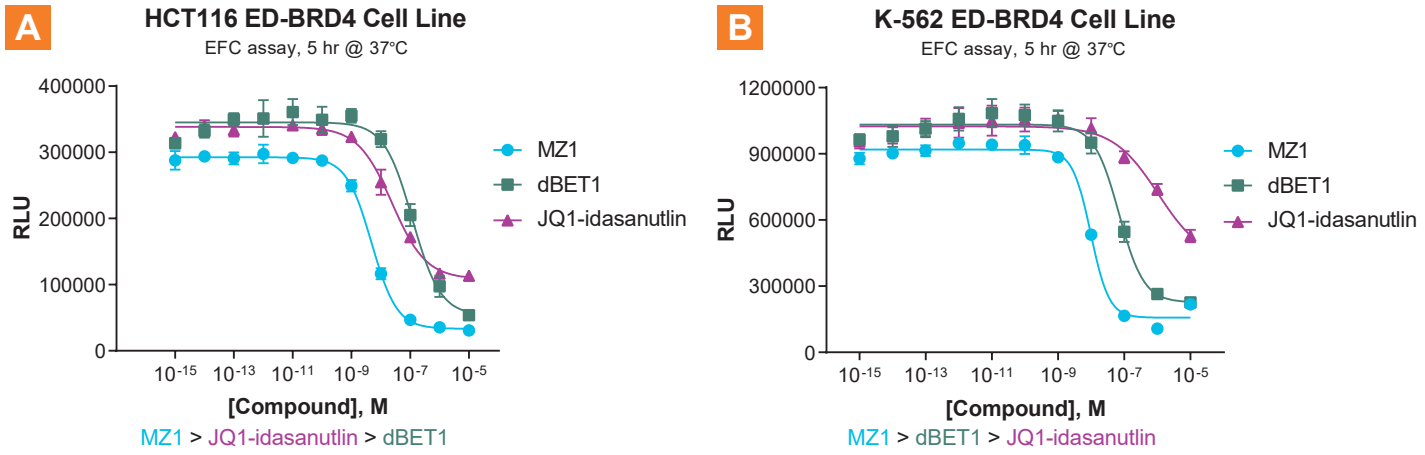

Figure 3. Select PROTACs display distinct efficacies among different cell types. A. SPRINTer HCT116 ED-BRD4 and B. SPRINTer K-562 ED-BRD4 cell lines were treated with three BRD4 PROTACs. Results reveal differences in rank order and potency related to engaging to different E3 ligases for each cell model with JQ1-idasanutlin showing to be more efficacious in the HCT-116 cell type compared to the K-562 cell type.

QUANTIFY INHIBITION OF THE UBIQUITIN-PROTEASOME PROTEIN DEGRADATION SYSTEM

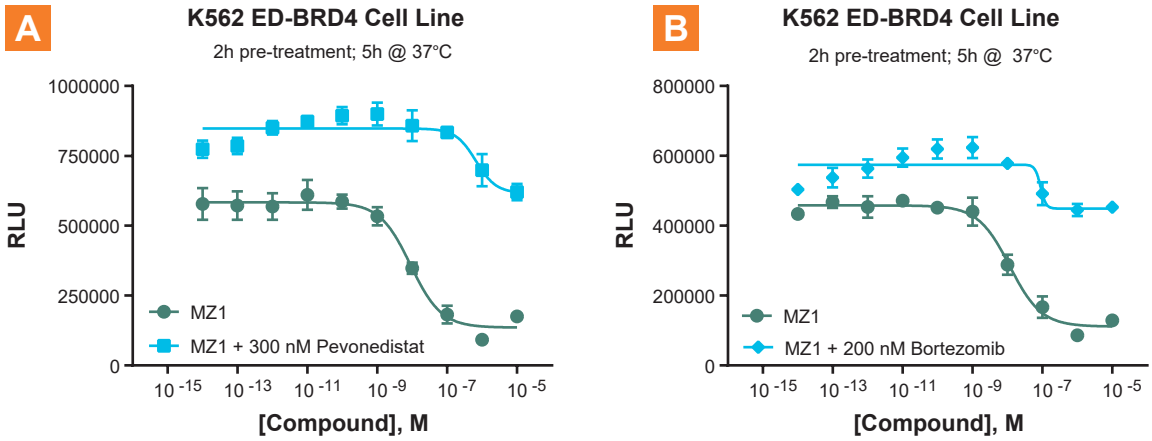

Figure 4. Comparison of two inhibitors, Pevonedistat and Bortezomib, of ubiquitin-proteasome protein degradation system using the same SPRINTER™ K562 BRD4 Protein Turnover Cell Line. A. & B. After treating the cells with the two inhibitors, MZ1 induced degradation of BRD4 was greatly reduced, indicating these assays are truly measuring target degradation mediated through the ubiquitin-proteasome system.