CeTPD Journal Club

February – March 2026

Targeted protein degradation, medicinal chemistry, chemical structural biology & cell biology

Centre for Targeted Protein Degradation
University of Dundee

innovate
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MEET THIS MONTH'S EDITORS

Click here for info on the editor

MATYLDA IZERT-NOWAKOWSKA

Matylda completed her PhD at the University of Warsaw where she worked on developing peptide-based degraders for Gram-negative bacteria. In 2024 she joined Will Farnaby's group as a postdoctoral researcher where she combines cellular assays with biophysical methods for development of mitophagy regulating molecules.

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CLAUDINE GREENWOOD

Claudine completed her Master's degree in Pure and Applied Chemistry, including an industrial placement, at the University of Strathclyde in 2021. She then undertook an Industrial PhD in Chemical Biology at GSK, which she completed in 2025. Her doctoral research focused on the development of covalent tools to study essential parasite proteins. Following her PhD, Claudine joined the LITE team at the CeTPD as a Chemical Biologist, where she works on investigating novel strategies to modulate LRRK2 activity in Parkinson's disease.

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DYLAN M. LYNCH

Dylan is a postdoctoral researcher from Dublin, Ireland. He conducted his PhD at Trinity College Dublin, where he researched glycopeptides and radical-based ligation methodology. Following a research stay at the University of Washington, he joined the Ciulli group in 2022, where he currently researches small-molecule probes for new E3 ligases. His personal interests include film photography, vegan cooking, and arguing about ways to make coffee.

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ALEXANDRA HARRIS

Alexandra completed her Master's by research degree in Chemical Biology at the University of Dundee in September 2023, where she worked on the development of CRBN-recruiting BromoTag degraders with Prof. Alessio Ciulli. She rejoined the CeTPD as a PhD student, now in her third year, developing multivalent modalities in the Ciulli group. Outside of research, she is a flautist who enjoys socialising, travelling and learning Italian.

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TARGETED PROTEIN DEGRADATION

CHEMISTRY | STRUCTURAL BIOLOGY & BIOPHYSICS | CELL BIOLOGY | MODELLING

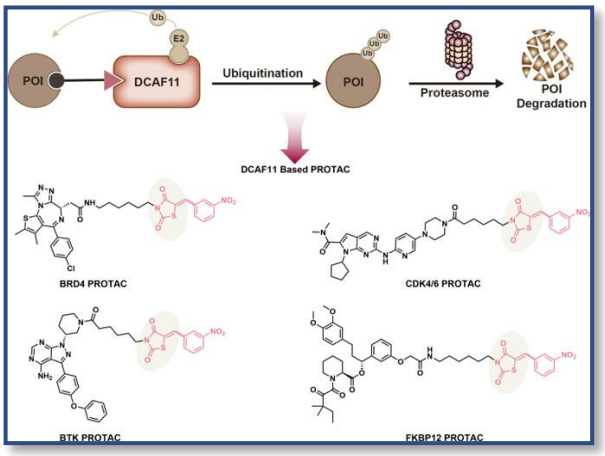
"Every two months, we spotlight the latest and most significant literature in the field of targeted protein degradation, spanning chemistry, biophysics, cell biology, and computational modeling"

Literature review from 21st January to 20th March 2026

| *Claudine*

Arylidene-Thiazoldione Scaffold Acts as the E3 Ligand of DCAF11 for PROTAC Design

Jinyi Liang§, Yuyang Liu§, Man Zhao§, …, Ming Zhang*, Liang Hong*, Rui Wang*, Guofeng Li Wang*
J. Med. Chem. ***2026,*** *69, 3, 2349–2369*



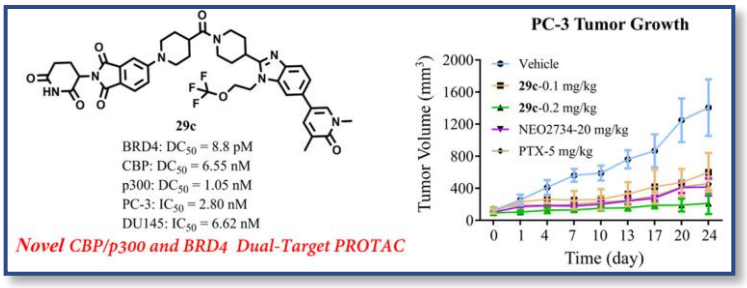
The identification of novel E3 ligands remains a key bottleneck in expanding TPD beyond CRBN and VHL recruiters. This paper describes the discovery of a new DCAF11-recruiting ligand, based on an α,β-unsaturated arylidene-thiazoldione scaffold. Building on recent reports of DCAF11 electrophilic ligands, the authors used BRD4 PROTACs as a discovery platform to optimise this novel chemotype. LGF308 was identified as their lead PROTAC, showing potent, DCAF11-dependent BRD4 degradation alongside anti-tumour activity in breast cancer cell-lines. The scaffold's generality was then demonstrated through the synthesis of functional PROTACs targeting CDK4/6, BTK, and FKBP12. The authors do appropriately highlight the nitro group within the DCAF11 warhead as a potential toxicophoric and metabolic liability, noting that further optimisation is ongoing.

The work by Liang et al. expands the DCAF11 ligand toolbox to include an arylidene-thiazoldione α,β-unsaturated electrophile. With increasing chemical matter emerging for DCAF11, it would be interesting to carry out more systematic profiling of engagement kinetics, stability, and selectivity. This would help to benchmark the available chemotypes and identify any advantages of α-chloroacetamides, alkenyl-oxindoles, or cyanoacrylamides relative to these α,β-unsaturated electrophiles.

| *Alexandra*

Discovery of Novel CBP/p300 and BRD4 Dual-Target PROTACs with Potent Antitumor Activity in Prostate Cancer

Yi-Zhe Zhang§, Hui-Juan Zhu§, Xiao-Xiao Zhou§, …, Yong-Tao Xu*, Sai-Qi Wang*, Ying-Chao Duan*
J. Med. Chem. ***2026****, 69, 4, 4512–4547*



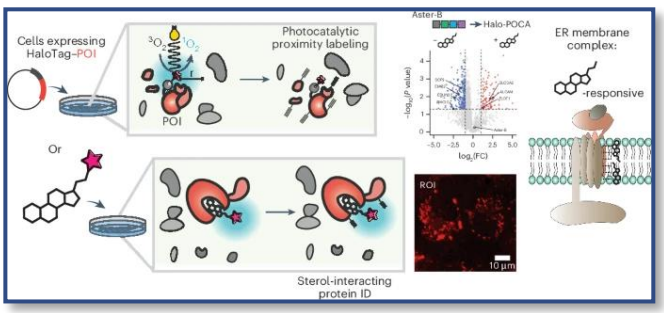
This paper describes the rational design, synthesis and biological characterisation of CRBN-recruiting CBP/p300 and BRD4 dual-targeting PROTAC, proteins both reported to synergistically drive prostate cancer progression. The solvent exposed pyran ring of the dual-targeting inhibitor NEO2734 was replaced with a piperidine to serve as a suitable exit vector and conjugated to various thalidomide-bearing linkers and their anti-proliferation activity evaluated in PC-3 cancer cells. PROTAC 29c, featuring a piperidin-4-carbonyl linker conjugated to the C5'-position of thalidomide, was identified as the most promising compound with 82% inhibition of growth and an IC50 of 2.8 nM. By western blot, they showed all targets are degraded in a dose- and time-dependent manner and the authors also nicely demonstrate proteasome and neddylation dependence through the use of inhibitors. In PC-3 cancer cells, 29c induced degradation of both CBP/p300 and BRD4 with DC50 values ranging from 8.8 pM to 10.5 nM, and authors highlighted nicely how this translates to DU145 and RM-1 cancer cell lines. Importantly, PC-3 xenograft mouse models showed 81.5% inhibition of tumour growth with only 0.2 mg/kg every second day.

This work nicely illustrates yet another example of PROTACs utilising a dual-targeting approach. The authors neatly show how degradation of their targets with 29c translates into downregulation of known downstream proteins. Further characterisation of PROTAC selectivity (global proteomics) would have been a useful addition to the study.

| *Claudine*

Photosensitizer proximity labelling captures the lipid and protein interactomes

Andrew P. Becker, …, Keriann M. Backus*
Nature Chem. Biol. DOI 10.1038/s41589-026-02140-1



This study introduces POCA (Photosensitizer-Dependent Oxidation and Capture by Amine), a singlet oxygen-based proximity labelling method that can map both protein and lipid interactomes in living cells. To study these interactomes, the authors took two complementary approaches: the first leveraged the HaloTag system (Halo-POCA), where Halo-tagged proteins were used as bait to recruit the photosensitiser and capture nearby

proteins after light activation. This enabled them to profile protein complexes and to show that POCA could detect dynamic, state-dependent interactions such as the cholesterol-sensitive behaviour of Aster-B. The method was then extended to lipid interactomics using functionalised cholesterol (chol-POCA), allowing the authors to identify known and novel cholesterol-binding proteins, as well as proteins involved in cholesterol uptake and membrane organisation.

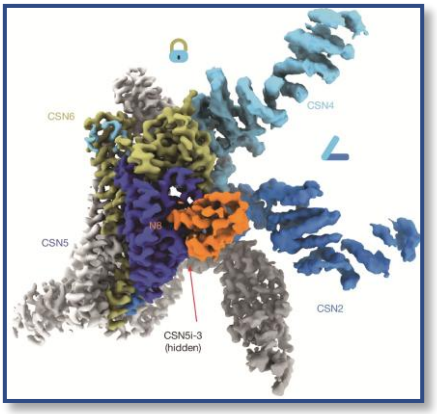
Overall, POCA is presented as a versatile and adaptable proximity labelling platform. Its ability to be directed by HaloTag or functionalised probes offers an advantage over existing approaches. The use of singlet oxygen enables high spatiotemporal precision, capturing local, dynamic interactions. It will be exciting to see how broadly this platform can be extended to other lipid systems in the future.

| *Matylda*

CSN5i-3 is an orthosteric molecular glue inhibitor of COP9 signalosome

Huigang Shi, …, Lan Huang*, Ning Zheng*
Nature ***2026*** *DOI 10.1038/s41586-026-10129-y*

Discussed internally



In this work the authors present structural studies on CSN5i-3 as a unique orthosteric molecular glue. CSN5i-3 was first published in 2016 by Novartis as an inhibitor of COP9 signalosome (CSN) subunit CSN5, with antiproliferative effect on cancer cell lines. The compound inhibits deneddylation of cullin Ring ubiquitin ligase (CRL) complexes by CSN. Despite being a highly potent deneddylation inhibitor, it has relatively weak, micromolar affinity towards CSN5. The in-depth structural analysis of CSN-CRL1 complex with NEDD8 helped to identify the interactions within the complex and identify how CSN recognises and cleaves NEDD8. The structure of a full CSN-CRL1-NEDD8 complex with CSN5i-3 revealed that binding of the inhibitor displaces NEDD8 iso-peptide bond from the active site of CSN5 and changes complex topology introducing new contacts between the proteins. BLI measurements revealed that CSN5i-3 acts as a molecular glue and greatly enhances NEDD8 and CSN affinity and the proteomics analysis revealed how CSN5i-3 alters CSN interactome.

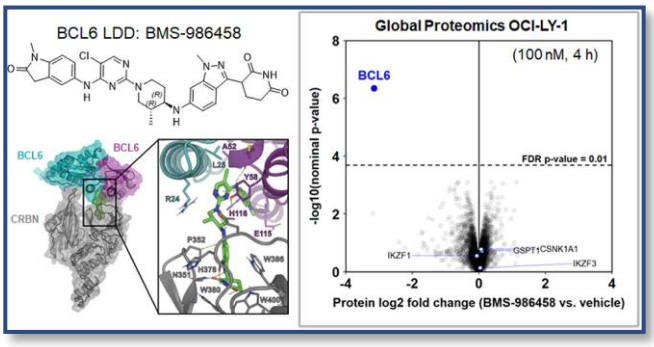
This work presents a very interesting case of identification of an inhibitor acting as molecular glue. Although the discovery was serendipitous, future developments on the field of molecular glue inhibitors could be an exciting approach for targeting specific substrates of multifunctional proteins.

| *Alexandra*

Discovery of BMS-986458, a Potent and Selective B-Cell Lymphoma 6 Protein Ligand-Directed Degrader, for the Treatment of B-Cell Non-Hodgkin Lymphoma

Deborah S. Mortensen* *et al.*
J. Med. Chem. ***2026**, 69, 4, 4424−4438*

Discussed internally



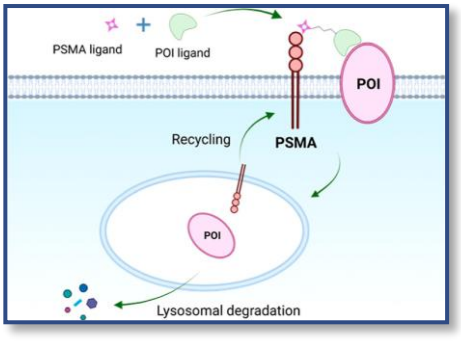
In this study the authors detail the structural activity relationship (SAR) exploration and optimisation of lead PROTAC 3, targeting B-cell lymphoma 6 protein (BCL6) with the E3 ligase Cereblon (CRBN) for the treatment of non-Hodgkin lymphoma. The authors aimed to improve the overall potency of compound 3 while maintaining the oral bioavailability through rounds of SAR optimisation to achieve a clinical candidate. Optimisation and examination of the stereoselective configuration of the linker region proved crucial in enhancing potency and degradation depth, ultimately modifying the original NH-piperidine of PROTAC 3 with a methyl substituent in the 3-positions to generate PROTAC BMS-986458. The optimal configuration of the linker was confirmed as 3R,4R - possessing an EC_{50} of 2.2 nM and Y_{min} of 13%. In a 3-day PK/PD study, statistically significant BCL degradation was maintain across all timepoint and dose-dependent tumour volume reduction of 84% was observed at treatments of 45 mg/kg b.i.d. The authors also further profile BMS-986458, confirming selectivity for BCL6 with global proteomics, proteasome dependence with known proteasome inhibitors, and CRBN dependence using $CRBN^{-/-}$ cell lines.

This work highlights an elegantly executed example of lead compound optimisation to the first BCL6 heterobifunctional clinical candidate. It nicely illustrates the significance of linker optimisation and stereochemical configuration when attempting to fine-tune PROTAC potency.

| *Matylda*

Development of Prostate-Specific Lysosome-Targeting Degraders

Deqin Cai§, Xuankun Chen§, Yaxian Zhou§, ..., Weiping Tang*
JACS ***2026** 148, 7, 7171-7180*



This article presents a new approach targeted lysosomal degradation. Several examples of targeted degradation of extracellular and membrane proteins via lysosomal targeting receptors have been published, however obtaining tissue specificity remains challenging. Here, the authors present a new class of molecules which can induce protein degradation by targeting them to prostate cancer specific PSMA receptor using PSMA TArgeting Chimeras (PTACs). First, they tested a small array of biotinylated linkers in fusion with PSMA ligand to assess how they affect the cellular uptake. Using western blotting and fluorescent

microscopy, they identify the most promising linkers and show the specificity of their approach by testing the molecules in cell lines with different levels of PSMA expression. Then using copper-free click chemistry, they created PTAC molecules with clinically approved antibodies targeting EGFR and PD-L1. The resulting PTACs can selectively degrade their target proteins in PSMA expressing cell lines at DC_{50} in picomolar range. Finally, they created a fully small-molecule based PTACs targeting PD-L1 however, these molecules required much higher concentration to obtain a comparable level of degradation.

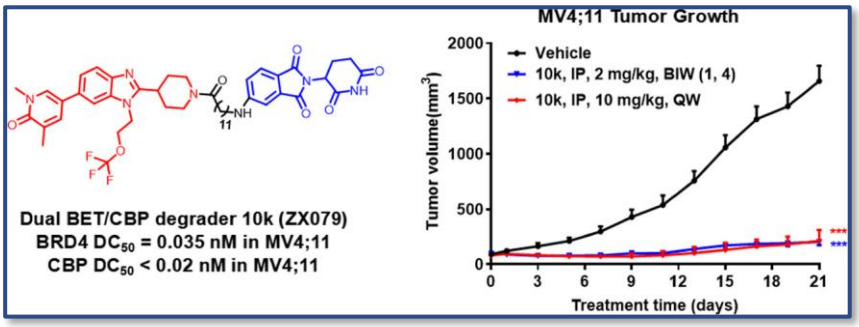
This article presents a new approach to tissue-selective targeted lysosomal degradation. Several examples of targeted degradation of extracellular and membrane proteins via lysosomal targeting receptors have been published, however obtaining tissue specificity remains challenging. The molecules described in the article are a promising tool for specific targeting of PSMA-positive cancers and other diseases.

| *Dylan*

Discovery of ZX079 as a Dual PROTAC Degrader Targeting BRD4/CBP in Acute Myeloid Leukemia

Qiuping Xiang§, Yanan Wang§, Mengli Gu§, Junchen Yao§, Yanping Zhang§, …, Shuo Yang*, Yong Xu*, Dongsheng Zhu**
J. Med. Chem. 2026, 69, 4, 4132–4159

Discussed internally



Epigenetic regulators, such as BET proteins, have consistently been targeted with degraders as the field of TPD has developed. BRD4 plays a vital role in acute myeloid leukemia progression, but traditional inhibitory approaches have been rendered unsuitable due to dose-limiting toxicity and treatment-induced resistance. The CBP/p300 proteins have been implicated in this resistance to BET-inhibition, due to their compensatory translational activation. In this account, Xiang *et al.* propose a dual PROTAC degrader, drawing from prior knowledge of dual BET/CBP inhibitors, CBP degraders, and BET degraders. Following a dive into linkerology, the authors disclosed a potent dual degrader of BRD4/CBP, which also decreases c-Myc expression (which plays a vital role in the BRD4/CBP signalling axis). Their lead candidate **ZX079** (referred to as **10k** in the main text) boasts DC_{50} values of 0.035 nM and <0.02 nM against BRD4 and CBP respectively, and over 90% tumour regression in a MV4-11 xenograft mouse model.

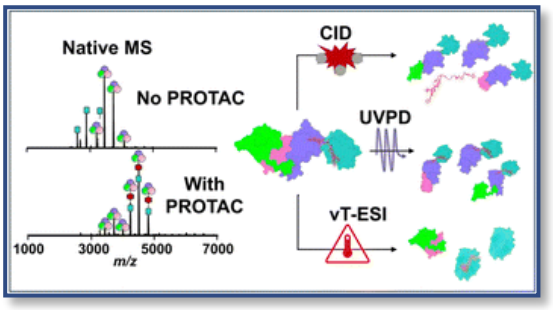
The authors have developed SAR for these compounds, it would have been interesting to see a more diverse array of linker types employed for their future development of this compound. Furthermore, there does seem to be a slight aspecificity within the BET proteins herein, although the authors highlight this as a point for further investigation.

| *Claudine*

Unveiling BCL-xL-specific PROTAC efficiency and dissociation pathways using native mass spectrometry

Mohamed I. Gaddalah, …, Jennifer S. Brodbelt*
Chem. Sci., ***2026***, *Advance Article*

Discussed internally



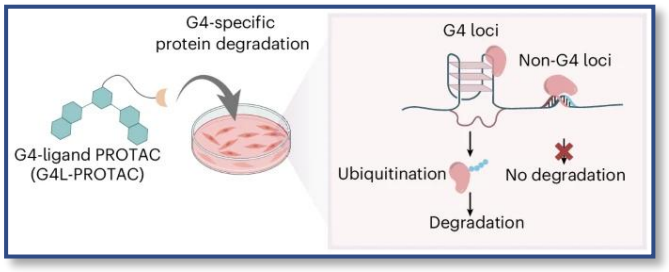
Understanding and characterising full ternary complex assembly is a key part of PROTAC design. In this study, the authors use native mass spectrometry to probe interactions between BCL-xL, a series of PROTACs, and the VHL E3 ligase complex. This label-free approach enables profiling of binary binding, competition experiments, and ternary complex formation and stability. They show that PROTAC engagement occurs first with BCL-xL, which then promotes recruitment of the ligase to form stable ternary complexes. Using CID, UVPD, and variable-temperature ESI, they compare different methods for interrogating these assemblies, showing that UVPD better preserves native topology, whereas CID can introduce artefactual dissociation pathways. Thermal studies indicate broadly similar stability across the PROTACs tested. Overall, the work demonstrates how native MS can be used to gain mechanistic insight into PROTAC-induced complex formation and stability.

This paper highlights how native MS can be used to study and characterise PROTACs, with approaches that could also be applied to other modalities such as molecular glues. These methods provide complementary insight alongside established biophysical techniques like SPR, which offer more detailed kinetic information. It would have been interesting to see a broader range of PROTACs with more varied affinities to better demonstrate the scope and general applicability of native MS.

| *Matylda*

Degradation of G-quadruplex-binding proteins in chromatin using G4-ligand-based proteolysis-targeting chimeras

Zixuan Wang, …, Shankar Balasubramanian*
Nature Chemistry ***2026*** *DOI 10.1038/s41557-026-02111-y*



This article presents work on new G-quadruplex (G4) PROTACs. The G4L-PROTACs use a small molecule PDS ligand binding to G4. The authors explored several flexible linkers which differed in length and composition as well as E3 ligands for VHL (VH032) and cereblon (thalidomide and pomalidomide). They confirm efficient binding of the PROTACs to E3 ligases using an FP assay. They also confirmed G4 binding and stabilisation of the structures using different known DNA fragments containing G4 structures. The compounds however showed poor cell permeability which was effectively enhanced by co-treatment with Endo-Porter peptide which promotes endocytosis. Cellular profiling showed efficient reduction in levels of several protein known to bind to the G4 regions, such as SMARCA4 and FUS. The

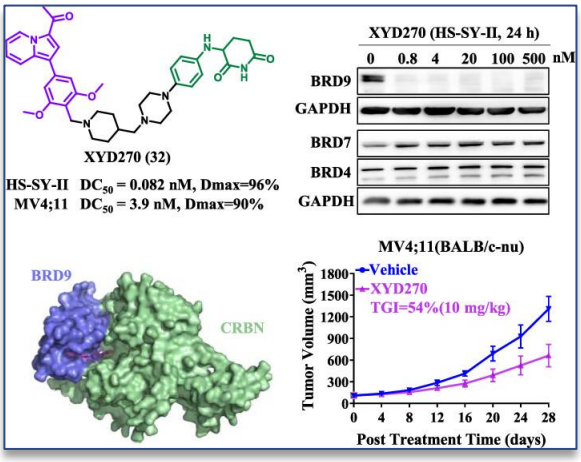
proteomics experiment revealed dramatic changes in cell proteome upon PROTACs treatment. Interestingly, PROTACs with different linkers showed different specificity towards G4-binding proteins and different anti-proliferative effects which were assessed by cell cycle analysis. Finally, several unexpected findings from proteomics profiling were validated by western blotting and ELISA which identified SOX2 and SNRNP70 as new proteins binding to G4.

This work presents another advancement towards development of PROTACs targeting transcription factors using fully small-molecule chimeras. Previously published PROTACs targeting G4-binding proteins required transfection of G4-containing DNA PROTACs. Here, the authors used a small-molecule ligand binding to G4 structures. Further work on optimising PROTACs permeability can result in developing a useful research tool with potential therapeutic applications.

| *Dylan*

Discovery of XYD270 as a Potent, Selective, and Orally Efficacious BRD9 PROTAC for Cancer Therapy

Yumin Huang§, Guizhen Cheng§, Xin Tang§, …, Bin Lin, Hui Shen*, Yong Xu**
J. Med. Chem. ***2026****, 6, 4, 4132–4159*



BRD9 remains a widely targeted therapeutic target in the field of TPD, with mounting evidence of its role as a driver in multiple forms of cancer. Its role as an oncogenic driver is particularly well established in synovial sarcoma, which has been previously investigated by academics and industry alike. In this work, Huang et al. develop a CRBN-based degrader via an elegant SAR study, which boasts low-to-sub nanomolar DC50 values and >95% ablation of BRD9 protein levels. While the majority of BRD9 degraders employ BI-7273 as the BRD9 binding warhead, the authors instead employ a different warhead reported previously in a separate paper by the senior author, Yong Xu.

Huang et al. report a full investigation of the degradation mechanism for XYD270, including AlphaScreen assays for ternary complex formation. Furthermore, oral administration of the lead compound at 10 mg/kg q.d. in mice resulted in >50% tumour growth inhibition.

The authors delve deep into linkerology and CRBN binder scope to develop XYD270, and it is refreshing to not only see a new BRD9 warhead, but also an N-arylglutarimide binder as the CRBN recruiter. This account is an excellent example of the range of chemical space one needs to explore to find potent and effective degraders. Overall, this represents a potent and orally bioavailable PROTAC against a highly relevant target, with excellent scope exploration and a refined exploration of SAR in their compound set.

PRE-PRINTS

| *Alexandra*

Developing potent and selective TBK1 molecular glue degraders for cancer immunotherapy

John J. Caldwell§, Patrick R. A. Zanon§, Iona Ferguson§, Stephen T. Hallett§, ..., Rob L. M. van Montfort, Pascal Meier*, Henrik Daub*, Zoran Rankovic**

In this work they utilise high-throughput proteomic screening of a molecular-glue library, resulting in the identification a rapid, potent and selective first-in-class TBK1 molecular glue degrader, CCT412020. Their cryo-EM structure highlights CCT412020 as a mechanistically distinct TBK1 degrader, as it binds as an unconventional site at the TBK1 dimer interface, a strategy that could be applied to overcome cancer immunotherapy resistance.

| *Alexandra*

Rational scaffold design mitigates mitochondrial complex I off-target inhibition of bifunctional degraders

*Nick Richert§, Hana Nůsková§, ..., Aubry K. Miller**

This paper details the identification of a novel mitochondrial complex I inhibitor scaffold and discusses strategies, such as the introduction of a bump or kink in the linker, used to ease mitochondrial complex I inhibition exhibited by bifunctional degraders. They examine this in the context of androgen receptor clinical candidate, highlighting mitotoxicity as a concern in PROTAC design and establish general structural principles to circumvent mitochondrial complex I inhibition.

| *Dylan*

Direct-to-Biology Enables Rapid Identification of Potent FBXO22 Degraders

Carla Brown§, Sarvatit Patel§, ..., Dalia Barsyte-Lovejoy*, Vijayaratnam Santhakumar*

Brown *et al.* report their efforts on harnessing a novel E3 ligase in this pre-print. This account follows a recent publication that the E3 ligase FBXO22 is recruitable for TPD *via* a bioconversion of simple amines to aldehydes, followed by covalent labelling of Cys326 in FBXO22. Employing a relatively limited screen of 175 compounds, they observed no FBXO22-dependent degradation of a range of POIs (BRD4, BTK, and more). However, their direct-to-biology approach did furnish CRBN and VHL-based degraders of FBXO22, and homoPROTACs.

| *Dylan*

Indazolone-Based Molecular Glue Degraders as a Tunable Platform for Reprogramming Cereblon Substrate Specificity

Hui-Jun Nie§, Jiamin Wang§, Hao Xu§, …, Jia Li, Xiao-Hua Chen**

This preprint showcases a further expansion in the scope of CRBN-binding ligands. Nie et al. disclose an indazolone-based discovery platform for CRBN-driven molecular glue degraders (MGDs), developed through rational design and mechanistic insights into the plasticity of CRBN-MGD complexes, moving beyond traditional isoindolinone-glutarimide scaffolds. The authors report variable degradation selectivity against the usual CRBN neo-substrates (IZKF1/3, CK1a, etc.) with their platform, including potent multi-target degraders, and highly specific MGDs: for example, compound IBA-12 which specifically depletes IKZF2 without degrading IKZF1/3 or GSPT1. Additionally, they note that their CK1a selective degrader, IBA-11, offers a therapeutic intervention for acute myeloid leukemia.

| *Claudine*

A Scalable Design for Proximity-Inducing Molecules

Endri Karaj§, *Varsha Venkatarangan§*, Shaimaa H. Sindi§, Surached Siriwongsup§, Chaiheon Lee§, …, *Amit Choudhary**

The authors introduce GRIPs (group-transfer chimeras), a new induced proximity strategy that repurposes small-molecule enzyme inhibitors to recruit endogenous PTM writers/erasers for targeted protein modification. By attaching group-transfer handles to inhibitors, they enable covalent recruitment of enzymes to proteins of interest, achieving controlled phosphorylation, acetylation, and O-GlcNAcylation across 16 enzyme-POI pairs at endogenous levels. GRIPs expand proximity pharmacology beyond degradation into PTM editing by leveraging abundant inhibitor chemical space, establishing a scalable new modality for controlling protein function.

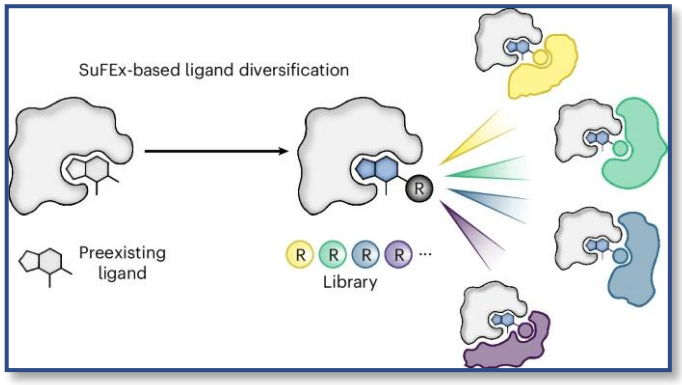
PAPERS AND PRE-PRINTS FROM CeTPD

| *Hiro*

High-throughput ligand diversification to discover chemical inducers of proximity

James B. Shaum§, Miquel Muñoz i Ordoño§, …, Georg E. Winter*, Michael A. Erb*
Nat. Chem. Bio. ***2026*** *DOI 10.1038/s41589-025-02137-2*

CeTPD authors (past and present): Zoe J. Rutter, Hirotake Furihata and Alessio Ciulli



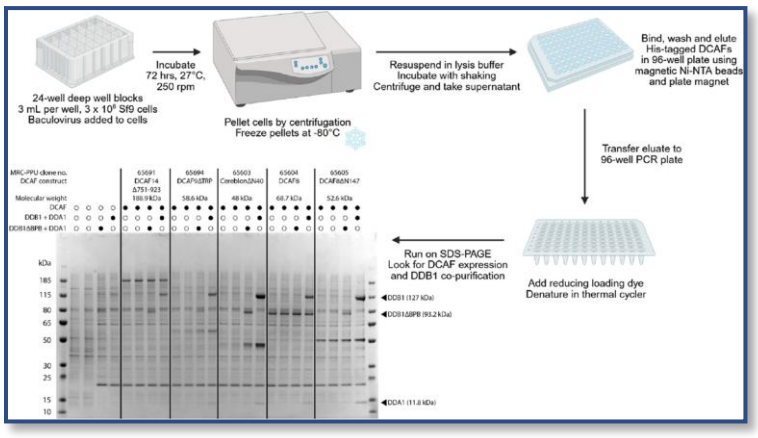
A collaborative study with Michael A. Erb presents a new strategy to discover chemical inducers of proximity (CIPs) - molecules that bring proteins together to trigger the rewiring of cellular biochemistry. Unlike traditional design approaches, this method uses high-throughput sulfur(VI) fluoride exchange (SuFEx) chemistry to rapidly generate and test thousands of compounds. This platform led to the discovery of dHTC1, which recruits the $CRL4^{CRBN}$ ligase to the target protein ENL, and dHTC3, a Brd4-targeting molecular glue that engages the previously unexplored SCF^{FBXO3} ligase. Structural analyses further revealed how even rather weak affinity for CRBN can be leveraged to form functional ternary complexes with ENL engagement that drive protein degradation. Looking ahead, this approach opens the door to systematically exploring new ligases, targets, and chemistries, expanding the reach of proximity-based therapeutics.

| *Matylda*

Scalable insect cell expression and purification screening applied to CRL4-DCAF substrate receptors

Angus D. Cowan§*, Stefan Jaekel, Alessio Ciulli*
Protein Expression and Purification ***2026,*** *241, 106907*

CeTPD authors (past and present): Angus D. Cowan and Alessio Ciulli



This work lead by Angus presents a valuable resource for researchers working on recombinant expression of DCAF proteins. Using a high-throughput plate-based insect cell expression, Angus screened 54 constructs covering 24 human DCAF proteins and identified their dependence on DDB1 for efficient expression. Further purification of the proteins helped to identify DCAFs which formed stable complexes with DDB1. The small-scale expression can be efficiently scaled up which was demonstrated in

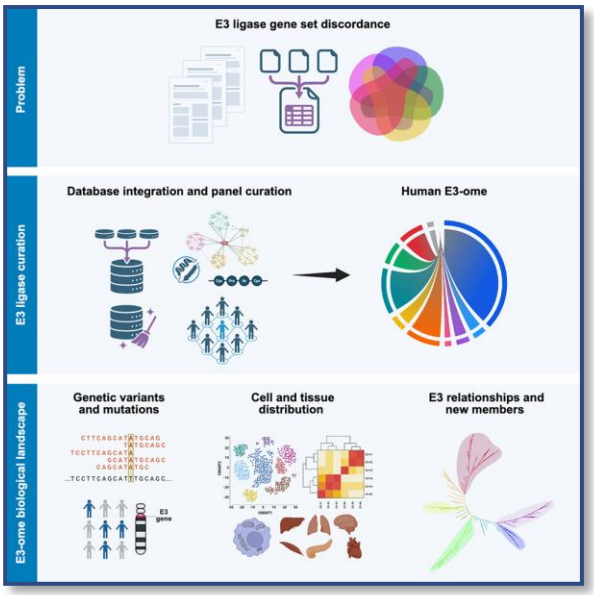
previously published works from CeTPD on bivalent molecular glue degraders (IBGs) and SMARCA2/4 molecular glues. This work and the presented methodology might be of great interest for researchers exploring E3 ligases for structural and functional studies or for recruitment of DCAFs for targeted protein degradation.

| *Alexandra*

The E3-ome gene-centric compendium reveals the human E3 ligase landscape

Ngee Kiat Chua, …, Rebecca Feltham*
Cell. ***2026****, 189, 1-22*

CeTPD authors (past and present): Mark A. Nakasone and Alessio Ciulli



In this monumental work championed by Ngee Kiat Chua and Rebecca Feltham, the authors curated all currently known human E3 ligases into a standardised reference database, integrating years of biological, structural and functional information to build a unified framework for E3 classification and annotation. The authors use the E3-ome to map E3 ligases across different subcellular locations, cell types, and tissues, highlighting disease relevance and associations, exemplifying how this resource could be used to reveal how E3 ligase mutations alter function, change substrate specificity, or drive abnormal protein degradation pathways. This resource represents an invaluable tool for the future TPD research and wider ubiquitin community, especially as the field seeks to expand the repertoire of E3 ligases currently co-opted by small molecule degraders.

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