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INDUSTRY FOCUS

Drug Discovery

An exclusive collection featuring top-tier articles, visionary experts, and essential industry insights

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Foreword

Welcome to the latest edition of our Industry Focus eBook, where we explore the ever-evolving landscape of **Drug Discovery.** This field continues to push scientific boundaries, combining innovation, precision, and cross-disciplinary collaboration to address some of the world's most urgent health challenges. Sponsored by **Sino Biological**, this edition brings together a compelling selection of articles that reflect the diversity and depth of breakthroughs shaping the next generation of therapeutics.

From the plant kingdom to the lab bench, **Plant-based fitness supplements for reversing metabolic syndrome** highlights promising natural compounds that may help counter a condition affecting millions worldwide. In the realm of oncology, **Drug combination shows promise for treating aggressive T-cell lymphomas** and **PPP2R1A mutations linked to improved survival in ovarian clear cell carcinoma** both underscore how molecular insights are translating into more effective, personalized treatment strategies.

Looking at cancer from a biomechanical perspective, **Measuring tumor force offers new clues for brain cancer treatment** introduces a novel method that could transform how we understand and target gliomas. Meanwhile, **New index helps optimize picosecond laser treatment for nevus of Ota** brings a dermatological lens to drug discovery, showcasing innovations that bridge diagnostics and therapeutics.

Immunology also takes centre stage with **Shingles and RSV vaccines with AS01 adjuvant reduce dementia risk**, pointing to a remarkable connection between vaccination and long-term cognitive health. On the cutting edge of molecular biology, **The role of transcription factors in next-gen drug discovery** explores how gene regulation is unlocking new therapeutic targets.

We also look beyond cancer with **Antibody-drug conjugates beyond oncology**, which examines how this powerful technology is being reimagined for a wider array of diseases. Finally, **What makes PROTACs and MGDs game-changers in drug discovery?** dives into the mechanisms behind two of the most exciting therapeutic modalities emerging today.

As you journey through this eBook, we invite you to explore how science is not only treating disease but reshaping the very concept of what's possible in medicine.

What makes PROTACs and MGDs game-changers in drug discovery?

Stick, tag, destroy: The science of PROTACs and MGDs

Traditional drug research has focused on creating inhibitors that occupy the active areas of disease-related proteins, preventing them from functioning properly.

But this strategy leaves a considerable amount of the human proteome, estimated to be around 80 % of disease-related proteins, "undruggable", due to the absence of specific active sites or binding pockets.[1,2]

Targeted Protein destruction (TPD) may be a revolutionary alternative, using small chemicals to trigger ubiquitination and then destruction of target proteins via the cell's natural proteasomal or lysosomal pathways.[2]

Within the TPD landscape, Proteolysis-Targeting Chimeras (PROTACs) and Molecular Glue Degraders (MGDs) stand out as the leading strategies[1-3].

PROTACs (Proteolysis-targeting chimeras)

A PROTAC molecule is typically a heterobifunctional compound made of three important parts: a ligand that binds to the protein of interest (POI), another ligand that recruits an E3 ubiquitin ligase, and a chemical linker that joins the two (Figure 1).[4,5]

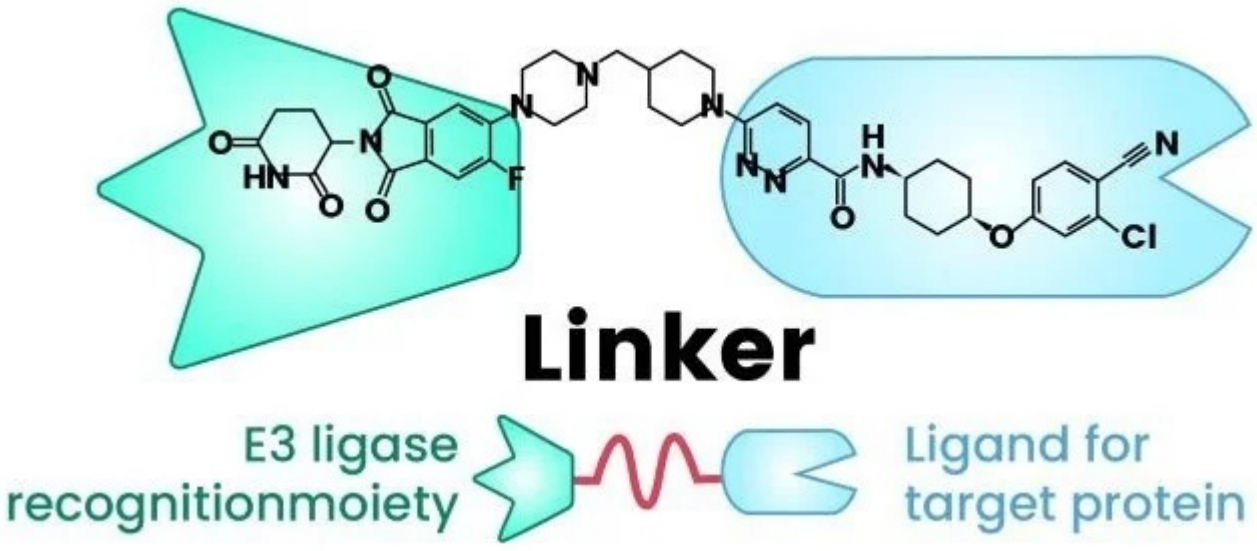


Figure 1. *Structure of a PROTAC. The molecule links an E3 ligase-binding domain to a*

target protein ligand via a flexible chemical linker, enabling targeted ubiquitination and subsequent proteasomal degradation[6]. Image Credit: PROTAC, A "Revolutionary" Technology in Small Molecule Drug Discovery- CUSABIO

PROTAC activity is based on its capacity to bring the POI and an E3 ligase into close proximity with each other, resulting in a ternary complex. This closeness promotes the transfer of ubiquitin tags from the E2 conjugating enzyme (which interacts with the E3 ligase) to the POI.[2,3]

Once polyubiquitinated, the 26S proteasome identifies and quickly destroys the POI (Figure 2). A significant advantage is that after the target protein is destroyed, the PROTAC molecule is released and regenerated to target another copy of the POI, allowing for continued degradation even at catalytic drug concentrations.[1,2]

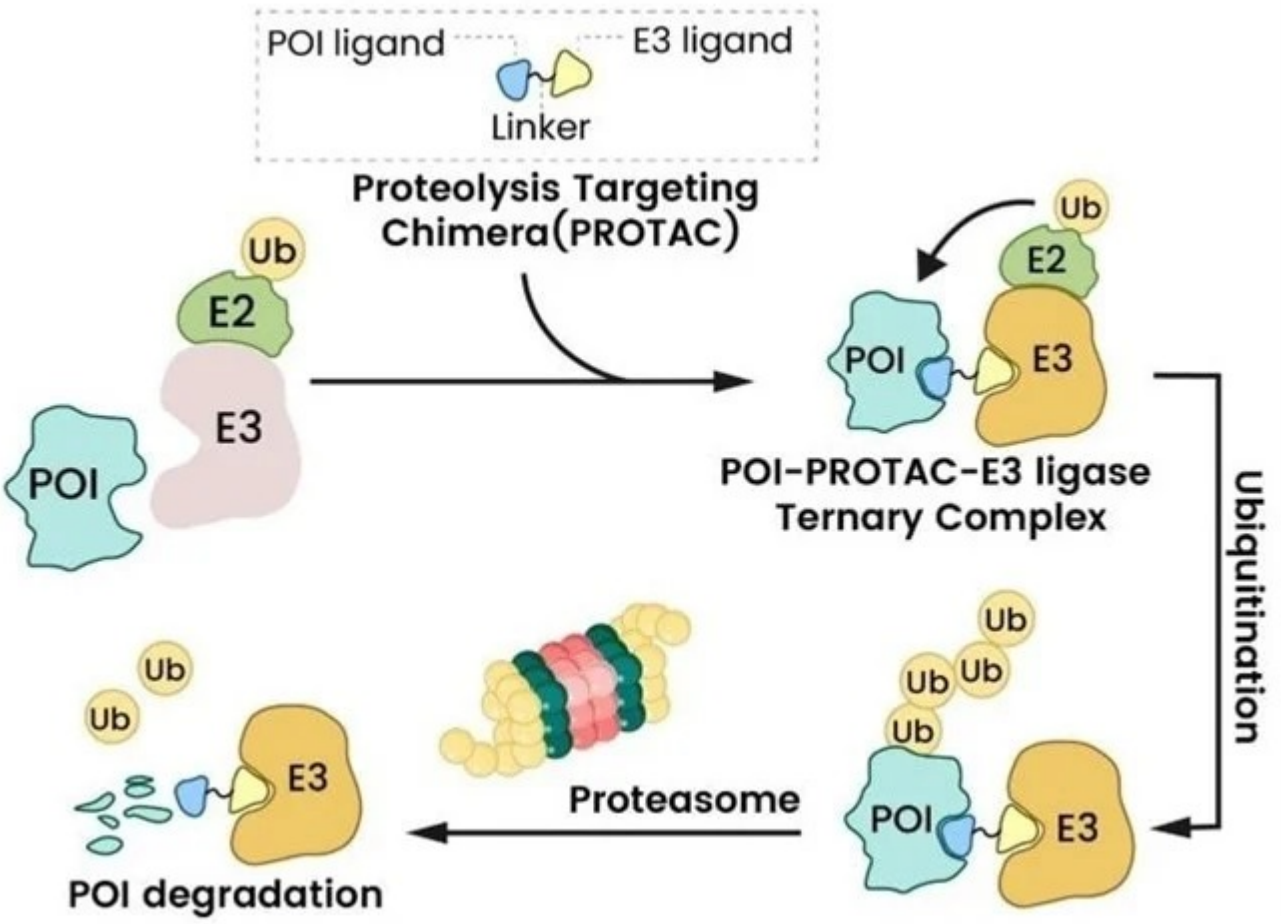


***Figure 2**. PROTAC mechanism of action. The PROTAC bridges a target protein and E3 ligase, triggering ubiquitination and proteasomal degradation[1]. Image Credit: Sino Biological Inc.*

Historical development and clinical progress

The concept of PROTACs was established in 1999, with the first peptide-based PROTAC molecule (PROTAC-1) created in 2001.[7] These early PROTACs demonstrated the notion of targeted protein degradation, but were restricted by low cell permeability, limited oral bioavailability, and proteolytic instability.

The first entirely small molecule PROTAC, PROTAC 4, was introduced in 2008. It demonstrated significantly improved cell permeability and paved the way for finding small-molecule ligands for important E3 ligases.[8]

Cereblon (CRBN) sprang to prominence in 2010 as the principal target of thalidomide and its analogs. Von-Hippel-Lindau (VHL)-recruiting ligands were later found in 2012.[1-3] CRBN and VHL are now the most commonly used E3 ligases in PROTAC design due to their drug-like characteristics.

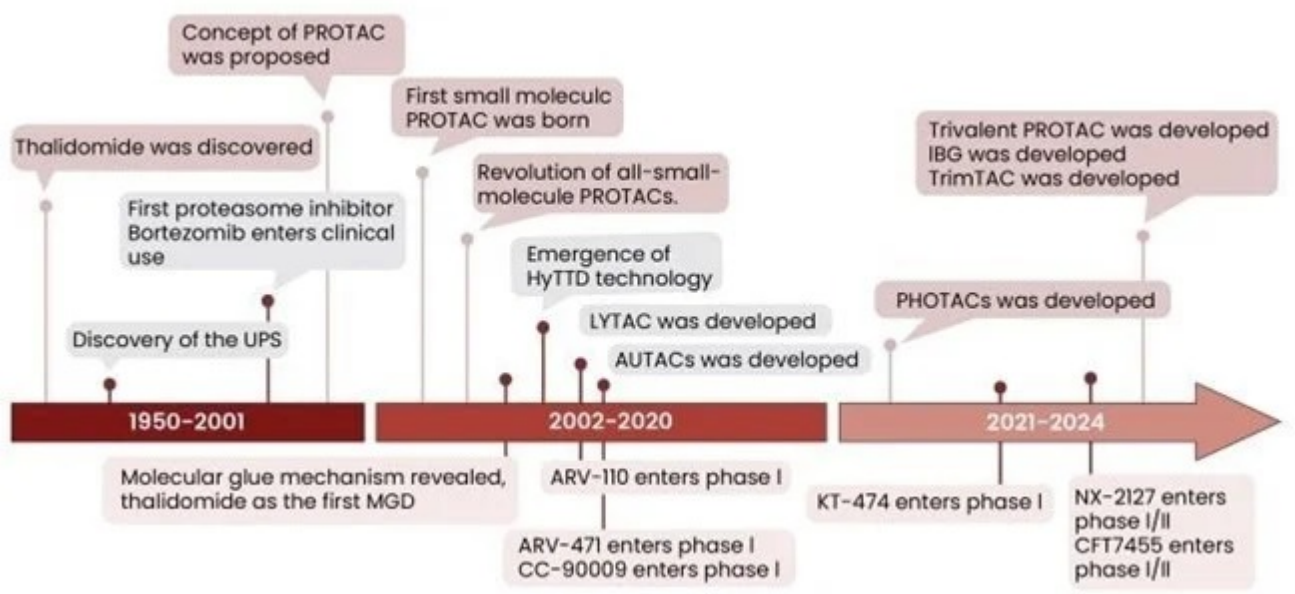


***Figure 3**. Key milestones in PROTAC development, from its initial conceptualization and peptide-based molecules to the first small-molecule PROTACs and the emergence of CRBN and VHL as E3 ligase targets[2]. Image Credit: Sino Biological Inc.*

Since then, there has been rapid clinical development in the area, with numerous PROTACs entering clinical trials. Bavdegalutamide (ARV-110), an androgen receptor (AR)-targeting PROTAC, has completed Phase II studies for prostate cancer.[9]

Vepdegestrant (ARV-471), which targets the estrogen receptor (ER), has advanced to NDA/BLA for ER+/HER2− breast cancer.[2,10] NX-2127, a Bruton's tyrosine kinase (BTK) degrader, has demonstrated efficacy in overcoming treatment resistance in B-cell malignancies.[11]

There are over 30 heterobifunctional protein degraders currently studied in Phase I-III trials1. Table 1 lists the representative clinical-stage PROTACs, their target proteins, the E3 ligases they recruit, and their current clinical stages.

Table 1. Representative clinical-stage PROTACs, their target proteins, and the E3 ligases they recruit[1-3]. Source: Sino Biological Inc.

Molecule	Target Protein	E3 Ligase	Clinical Phase
ARV-471	ER	CRBN	NDA/BLA
ARV-766	AR	CRBN	Phase II
ARV-110	AR	CRBN	Phase II
DT-2216	Bcl-XL	VHL	Phase I/II
NX-2127	BTK	CRBN	Phase I
NX-5948	BTK	CRBN	Phase I
CFT1946	BRAF V600	CRBN	Phase I
KT-474	IRAK4	CRBN	Phase II

Challenges and optimization

Despite their potential, PROTACs have a few issues that prevent their widespread adoption, such as complex structures and large molecular weight (typically >700 Da), which frequently place them outside of the "rule of five". This can cause decreased cell permeability, metabolic instability, and adverse pharmacokinetic (PK) profiles.[2,12]

Rational design approaches address these issues by focusing on linker and E3 ligase ligand optimization.[13] Incorporating rigid structures, such as spirocycles or piperidines, into the linker can significantly improve degradation potency and oral bioavailability.[2]

Optimizing E3 ligands entails creating novel scaffolds, such as phenyl glutarimide (PG) derivatives and TX-16, which have higher stability and affinity than standard thalidomide derivatives.[2,4,12,13]

Molecular glue degraders (MGDs)

MGDs are small, monovalent molecules, as opposed to the bivalency of PROTACs. They work by initiating or maintaining new protein-protein interactions (PPIs) between an E3 ligase and a target protein (POI). This interaction marks the target protein for destruction using the ubiquitin-proteasome pathway.[2,3]

MGDs achieve this by changing the surface properties of substrate receptors and E3 ligases, resulting in "non-native" interactions that enhance ubiquitination and degradation.[3,14]

MGDs were discovered mostly through serendipitous observation or repurposing existing pharmacological compounds, making rational design difficult due to the unpredictable nature of these generated interactions.[15]

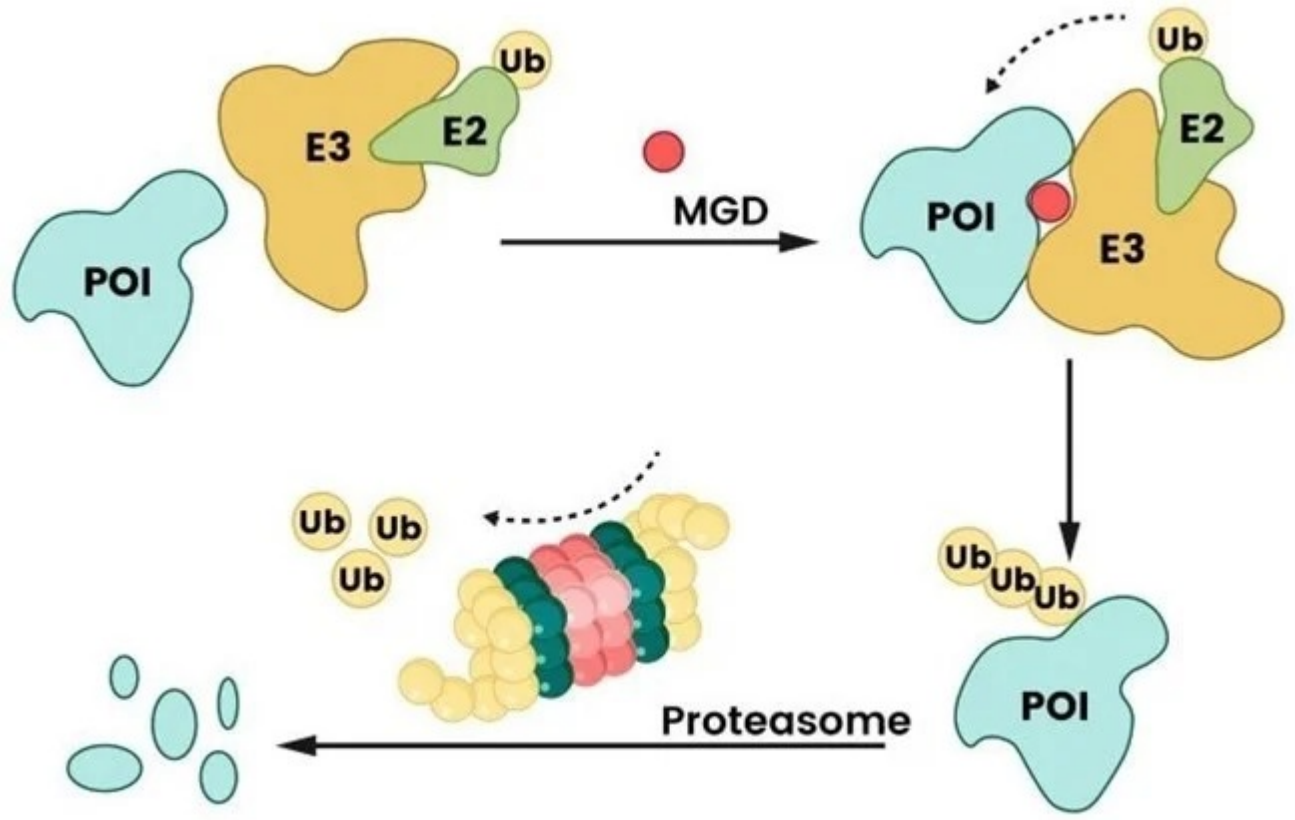


Figure 4. *Degradation mechanism of MGD. MGD facilitates the interaction between a protein of interest (POI) and an E3 ligase by binding to either the E3 ligase or the POI, thereby promoting ubiquitination and subsequent proteasomal degradation[2]. Image Credit: Sino Biological Inc.*

Advantages and challenges

MGDs have many encouraging characteristics in therapeutics. Their monovalent structure produces smaller molecules with lower molecular weights that are more easily subject to "Lipinski's rule of five". This often results in greater drug-likeness and pharmacokinetic characteristics than PROTACs.[2]

In addition, MGDs may not always require a binding pocket on the target protein, which broadens the list of "undruggable" proteins they can degrade.[1,2]

Thalidomide, lenalidomide, and pomalidomide were among the first MGDs identified and are now licensed to treat erythema nodosum, myelodysplastic syndromes, and multiple myeloma, respectively.[1,2]

Other MGDs, including CC-90009 (targeting GSPT1) and E7820 (targeting RBM39), are also in clinical trials.[2,3]

Designing sensible MGDs is still a challenge in this area. Their mechanisms are fundamentally unpredictable, and clinical translation faces challenges such as varying degradation efficiencies across tissues, a lack of prognostic biomarkers, and unexpected off-target consequences.

Recent efforts in rational MGD design have included tactics such as adding covalent handles to existing inhibitors, which effectively convert them into degradation-competent MGDs.[1-3,12,15]

Conclusion and future outlook

TPD technologies, particularly PROTACs and MGDs, represent a paradigm shift in drug development by completely eliminating target proteins rather than merely inhibiting them.

This ability to destroy "undruggable" proteins opens up new therapeutic paths for various disorders, particularly cancer.

Despite impressive progress, problems remain, such as enhancing metabolic stability, addressing potential off-target effects, and broadening the range of accessible E3 ligases beyond the currently dominating CRBN and VHL.

The combination of modern computational tools, such as AI-aided drug design, with comprehensive analytical methodologies, such as multi-omics profiling, is expected to speed the discovery of novel degraders while improving selectivity and efficacy.[2,3]

PROTAC and MGD technologies promise to open new therapy options for diseases previously considered unattainable.

SignalChem Biotech’s contribution to targeted protein degradation research

As targeted protein degradation technologies evolve, SignalChem Biotech provides researchers with a comprehensive suite of recombinant E3 ligases, including essential molecules such as CRBN and VHL, and a diverse array of target proteins, antibodies, and functional assay reagents.

These high-quality, validated proteins and reagents allow for rapid screening, mechanistic probing, and optimization of novel PROTACs and molecular glue degraders.

Partial list of ubiquitin enzymes - E3

Source: Sino Biological Inc.

Name	Cat#	Species	Tag	Expression	Sequence
BIRC3, Active	B280-380G	Human	GST	Sf9 Cells	Full Length
BIRC7, Active	B281-380G	Human	GST	Sf9 Cells	Full Length
HERC4, Active	H265-381G	Human	GST	Sf9 Cells	642-end
MGRN1, Active	M287-380G	Human	GST	Sf9 Cells	2-end
RanBP2, Active	R230-381H	Human	His	E.coli	2553-2838
RNF34 (CARP), Active	R296-380G	Human	GST	Sf9 Cells	Full Length
RNF34L (CARP2), Active	R297-380G	Human	GST	Sf9 Cells	Full Length
TRIM37, Active	T292-380G	Human	GST	Sf9 Cells	Full Length
WWP2, Active	W297-380G	Human	GST	Sf9 Cells	Full Length
CBL Protein	C272-381G	Human	GST	E.coli	1-375

References

1. Pan, M., *et al*. (2025). Proteolysis-Targeting Chimera (PROTAC): A Revolutionary Tool for Chemical Biology Research. *Small Methods*. https://doi.org/10.1002/smtd.202500402.
2. Pan, Y., Wang, Y. and Gou, S. (2025). Proteolysis targeting chimera, molecular glue degrader and hydrophobic tag tethering degrader for targeted protein degradation: Mechanisms, strategies and application. *Bioorganic Chemistry*, (online) 161, p.108491. https://doi.org/10.1016/j.bioorg.2025.108491.
3. Zhang, B., *et al*. (2025). Rational Design of Dual Degraders by Incorporating Molecular Glue Structural Features into PROTAC Degraders. *Journal of Medicinal Chemistry*. https://doi.org/10.1021/acs.jmedchem.5c00443.
4. Ito, T. (2023). Protein degraders -from thalidomide to new PROTACs. *Journal of Biochemistry/The journal of biochemistry*. https://doi.org/10.1093/jb/mvad113.
5. Rutherford, K.A. and McManus, K.J. (2024). PROTACs: Current and Future Potential as a Precision Medicine Strategy to Combat Cancer. *Molecular cancer therapeutics*,

(online) 23(4), pp.454–463. https://doi.org/10.1158/1535-7163.mct-23-0747.
6. Pagan, J., *et al*. (2013). Role of the Ubiquitin Proteasome System in the Heart. *Circulation Research*, 112(7), pp.1046–1058. https://doi.org/10.1161/circresaha.112.300521.
7. Sakamoto, K.M., *et al*. (2001). Protacs: Chimeric molecules that target proteins to the Skp1-Cullin-F box complex for ubiquitination and degradation. *Proceedings of the National Academy of Sciences*, 98(15), pp.8554–8559. https://doi.org/10.1073/pnas.141230798.
8. Schneekloth, A.R., *et al*. (2008). Targeted intracellular protein degradation induced by a small molecule: En route to chemical proteomics. *Bioorganic & Medicinal Chemistry Letters*, (online) 18(22), pp.5904–5908. https://doi.org/10.1016/j.bmcl.2008.07.114.
9. Chirnomas, D., Hornberger, K.R. and Crews, C.M. (2023). Protein degraders enter the clinic — a new approach to cancer therapy. *Nature Reviews Clinical Oncology*. https://doi.org/10.1038/s41571-023-00736-3.
10. Hamilton, E.P., *et al*. (2022). ARV-471, an estrogen receptor (ER) PROTACdegrader, combined with palbociclib in advanced ER+/human epidermal growth factor receptor 2–negative (HER2-) breast cancer: Phase 1b cohort (part C) of a phase 1/2 study. *Journal of Clinical Oncology*, 40(16_suppl), pp.TPS1120–TPS1120. https://doi.org/10.1200/jco.2022.40.16_suppl.tps1120.
11. Robbins, D.W., *et al*. (2024). Discovery and Preclinical Pharmacology of NX-2127, an Orally Bioavailable Degrader of Bruton's Tyrosine Kinase with Immunomodulatory Activity for the Treatment of Patients with B Cell Malignancies. *Journal of medicinal chemistry*, 67(4). https://doi.org/10.1021/acs.jmedchem.3c01007.
12. Pu, C., *et al*. (2023). Current strategies for improving limitations of proteolysis targeting chimeras. *Chinese Chemical Letters*, 34(6), pp.107927–107927. https://doi.org/10.1016/j.cclet.2022.107927.
13. Zagidullin, A., *et al*. (2020). Novel approaches for the rational design of PROTAC linkers. *Exploration of Targeted Anti-tumor Therapy*, 1(5), pp.381–390. https://doi.org/10.37349/etat.2020.00023.
14. Malone, M.L., *et al*. (2025). Application of DELs for E3 Ligase Ligand Discovery and Targeted Protein Degradation. *DNA-encoded Library Technology for Drug Discovery*, pp.134–156. https://doi.org/10.1039/9781788016032-00134.
15. Liu, Y., *et al*. (2025). Routes to molecular glue degrader discovery. *Trends in Biochemical Sciences*. (online) https://doi.org/10.1016/j.tibs.2024.12.006.

About Sino Biological Inc.

Sino Biological is an international reagent supplier and service provider. The company specializes in recombinant protein production and antibody development. All of Sino

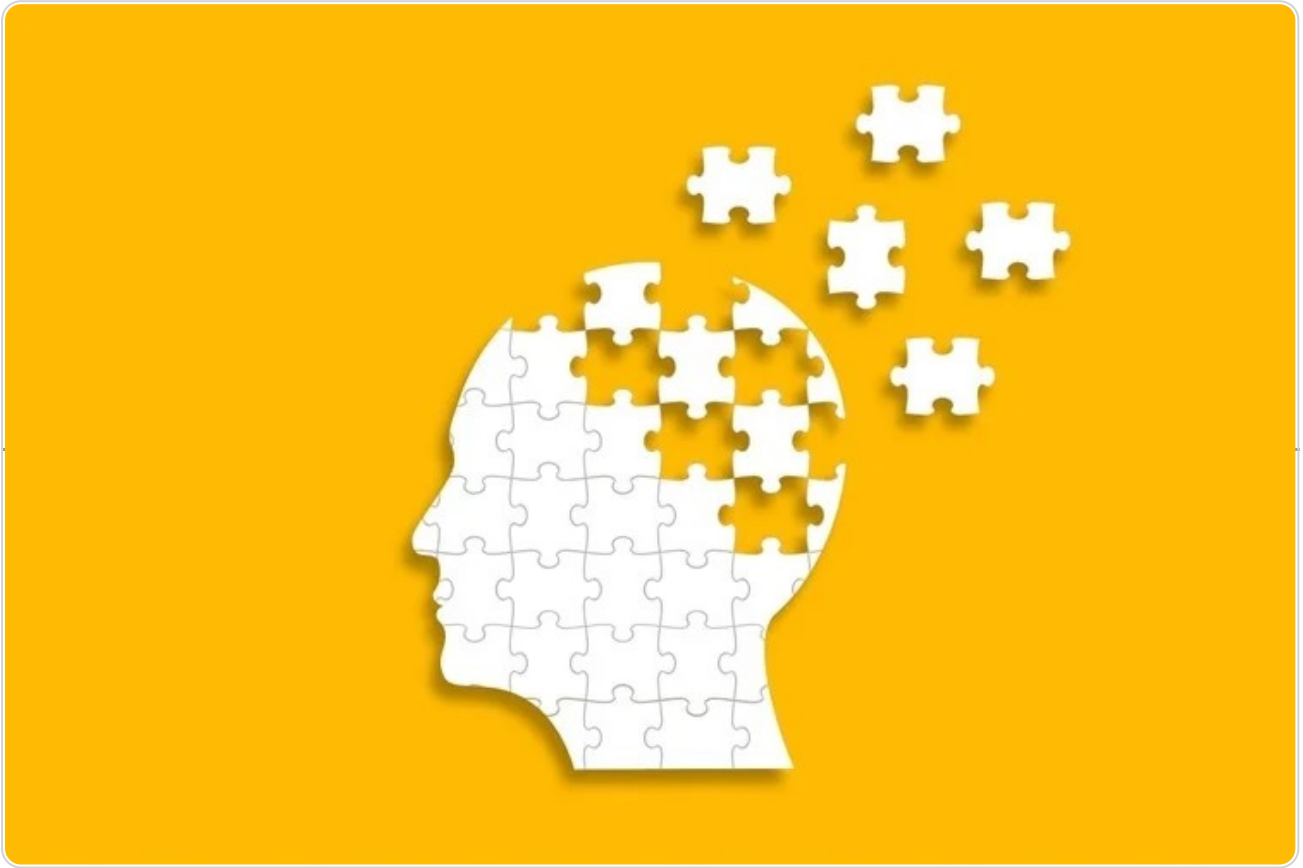
Biological's products are independently developed and produced, including recombinant proteins, antibodies and cDNA clones. Sino Biological is the researchers' one-stop technical services shop for the advanced technology platforms they need to make advancements. In addition, Sino Biological offer pharmaceutical companies and biotechnology firms pre-clinical production technology services for hundreds of monoclonal antibody drug candidates.

Sino Biological's core business

Sino Biological is committed to providing high-quality recombinant protein and antibody reagents and to being a one-stop technical services shop for life science researchers around the world. All of our products are independently developed and produced. In addition, we offer pharmaceutical companies and biotechnology firms pre-clinical production technology services for hundreds of monoclonal antibody drug candidates. Our product quality control indicators meet rigorous requirements for clinical use samples. It takes only a few weeks for us to produce 1 to 30 grams of purified monoclonal antibody from gene sequencing.

Shingles and RSV vaccines with AS01 adjuvant reduce dementia risk

New research reveals that vaccines enhanced with the AS01 adjuvant may help shield the aging brain from dementia, potentially redefining vaccine benefits beyond infectious disease protection.



Study: Lower risk of dementia with AS01-adjuvanted vaccination against shingles and respiratory syncytial virus infections. Image Credit: ahmetmapush / Shutterstock

In a recent study in ***npj Vaccines***, researchers demonstrated the short-term (18-month) protective effects of the AS01 adjuvant against the risk of subsequent dementia. This retrospective research leveraged electronic health record data (EHR) from the TriNetX US Collaborative Network, comprising more than 436,000 US adults, approximately half of whom were administered an AS01-adjuvanted vaccine, while the rest received a comparable non-AS01-adjuvanted flu vaccine.

Study findings revealed that participants administered AS01-adjuvanted vaccines (Shingrix or Arexvy) were at a significantly lower risk of dementia over the following 18 months than participants who received the flu vaccine. This result remained robust, irrespective of vaccine type or participant sex, suggesting that the protective effects may be attributed mainly to the adjuvant (AS01) and its potential neuroprotective immune responses. These findings open a

new frontier in preventive neurology, potentially positioning AS01-adjuvanted vaccines as promising candidates for delaying or preventing dementia.

Background

Dementia is an umbrella term for several age-associated progressive cognitive declines that can severely hamper daily activities. Dementia represents a global public health concern, estimated to impact more than 57 million people (2021), most of whom are women. In today's aging world, dementia prevalence continues to rise, with projections suggesting that 139 million adults will have dementia by 2050.

> ***Flu Vaccine as Comparator: Researchers specifically chose the flu vaccine for comparison because, like RSV, it affects the respiratory system, offering a relevant baseline while lacking the AS01 adjuvant.***

Unfortunately, dementia remains without a cure, with current research efforts focused on identifying its risk factors and developing effective preventive interventions. In light of this, the current research group made an intriguing discovery in their previous work: Shingrix, a shingles vaccine, was associated with a lower risk of dementia compared to live anti-varicella-zoster virus vaccines.

Researchers hypothesized that this either meant that shingles was linked to dementia, or AS01, an adjuvant added to Shingrix to improve its efficacy (no AS01 in live vaccines), was contributing to the observed reduced dementia risk. However, these findings were observational, which raises questions about whether this benefit was derived from better viral protection (against shingles or the varicella-zoster virus) or from interactions between the immune-boosting agents.

About the study

In the present study, researchers sought to isolate the effects of potential shingles-dementia associations by explicitly investigating if AS01 can alter the short-term risk of dementia diagnosis. To do this, they compared individuals who received AS01-adjuvanted vaccines with controls who received a flu vaccine devoid of AS01.

> ***Measuring the Benefit: The reduced dementia risk translated to extra time lived without a diagnosis: 87 extra days for RSV vaccinees, 53 days for shingles vaccinees, and 113 days for those getting both, among those diagnosed within 18 months.***

The study compared the relative risk of dementia

diagnosis among members of each cohort over the subsequent 18 months. Participant data was obtained from the United States (US) TriNetX Collaborative Network. The electronic health record (EHR) dataset comprised 436,788 US adults (60+ yrs; majority between 70-73) who were administered Shingrix (n = 103,798), Arexvy (another AS01-adjuvanted RSV vaccine; n = 35,938), or a non-AS01-adjuvanted vaccine against the common flu.

Notably, the controls were sociodemographically and medically matched (66 variables) to cases via propensity score matching. Outcomes of interest included positive dementia diagnoses (International Classification of Diseases [ICD-10] codes) within the 18 months following study enrolment/vaccine administration.

Statistical analyses included the Kaplan-Meier estimator for calculating incidences of outcomes, the generalised Schoenfeld approach for assumption testing, and clinically meaningful estimations using a restricted mean time lost (RMTL) model. The primary statistical comparisons were between these vaccine-defined cohorts, and analyses were also stratified by sex.

Study findings

The study demonstrated several compelling findings. First, AS01-adjuvanted vaccines showed impressive short-term (18 months) protective effects against the risk of dementia. Participants who received Arexvy showed a 29% lower risk of dementia compared to controls, while those who received Shingrix showed an 18% reduction. Those who received both vaccines saw a 37% lower risk.

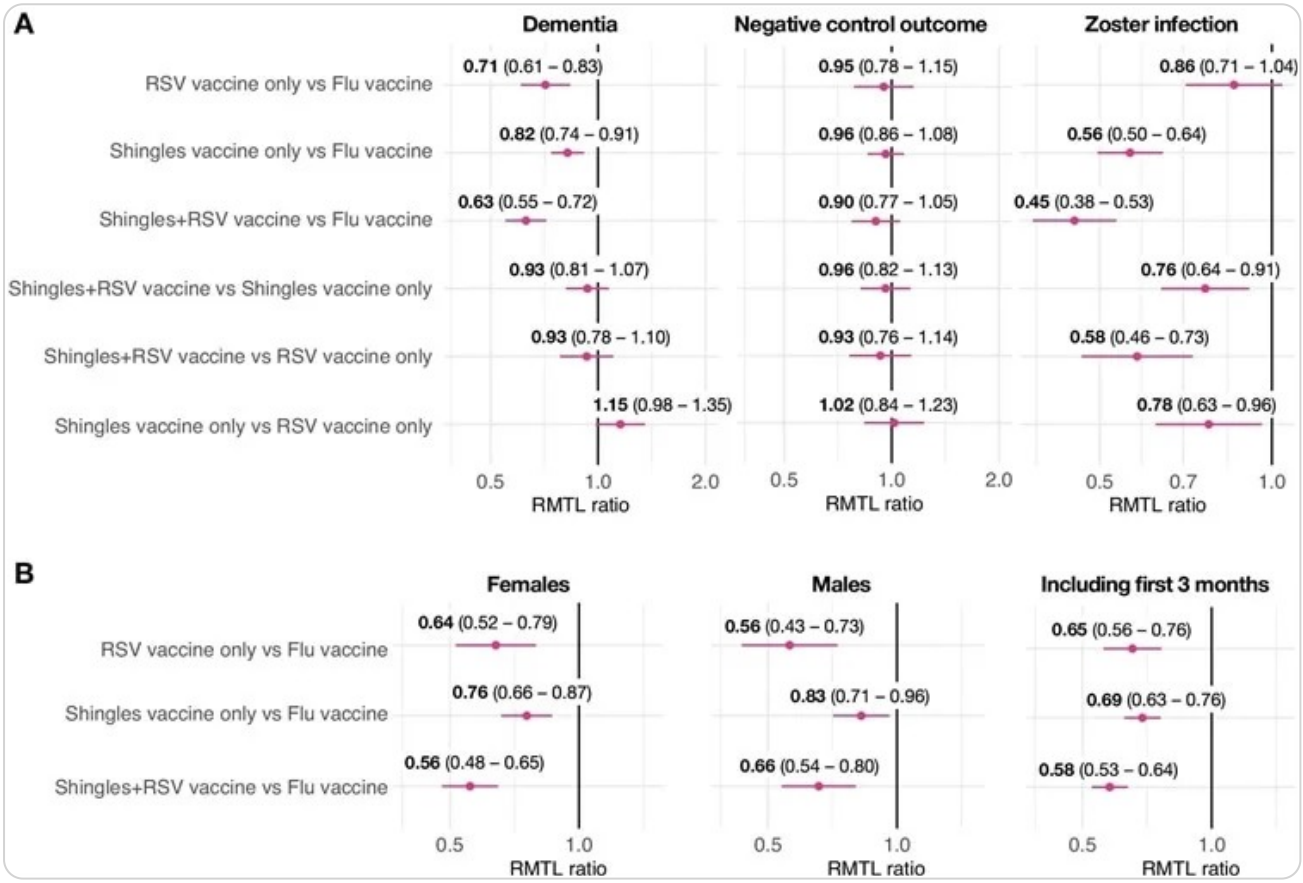
> ***Mouse Model Insight: Laboratory work cited in the paper suggests a specific ingredient in AS01 (monophosphoryl lipid A, or MPL) improved Alzheimer's disease pathology in mice, offering a potential biological pathway for the observed effect.***

Notably, the protective impacts of these vaccines were statistically indistinguishable, strengthening support that the AS01 adjuvant, the only commonality between the vaccines, is a plausible explanation for the observed protective effect. Independent laboratory studies bolster this idea, though the paper's authors note that the exact mechanisms remain speculative. They highlight that AS01 activates innate immune cells, such as microglia, thereby enhancing pathogen clearance and reducing inflammation processes implicated in Alzheimer's disease and the risk and progression of dementia.

Interestingly, the authors report a key limitation that may mean the protective effect is even

stronger than observed. The RSV vaccine group likely included some patients who received a non-AS01 vaccine, suggesting the true impact of the AS01-adjuvanted vaccine (Arexvy) may be underestimated.

In contrast, the hypothesized anti-viral benefits of these vaccines on dementia risk (and by extension, the potential associations between the diseases and dementia) remain unlikely. These results remained robust following sensitivity testing and adjustments for vaccine type and sex. However, the authors stress that, because the study is observational, it reveals that unmeasured confounding factors may influence an association rather than a proven causal link, and the findings.



A. *Association between AS01-adjuvanted vaccines and risk of dementia, negative control outcome, and zoster infection. Each dot and bold number represent the ratio of restricted mean time lost (RMTL) for the comparison between two cohorts, while horizontal lines and numbers in brackets are 95% confidence intervals. RMTL ratios below 1 indicate that the risk is lower in the first cohort (e.g., recipients of the RSV vaccine on the first line) than in the second (e.g., recipients of the flu vaccine).* ***B.*** *Associations between AS01-adjuvanted vaccines (compared to flu vaccine) and risk of dementia in females, males, and in the cohorts including people who developed dementia within the first 3 months post-vaccination.*

Conclusions

This real-world study contributes to the growing body of evidence that AS01-adjuvanted vaccines may protect brain health beyond their intended viral targets. With both RSV and shingles vaccines showing significant dementia risk reduction (29% for RSV and 18% for shingles), their shared efficacy, rather than specific disease prevention, appears key to their holistic dementia-preventive effects.

The findings strongly support the need for future randomized clinical trials to confirm these effects and test AS01 boosters for the prevention of dementia. If confirmed, we may be able to harness vaccine platforms not just for infectious disease control, but as tools to delay or prevent cognitive decline, thereby representing a significant paradigm shift in preventive geriatrics.

Journal reference:

- Taquet, M., Todd, J.A. & Harrison, P.J. Lower risk of dementia with AS01-adjuvanted vaccination against shingles and respiratory syncytial virus infections. npj Vaccines 10, 130 (2025), DOI — 10.1038/s41541-025-01172-3, https://www.nature.com/articles/s41541-025-01172-3

New index helps optimize picosecond laser treatment for nevus of Ota

In recent years, the application of picosecond laser (PSL) treatment for skin discoloration caused by nevus of Ota has been advancing in the fields of dermatology, plastic surgery, and cosmetic surgery. However, setting appropriate irradiation conditions is necessary to achieve effectiveness. This poses a challenge as previous meta-analyses on laser treatment research did not account for proper laser irradiation levels. Further, such analyses included results from cases with over- and under-irradiation, prompting the need for a more accurate evaluation.

A research team led by Postdoctoral Fellow Yu Shimojo, Specially Appointed Professor Toshiyuki Ozawa, and Professor Daisuke Tsuruta from the Graduate School of Medicine developed the EICF (Excessive Setting Index of Clinical Fluence) indicator using an in-silico mathematical model to determine the appropriate laser irradiation conditions. Based on this index, the irradiation parameters used in clinical practice were evaluated. The team then conducted a meta-analysis on treatment studies that were consistent with theoretical irradiation conditions.

In the case of nevus of Ota, a comparison of PSL and nanosecond laser (NSL) treatments revealed that PSL treatment demonstrated higher efficacy and equivalent safety under proper conditions.

> *This achievement provides scientific evidence that answers questions such as 'Why was it effective?' and 'Why did side effects occur?' in PSL treatment. Although further verification is needed, we hope EICF can be used to ensure safer and more effective laser irradiation conditions."*
>
> *Dr. Yu Shimojo, Postdoctoral Fellow*

The findings were published in *JAAD Reviews*.

Source:

Osaka Metropolitan University

Journal reference:

Shimojo, Y., *et al.* (2025) Association between irradiation parameters and outcomes for

picosecond laser treatment of nevus of Ota: An in-silico-supported meta-analysis. *JAAD Reviews*. doi.org/10.1016/j.jdrv.2025.06.001.

Antibody-drug conjugates beyond oncology

Antibody-drug conjugates (ADCs) have revolutionized the oncology field, offering targeted cancer treatments that improve efficacy without adversely affecting healthy cells.[1]

ADCs' potential extends far beyond cancer care, however, with advances in ADC technology paving the way for breakthroughs across a range of therapeutic areas from metabolic disorders to autoimmune diseases.[2] This article looks at how ADCs are improving patient outcomes and redefining treatment paradigms across diverse fields of medicine.

ADCs are a pioneering class of therapeutics that combine cytotoxic drugs and monoclonal antibodies, connected via chemical linkers.

The monoclonal antibody specifically binds to antigens on diseased cells, facilitating precise drug delivery. The linker is cleaved once the monoclonal antibody has been internalized by the target cell, releasing the cytotoxic drug to apply its therapeutic effect.[1,3]

ADCs were originally developed as a means of treating cancer, but they have since demonstrated a unique ability to target diseases at a molecular level, offering reduced toxicity and improved precision versus traditional therapies.[2]

Advances in linker technology, payload engineering, and antigen discovery have seen ADCs fueling innovation across a range of therapeutic areas, including inflammatory conditions, infectious diseases, autoimmune diseases, neurological disorders, and metabolic diseases.[2,3,4]

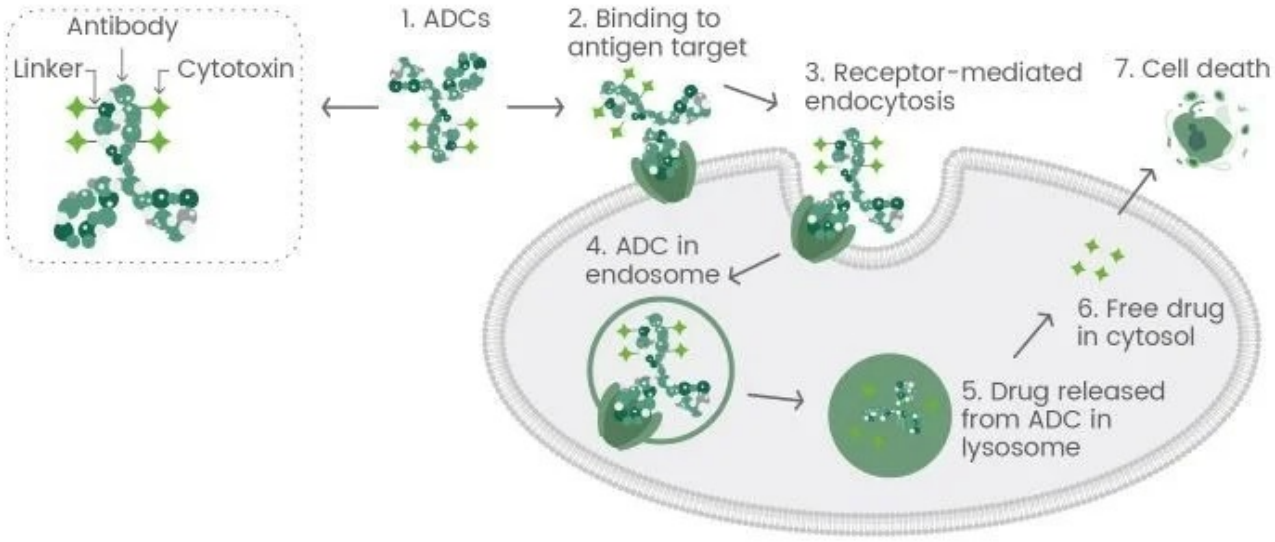


Figure 1. *The general mechanism of action for antibody-drug conjugates (ADCs). Image Credit: Sino Biological Inc.*

Autoimmune diseases: Precision in immune modulation

Autoimmune diseases have become a major focus for non-cancer-related ADC development. Conditions such as lupus, psoriasis, rheumatoid arthritis, ulcerative colitis, and scleroderma are typically driven by dysregulated immune responses that prompt the body to attack its own tissues.

While conventional immunosuppressive therapies are effective, these often come coupled with serious side effects due to their lack of specificity.

ADCs offer a highly targeted strategy for the treatment of autoimmune diseases such as rheumatoid arthritis (RA), however.

For instance, ABBV-3373 from AbbVie combines adalimumab (an anti-TNF monoclonal antibody) with a glucocorticoid receptor modulator (GRM), specifically delivering the GRM payload to immune cells expressing TNFα, modulating inflammatory pathways while minimizing systemic side effects.[5]

ADCs targeting CD6 are another promising development. These ADCs selectively eliminate pathogenic T cells implicated in autoimmune disorders such as lupus and graft-versus-host disease.[6]

CD45-targeted ADCs also aim to reset the immune system through the eradication of autoreactive immune cells, facilitating autologous hematopoietic stem cell transplants in conditions such as multiple sclerosis.[7]

ADCs also have the potential to treat inflammatory bowel diseases, targeting gut-specific inflammatory markers in order to ensure that anti-inflammatory agents are precisely delivered to the intestines.[8]

Combating infectious diseases

ADCs represent a promising solution to the mounting threat of antimicrobial resistance.

RG7861 is one notable example. This ADC uses a monoclonal antibody that binds to wall teichoic acid—a key bacterial structure—conjugated with a rifamycin analog. This design allows RG7861 to penetrate bacterial defenses and deliver its therapeutic payload effectively. Clinical trials have shown promising results, highlighting its potential as a next-generation antibiotic.[9,10]

Research is also ongoing to develop ADCs for treating HIV-1, aiming to block viral entry and replication via the linking of monoclonal antibodies able to target viral proteins such as gp41

and gp120 to small-molecule antivirals.[11]

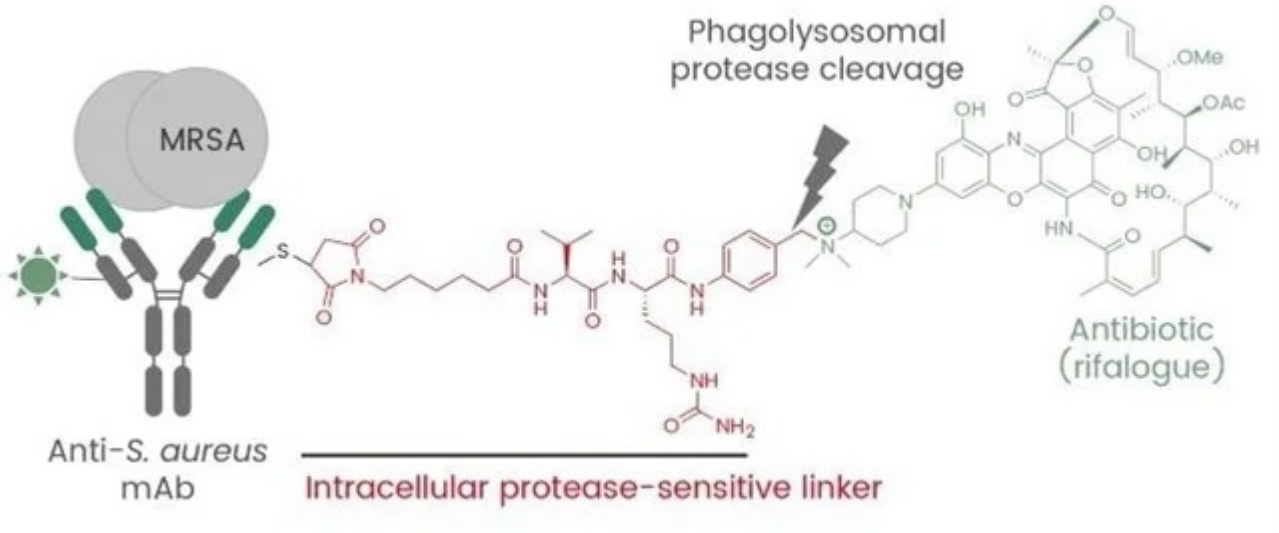


Figure 2. *Antibody-antibiotic conjugate for treatment of S. aureus infections. Image Credit: DOI: 10.1038/nature16057*

Fighting neurological disorders

Amyloid-beta plaques or tau protein aggregates are also known to contribute to cognitive decline in Alzheimer's disease, meaning that ADCs designed to target these proteins could inhibit disease progression.[12]

ADCs also aim to modulate pathogenic immune cells or inflammatory pathways within the central nervous system, helping to treat multiple sclerosis and other autoimmune neurological conditions.

New research is also exploring ADC applications for conditions such as Huntington's and Parkinson's disease, potentially improving patient outcomes via targeted drug delivery. While these approaches are still experimental, the potential to address drug delivery challenges in the brain represents a major advancement in the treatment of a range of neurological disorders.[2,13]

Addressing metabolic disorders

ADC technology is seeing increased use in the targeting of metabolic disorders, such as atherosclerosis, diabetes, and obesity.[2,14,15]

Unlike traditional ADCs, metabolic applications typically involve non-cytotoxic payloads that have been specifically designed to precisely modulate biochemical pathways.

For instance, ADCs targeting lipid metabolism are currently being developed to address

atherosclerosis. An LXR agonist–ADC is also being designed to deliver its payload to specific lipid pathways, helping to reduce plaque formation and modulate cholesterol levels.[15,16]

Table 1. Selected ADCs that have been tested for indications other than oncology. Source: Sino Biological Inc.

Indications	ADCs	Antibody	Linkers	Payloads
Inflammation	Dexa-AbhEsel	Murine anti-E-selectin mAb (H18/7)	Succinate	Dexamethasone
Autoimmune models	Anti-CD74-flu449	Human anti-CD74 mAb	Pyrophosphate acetal	Fluticasone propionate
Atherosclerosis	Anti-CD1la LXR agonist	Humanized anti-CD11 mAb	PEG4-Phe-Lys	Amino acid para-acetylphenylalanine
Muscular diseases	Anti-CD71 siRNA	Murine anti-CD71	mAb Maleimide	siRNA
Systemic sclerosis	ADCETRIS	Chimeric anti-CD30 mAb	Val-Cit	MMAE
Non-alcoholic fatty liver disease	Anti-CD163-IgG-Dex	Anti-CD163 mAb	Hemisuccinate	Dexamethasone
Lung infection	VSX-D297 antimicrobial antibody conjugate	VSX	Enzymatically coupling with Sortase A	Antimicrobial peptides

Conclusion and future outlook

ADCs have progressed from being principally oncology-focused to being versatile tools with the potential to revolutionize a range of therapeutic areas. ADCs' capacity to combine precision targeting with potent therapies provides a viable pathway to the treatment of a range of complex diseases, from autoimmune disorders to metabolic and neurological conditions, as well as addressing the increasingly prevalent issue of antimicrobial resistance.

Future developments in antibody design, linker technology, and payload engineering are expected to further expand the applications of ADCs, while the integration of ADCs with emerging fields like nanotechnology, gene therapy, and personalized medicine has the potential to unlock new possibilities.

Clinical research continues to validate their safety and efficacy, meaning that ADCs are set to become central to modern therapeutics, improving patient outcomes and addressing unmet medical needs.[1–4,17–21]

Sino Biological's support for ADC development

Sino Biological is supporting pioneering ADC research with its diverse portfolio of products and services. The company's end-to-end solutions and seamless client support drive every stage of the ADC development process, from early discovery through clinical development.

Sino Biological's strong focus on recombinant protein production sees the company offer a diverse range of high-quality ADC target proteins available in multiple formats and species.

Its catalog includes well-known targets such as Nectin-4, EGFR, HER-2, TROP-2, CD19, and BCMA, along with emerging targets like GFRA1, EphA3, and CLEC7A.

The company also provides comprehensive solutions for research into the treatment of autoimmune diseases, including target proteins for nearly 50 diseases. These reagents are designed to support the application of innovative ADCs in the treatment of autoimmune diseases.

References and further reading

1. Tsuchikama, K., *et al.* (2024). Exploring the next generation of antibody–drug conjugates. *Nature Reviews Clinical Oncology*, (online) pp.1–21. https://doi.org/10.1038/s41571-023-00850-2.
2. Lal Bahadur Pal, Bule, P., Khan, W. and Naveen Chella (2023). An Overview of the Development and Preclinical Evaluation of Antibody–Drug Conjugates for Non-Oncological Applications. *Pharmaceutics*, 15(7), pp.1807–1807. https://doi.org/10.3390/pharmaceutics15071807.
3. Conilh, L., *et al.* (2023). Payload diversification: a key step in the development of antibody–drug conjugates. *Journal of Hematology & Oncology*, 16(1). https://doi.org/10.1186/s13045-022-01397-y.
4. Dumontet, C., *et al.* (2023). Antibody–drug conjugates come of age in oncology. *Nature Reviews Drug Discovery*, (online) 22(8), pp.641–661. https://doi.org/10.1038/s41573-023-00709-2.
5. McPherson, M.J., *et al.* (2024). An anti-TNF-glucocorticoid receptor modulator antibody-drug conjugate is efficacious against immune-mediated inflammatory diseases. *Science translational medicine*, (online) 16(739), p.eadd8936. https://doi.org/10.1126/scitranslmed.add8936.
6. Zhang, L., *et al.* (2023). A CD6-targeted antibody-drug conjugate as a potential therapy for T cell-mediated disorders. *JCI insight*, (online) 8(23), p.e172914. https://doi.org/10.1172/jci.insight.172914.
7. Brandish, P.E., *et al.* (2018). Development of Anti-CD74 Antibody–Drug Conjugates to

Target Glucocorticoids to Immune Cells. *Bioconjugate Chemistry*, 29(7), pp.2357–2369. https://doi.org/10.1021/acs.bioconjchem.8b00312.

8. Rimola, J., *et al*. (2024). ADC Values for Detecting Bowel Inflammation and Biologic Therapy Response in Patients With Crohn Disease: A Post Hoc Prospective Trial Analysis. *AJR. American journal of roentgenology*, (online) 222(1), p.e2329639. https://doi.org/10.2214/AJR.23.29639.
9. Lehar, S.M., *et al*. (2015). Novel antibody–antibiotic conjugate eliminates intracellular S. aureus. *Nature*, (online) 527(7578), pp.323–328. https://doi.org/10.1038/nature16057.
10. ADC Review. (2017). *DSTA4637S (Anti-S. aureus TAC; RG7861)» ADC Review*. (online) Available at: https://www.adcreview.com/drugmap/dsta4637s/.
11. Umotoy, J.C. and de Taeye, S.W. (2021). Antibody Conjugates for Targeted Therapy Against HIV-1 as an Emerging Tool for HIV-1 Cure. *Frontiers in Immunology*, 12. https://doi.org/10.3389/fimmu.2021.708806.
12. Punyakoti, P., *et al*. (2023). Postulating the possible cellular signalling mechanisms of antibody drug conjugates in Alzheimer's disease. *Cellular Signalling*, (online) 102, p.110539. https://doi.org/10.1016/j.cellsig.2022.110539.
13. Drug Target Review. (2024). *Exploring the potential of ADCs beyond oncology*. (online) Available at: https://www.drugtargetreview.com/article/151932/exploring-the-potential-of-adcs-beyond-oncology/.
14. Xue, D., *et al*. (2019). An anti-CD103 antibody-drug conjugate prolongs the survival of pancreatic islet allografts in mice. *Cell death & disease*, (online) 10(10), p.735. https://doi.org/10.1038/s41419-019-1980-8.
15. Liu, Y.-B., *et al*. (2024). A sterol analog inhibits hedgehog pathway by blocking cholesterylation of smoothened. *Cell chemical biology*, (online) 31(7), pp.1264-1276.e7. https://doi.org/10.1016/j.chembiol.2024.02.002.
16. AYYAPPAN, J.P., PAUL, A. and GOO, Y.-H. (2016). Lipid droplet-associated proteins in atherosclerosis (Review). *Molecular Medicine Reports*, (online) 13(6), pp.4527–4534. https://doi.org/10.3892/mmr.2016.5099.
17. Valsasina, B., *et al*. (2024). Present Scenario and Future Landscape of Payloads for ADCs: Focus on DNA-Interacting Agents. *Pharmaceuticals*, (online) 17(10), pp.1338–1338. https://doi.org/10.3390/ph17101338.
18. Ruiz, R. and Kirk, A.D. (2015). Long-Term Toxicity of Immunosuppressive Therapy. *Transplantation of the Liver*, pp.1354–1363. https://doi.org/10.1016/b978-1-4557-0268-8.00097-x.
19. Gu, Y., Wang, Z. and Wang, Y. (2024). Bispecific antibody drug conjugates: Making 1+1>2. *Acta Pharmaceutica Sinica B*. (online) https://doi.org/10.1016/j.apsb.2024.01.009.
20. Beck, A., *et al*. (2017). Strategies and challenges for the next generation of antibody–drug conjugates. *Nature Reviews Drug Discovery*, 16(5), pp.315–337. https://doi.org/10.1038/nrd.2016.268.

21. Carter, P.J. and Lazar, G.A. (2017). Next generation antibody drugs: pursuit of the 'high-hanging fruit'. *Nature Reviews Drug Discovery*, 17(3), pp.197–223. https://doi.org/10.1038/nrd.2017.227.

Acknowledgments

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About Sino Biological Inc.

Sino Biological is an international reagent supplier and service provider. The company specializes in recombinant protein production and antibody development. All of Sino Biological's products are independently developed and produced, including recombinant proteins, antibodies and cDNA clones. Sino Biological is the researchers' one-stop technical services shop for the advanced technology platforms they need to make advancements. In addition, Sino Biological offer pharmaceutical companies and biotechnology firms pre-clinical production technology services for hundreds of monoclonal antibody drug candidates.

Sino Biological's core business

Sino Biological is committed to providing high-quality recombinant protein and antibody reagents and to being a one-stop technical services shop for life science researchers around the world. All of our products are independently developed and produced. In addition, we offer pharmaceutical companies and biotechnology firms pre-clinical production technology services for hundreds of monoclonal antibody drug candidates. Our product quality control indicators meet rigorous requirements for clinical use samples. It takes only a few weeks for us to produce 1 to 30 grams of purified monoclonal antibody from gene sequencing.

Measuring tumor force offers new clues for brain cancer treatment

As brain tumors grow, they must do one of two things: push against the brain or use finger-like extensions to invade and destroy surrounding tissue.

Previous research found tumors that push - or put mechanical force on the brain - cause more neurological dysfunction than tumors that destroy tissue. But what else can these different tactics of tumor growth tell us?

Now, the same team of researchers from the University of Notre Dame, Harvard Medical School/Massachusetts General Hospital, and Boston University has developed a technique for measuring a brain tumor's mechanical force and a new model to estimate how much brain tissue a patient has lost. Published in *Clinical Cancer Research*, the study explains how these measurements may help inform patient care and be adopted into surgeons' daily workflow.

> *During brain tumor removal surgery, neurosurgeons take a slice of the tumor, put it on a slide and send it to a pathologist in real-time to confirm what type of tumor it is. Tumors that originally arise in the brain, like glioblastoma, are prescribed different treatments than tumors that metastasize to the brain from other organs like lung or breast, so these differences inform post-surgical care. By adding a two-minute step to a surgeon's procedure, we were able to distinguish between a glioblastoma tumor versus a metastatic tumor based on mechanical force alone."*
>
> *Meenal Datta, assistant professor of aerospace and mechanical engineering at Notre Dame and co-lead author of the study*

Datta and collaborators collected data from 30 patients' preoperative MRIs and their craniotomies, which include exposing the brain and using Brainlab neuronavigation technology. This technology provides surgeons with real-time, 3D visualization during brain surgeries and is considered commonly available for neurological procedures. Neurosurgeons can use this technique to measure the bulge caused by brain swelling from the tumor's mechanical forces before the tumor is resected.

Then this patient data was used to determine whether brain tissue was displaced by a tumor's mechanical force or replaced by a tumor. The researchers found that when there is more

mechanical force on the brain (displacement), the swelling will be more substantial. But when a tumor invades and destroys surrounding tissue (replacement), the swelling will be less significant.

The researchers created computational models based on a point system of measurements and biomechanical modeling that can be employed by doctors to measure a patient's brain bulge, to determine the mechanical force that was being exerted by the tumor, and to determine the amount of brain tissue lost in each patient.

Funded by the National Institutes of Health, National Science Foundation and various cancer research foundations, this study is among the first to show how mechanics can distinguish between tumor types.

"Knowing the mechanical force of a tumor can be useful to a clinician because it could inform patient strategies to alleviate symptoms. Sometimes patients receive steroids to reduce brain swelling, or antipsychotic agents to counter neurological effects of tumors," said Datta, an affiliate of Notre Dame's Harper Cancer Research Institute. Datta recently showed that even affordable and widely used blood pressure medications can counter these effects. "We're hoping this measurement becomes even more relevant and that it can help predict outcomes of chemotherapy and immunotherapy."

To get a better idea of what else mechanical force could indicate, the research team used animal modeling of three different brain tumors: breast cancer metastasis to the brain, glioblastoma and childhood ependymoma.

In the breast cancer metastasis tumor, researchers used a form of chemotherapy that is known to work in reducing metastasis brain tumor size. While waiting for the tumor to respond to the chemotherapy, the team found that a reduction in mechanical force changed before the tumor size was shown to change in imaging.

"In this model, we showed that mechanical force is a more sensitive readout of chemotherapy response than tumor size," Datta said. "Mechanics are sort of disease-agnostic in that they can matter regardless of what tumor you are looking at."

Datta hopes that doctors employ the patient models from the study to continue to grow the field's understanding of how mechanical force can improve patient care management.

In addition to Datta, co-lead authors include Hadi T. Nia at Boston University, Ashwin S. Kumar at Massachusetts General Hospital and Harvard Medical School, and Saeed Siri at Notre Dame.

Other collaborators include Gino B. Ferraro, Sampurna Chatterjee, Jeffrey M. McHugh, Patrick R. Ng, Timothy R. West, Otto Rapalino, Bryan D. Choi, Brian V. Nahed, Lance L. Munn and Rakesh K. Jain, all at Massachusetts General Hospital and Harvard Medical School.

Datta is also affiliated with Notre Dame's Eck Institute for Global Health, the Berthiaume Institute for Precision Health, NDnano, the Warren Center for Drug Discovery, the Lucy Family Institute for Data & Society and the Boler-Parseghian Center for Rare Diseases. She is also a concurrent faculty member in the Department of Chemical and Biomolecular Engineering and a faculty adviser for Notre Dame's graduate programs in bioengineering and materials science and engineering.

Source:

University of Notre Dame

Journal reference:

Nia, H. T., *et al.* (2025). Solid Stress Estimations via Intraoperative 3D Navigation in Patients with Brain Tumors. *Clinical Cancer Research*. doi.org/10.1158/1078-0432.ccr-24-4159.

PPP2R1A mutations linked to improved survival in ovarian clear cell carcinoma

Patients with ovarian clear cell carcinoma (OCCC) whose tumors have specific mutations in the PPP2R1A gene were found to have improved survival following immunotherapy compared to patients without these mutations, according to researchers from The University of Texas MD Anderson Cancer Center.

The findings, published today in *Nature*, suggest PPP2R1A mutations could be a valuable biomarker to help guide treatment for this difficult-to-treat ovarian cancer subtype and may offer a new therapeutic target to further improve outcomes in multiple cancer types.

Results of the study found that patients with PPP2R1A-mutant OCCC had a median overall survival (OS) of more than five years (66.9 months) after immunotherapy treatment, compared to just 9.2 months for patients without this mutation.

> *Developing effective immunotherapies for ovarian cancer, including rare subtypes like ovarian clear cell carcinoma, remains a significant unmet clinical need. Our study is the first to demonstrate the clinical importance of PPP2R1A mutations, and it opens the door to new strategies that could benefit many more patients."*
>
> *Amir Jazaeri, M.D., co-senior author, professor of Gynecologic Oncology and Reproductive Medicine*

In a Phase II trial, researchers investigated outcomes in a cohort of 34 patients with treatment-resistant OCCC who had been treated with a combination of immune checkpoint inhibitors – durvalumab and tremelimumab. Based on their findings in OCCC, experts also looked at two additional independent cohorts, one consisting of patients with endometrial cancer and the other including more than 9,000 patients with multiple cancer types who received immunotherapy treatment. Analyses confirmed the improved OS following immunotherapy in those with tumor PPP2R1A mutations.

In parallel, laboratory research showed that targeting PPP2R1A both in vitro and in vivo was also associated with improved response to immunotherapy, suggesting a causal link. This too indicates that therapies targeting PPP2R1A and the associated protein phosphatase 2A (PP2A) molecular pathway could be added to immunotherapy to further boost outcomes.

"Not only did we identify a new biomarker in ovarian cancer, but we also confirmed survival benefits in other cancer types," Jazaeri said. "Since PPP2R1A mutations are relatively uncommon, we believe the same benefits may be possible by targeting the PPP2A pathway — using drugs, and we currently are evaluating this in a clinical trial at MD Anderson."

The study represents an ongoing collaboration across multiple disciplines, led by co-senior authors Jazaeri; Linghua Wang, M.D., Ph.D., associate professor of Genomic Medicine and associate member of the James P. Allison Institute and focus area co-lead with the Institute for Data Science in Oncology; and Rugang Zhang, Ph.D., chair of Experimental Therapeutics.

This research was co-lead by first authors Yibo Dai and Minghao Dang, Ph.D., of the Wang laboratory; Anne Knisely, M.D., fellow in Gynecologic Oncology and Reproductive Medicine; and Mitsutake Yano, M.D., Ph.D., postdoctoral fellow in the Zhang laboratory. A full list of collaborating authors and their disclosures can be found in the paper.

This study was supported through grants from the National Institutes of Health/National Cancer Institute (T32 CA101642, R01CA202919, R01CA239128, R01CA243142, R01CA260661, R01CA276569, P50CA281701 and P50CA272218, K07CA201013), Dunwoody-Reese Philanthropic, MD Anderson's Ovarian Cancer Moon Shot, the U.S. Department of Defense (OC190181, OC210124, OC180193), the Cancer Prevention and Research Institute of Texas, Pennsylvania Department of Health CURE Funds, the Robert I. Jacobs Fund of The Philadelphia Foundation, the American Cancer Society (CA281701), and Frank McGraw Memorial Chair in Cancer Research.

Source:

University of Texas M. D. Anderson Cancer Center

Journal reference:

Dai, Y., *et al.* (2025). PPP2R1A mutations portend improved survival after cancer immunotherapy. *Nature*. doi.org/10.1038/s41586-025-09203-8.

The role of transcription factors in next-gen drug discovery

Transcription Factors (TFs) are pivotal regulators of gene expression and have been implicated in a variety of diseases, including cancer, neurological disorders, autoimmune conditions, and metabolic diseases. Once deemed "undruggable," TFs are now being therapeutically targeted through selective modulators, degraders, and innovative strategies such as PROTACs.

Recent approvals by the FDA, including belzutifan for VHL-associated renal cell carcinoma and elacestrant for breast cancer, underscore significant clinical advancements.

The development of PROTACs and direct small-molecule inhibitors, such as those targeting FOXA1, is broadening therapeutic options. Technologies like artificial intelligence, RNA interference, CRISPR, and engineered modulators are also expected to enhance precision in treatment.

These innovations are reshaping treatment paradigms, offering renewed hope for patients with previously untreatable or challenging diseases.

The master regulators

The human genome encodes approximately 1,600 TFs, representing one of the largest protein families within an intricate regulatory network that dictates the timing, location, and manner of gene expression.[1]

These molecular regulators achieve specificity through diverse DNA-binding domains that recognize particular nucleotide sequences, influencing cellular fate and responses to pathological conditions (see **Figure 1**).[1-3]

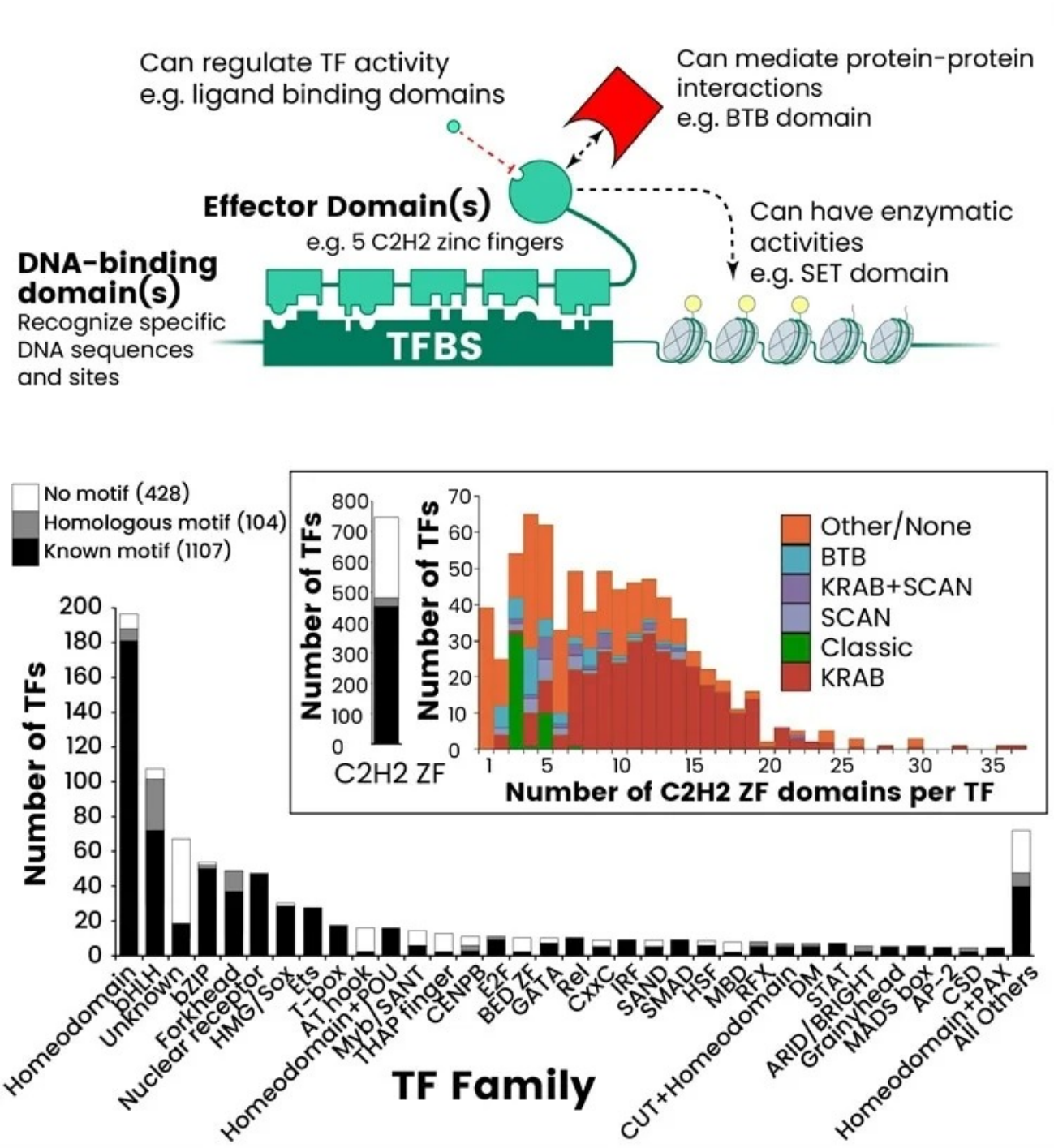

Figure 1. The Human TF Repertoire[1]. *(A) Schematic of a prototypical TF. (B) Number of TFs and motif status for each NA-binding domain (DBD) family. Inset displays the distribution of the number of C2H2-ZF domains for classes of effector domains (KRAB, SCAN, or BTB domains); "Classic" indicates the related and highly conserved SP, KLF, EGR, GLI GLIS, ZIC, and WT proteins. Image Credit: Sino Biological Inc.*

Disease mechanisms associated with TFs

Over 19% of TFs have been linked to at least one disease phenotype.[1] Cancer is the most extensively investigated category concerning transcription factor dysregulation, with multiple

TFs driving distinct oncogenic mechanisms.[2,4,5,6]

Hypoxia-inducible factors (HIFs), ETS-1, MYC, and β-catenin act as master regulators that constitutively activate oncogenic pathways, fostering tumor cell proliferation, survival, metastatic spread, and altered metabolism.

Conversely, mutations in p53 disrupt essential tumor suppression mechanisms, allowing uncontrolled cellular growth across breast, prostate, and hematologic malignancies.[2]

Hormone-dependent cancers significantly depend on FOXA1 and ESR1 for tumorigenesis in breast and prostate tissues, while STAT3 promotes cancer cell survival and facilitates immune evasion across various cancer types.[5] Furthermore, KLF5 and BRD4 regulate oncogenic transcription programs specifically in basal-like breast cancer.[5]

In autoimmune diseases, TFs disrupt immune homeostasis through various mechanisms. Tcf1 and Lef1 are crucial for maintaining CD8+ T-cell identity, and their disruption skews CD4+/CD8+ ratios, compromising immune function.[7]

STAT3 and STAT6 mediate inflammatory pathways in atopic dermatitis and hidradenitis suppurativa, while IRAK4 drives inflammation in hidradenitis suppurativa, presenting an attractive target for degrader therapies.[8] The NF-κB/STAT/AP-1 axis synergistically activates pro-inflammatory genes in synovial cells, perpetuating joint destruction in rheumatoid arthritis.[9-11]

Neurological disorders feature TFs that regulate neural development and survival pathways. POU3F2 governs genes involved in neocortical development, with dysregulation associated with schizophrenia and bipolar disorder.[12]

FOXO family members influence neuronal survival and autophagy, contributing to neurodegeneration when dysfunctional.[13] TFEB regulates lysosome biogenesis, and its impaired function exacerbates Alzheimer's pathology.[14,15]

Metabolic diseases predominantly involve TFs that regulate glucose homeostasis and adipose tissue function. HNF1α and HNF4α are key regulators of insulin production and glucose metabolism, with mutations leading to maturity-onset diabetes (MODY).[15]

HOXA5 regulates adipocyte differentiation and distribution; deficiencies in HOXA5 drive obesity-related inflammation and insulin resistance.[16] FOXM1 plays a role in diabetic complications through endothelial dysfunction.[17]

Cardiovascular diseases involve BRD4, MED1, and EP300, which stabilize DNA loops that regulate cardiac gene expression.[18] Their dysregulation contributes to congenital heart disease and atherosclerosis by disrupting cardiac transcriptional programs.[18]

TFs as therapeutic targets

Unlike enzymes with clearly defined active sites, TFs operate through relatively featureless protein-protein and protein-DNA interaction surfaces. Historically, TFs have been deemed "undruggable" due to the absence of traditional binding pockets amenable to small-molecule drugs.[19] However, advancements in research have begun to address these challenges.

In the 1970s, the development of tamoxifen—a selective estrogen receptor modulator—revolutionized breast cancer treatment by demonstrating that TFs could be targeted with competitive antagonists.[20,21]

This innovation marked one of the first rational drug design strategies aimed at directly inhibiting TFs. Similarly, extensive research has focused on the creation of compounds that inhibit the activation of hypoxia-inducible factor 1 (HIF-1) for cancer therapy.[22]

Nuclear hormone receptor modulators and indirect targeting strategies continue to be the gold standard for TF therapeutics.[23] Selective estrogen receptor modulators (SERMs) and degraders (SERDs), including fulvestrant, tamoxifen, and the recently approved elacestrant, are the most effective agents for hormone receptor-positive breast cancer. SERMs act as competitive antagonists to inhibit receptor activity, while SERDs promote receptor degradation through ubiquitin-proteasome pathways.[21]

Recently, belzutifan—the first direct small molecule inhibitor of HIF-2α—was approved in 2021 for von Hippel-Lindau (VHL) disease.[24] This advancement illustrates the potential for directly targeting TF protein-protein interaction domains.[25]

The FDA has approved seven drugs targeting TF for the treatment of cancers, cardiovascular diseases, and autoimmune diseases (shown in Table 1).

Table 1. Featured FDA-Approved TF Inhibitors. Source: Sino Biological Inc.

Drug Name	TF Target	Primary Indication(s)	FDA Approval Date
Dexamethasone	NR3C1 (Glucocorticoid R)	Cancer, asthma, immune disorders	October 30, 1958[26]
Carvedilol	HIF1A	Heart failure, hypertension	March 27, 2003[27]

Dimethyl fumarate	RELA (NF-κB subunit)	Multiple sclerosis, psoriasis	March 27, 2013[28]
Sulfasalazine	NF-κB	RA, IBD	April 13, 2005 (for juvenile rheumatoid arthritis)[29]
Eltrombopag	TFEB	Immune thrombocytopenia	June 11, 2015 (for pediatric ITP, ages ≥6)[30]
Belzutifan	Hypoxia-Inducible Factor 2α (HIF-2α)	Von Hippel-Lindau Disease, Renal Cell Carcinoma	August 13, 2021[25]
Elacestrant	Estrogen Receptor α (ERα)	ER+ Breast Cancer with ESR1 mutations	January 27, 2023[31]

Breakthroughs in TF therapeutics

Significant advancements in TF therapeutics have occurred over the past decade, propelled by innovative approaches such as proteolysis targeting chimeras (PROTACs), combination strategies, and direct TF inhibitors.

Breakthroughs in PROTACs

PROTACs are the most clinically advanced strategy for targeting TFs since their initial design by Sakamoto and Crews in 2001.[8,32,33,34] These bifunctional molecules concurrently bind target proteins and E3 ubiquitin ligases, facilitating selective protein degradation through the ubiquitin-proteasome system.[33] TF-PROTACs have demonstrated efficacy against NF-κB and E2F, paving the way for novel therapeutic options for various diseases.[34]

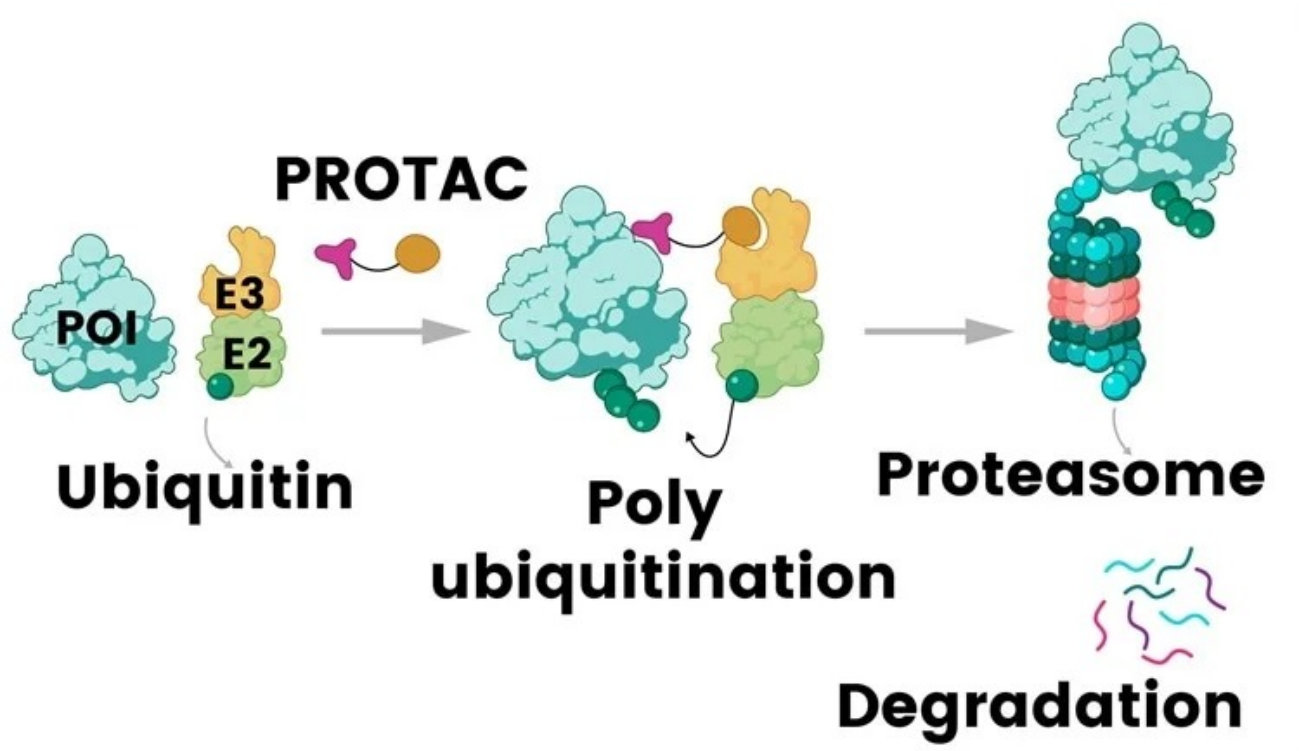

Figure 2. PROTAC (proteolysis-targeting chimera) mechanism: *a bifunctional molecule recruits E3 ligase to the protein of interest (POI), triggering its ubiquitination and subsequent degradation by the proteasome [32]. Image Credit: Sino Biological Inc.*

Table 2 outlines PROTAC compounds targeting TFs currently undergoing clinical trials.[35] Notably, ARV-471 (vepdegestrant), which degrades the estrogen receptor, and BMS-986365 (CC-94676), targeting the androgen receptor, have exhibited strong clinical efficacy, achieving protein degradation rates exceeding 90% in cancer patients.[36]

In February 2024, the FDA granted vepdegestrant Fast Track designation for the treatment of ER+/HER2- advanced or metastatic breast cancer in adults previously treated with endocrine therapy.[37]

Table 2. PROTACs Targeting TFs in Clinical Trials. Source: https://synapse.zhihuiya.com/

Drug	Company	Target	Indications	Status
Vepdegestran (ARV-471)	Arvinas/Pfizer	ER	ER + /HER2- breast cancer	Phase III
CC-94676 (BMS-986365)	BMS	AR	mCRPC	Phase III
ARV-110	Arvinas	AR	mCRPC	Phase II
ARV-766	Arvinas/Novartis	AR	mCRPC	Phase II

GT-20029	Kintor Pharma	AR	Skin and Musculoskeletal Diseases	Phase II
RT3789	Prelude Therapeutics	SMARCA2	Metastatic Solid Tumor, NSCLC	Phase II
HRS-5041	Jiangsu HengRui	ER	mCRPC	Phase I/II
HRS-1358	Jiangsu HengRui	AR	Breast cancer	Phase I/II
AC-176	AccutarBio	AR	mCRPC	Phase I
AC-699	AccutarBio	ERα	ER-positive/HER2-negative Br	Phase I
ARV-393	Arvinas	BCL6	Lymphoma	Phase I
HSK-38008	Haisco	AR-v7	mCRPC	Phase I
HP518	Hinova	AR	mCRPC	Phase I
KT-621	Kymera	STAT6	atopic dermatitis	Phase I
NX-2127	Nurix	IKZF1/3	R/R B-cell malignancies	Phase I

mCRPC = Metastatic Castration-Resistant Prostate Cancer; NSCLC = Non-Small Cell Lung Cancer

Breakthroughs in small molecules

Recent years have witnessed significant advancements in targeting challenging TFs through various mechanisms. Small molecule inhibitors targeting STAT3 have shown considerable promise in clinical trials.[38,39]

Although no STAT3 inhibitors have received FDA approval to date, the development of STAT3 PROTACs represents a promising approach to overcoming the difficulties associated with directly targeting this TF.[40]

NF-κB pathway inhibitors have also progressed through clinical development, with several small molecules targeting various components of this critical inflammatory TF pathway.[41]

These agents hold significant potential for treating inflammatory diseases, certain cancers, and autoimmune diseases driven by NF-κB. Notably, WX-02-23 represents a breakthrough as the first small molecule to directly bind the TF FOXA1, covalently targeting a cryptic cysteine residue (C258) when FOXA1 is bound to DNA, altering its binding specificity and demonstrating that TFs can be modulated through allosteric modulation.[19]

Future directions

Future therapeutics targeting TFs will focus on precision medicine and combination therapies. Artificial intelligence is accelerating drug discovery by utilizing machine learning to optimize drug design, predict binding sites, and identify patient-specific targets.[42,43,44]

Emerging technologies, such as CRISPR-based approaches, RNA interference, and engineered TF modulators, promise to transform the field.[45,46,47] Such platforms allow for highly precise targeting of specific TF functions while minimizing off-target effects.

Featured products of transcription protein

Source: Sino Biological Inc.

Cat#	Product Name	Species	Molecule	Expression System	Tag
S54-54BH	STAT3 Protein	Human	STAT3	Baculovirus-Insect Cells	N-His
S54-54G	STAT3 Protein	Human	STAT3	Baculovirus-Insect Cells	N-GST
S55-54H	STAT4 Protein	Human	STAT4	Baculovirus-Insect Cells	N-His
A09-54G	ATF1 Protein	Human	ATF1	Baculovirus-Insect Cells	N-GST
S57-30H	STAT6 Protein	Human	STAT6	Baculovirus-Insect Cells	N-His
C06-30G	Catenin beta Protein	Human	CTNNB1	Baculovirus-Insect Cells	N-GST
S52-50G	STAT1 alpha Protein	Human	STAT1	Baculovirus-Insect Cells	N-GST
E64-30G	ELK1 Protein	Human	ELK1	Baculovirus-Insect Cells	N-GST
S57-30G	STAT6 Protein	Human	STAT6	Baculovirus-Insect Cells	N-GST
T74-34G	TDP43 Protein	Human	TARDBP	Baculovirus-Insect Cells	N-GST
S11-30G	SMAD2 Protein	Human	Smad2	E. coli	N-GST
S52-54G	STAT1 beta Protein	Human	STAT1	Baculovirus-Insect Cells	N-GST
P07-31G	P300 Protein	Human	EP300	Baculovirus-Insect Cells	N-GST
S12-30G	SMAD3 Protein	Human	Smad3	E. coli	N-GST
S56-54BG	STAT5B Protein	Human	STAT5b	Baculovirus-Insect Cells	N-GST
S10-30G	SMAD1 Protein	Human	Smad1	E. coli	N-GST
N30-34G	NFE2L2 (NRF2) Protein	Human	NFE2L2	Baculovirus-Insect Cells	N-GST
N13-31G	NFKB2 Protein	Human	NFKB2	Baculovirus-Insect Cells	N-GST
N12-30G	NFATC1 Protein	Human	NFATC1	Baculovirus-Insect Cells	N-GST
S53-54G	STAT2 Protein	Human	STAT2	Baculovirus-Insect Cells	N-GST
S14-30G	SMAD5 Protein	Human	Smad5	E. coli	N-GST
C06-30H	Catenin beta Protein	Human	CTNNB1	Baculovirus-Insect Cells	N-His
N12-35G	NFKB1(p50) Protein	Human	NFkB1	Baculovirus-Insect Cells	N-GST
M86-30G	MYC Protein	Human	MYC	Baculovirus-Insect Cells	N-GST
S52-54H	STAT1 beta Protein	Human	STAT1	Baculovirus-Insect Cells	N-His
S56-54H	STAT5 Protein	Human	STAT5a	Baculovirus-Insect Cells	N-His
S12-31G	SMAD3 (del SXS) Protein	Human	Smad3	E. coli	N-GST
I20-30G	IkBA Protein	Human	NFKBIA	E. coli	N-GST
H25-30G	HSF1 Protein	Human	HSF1	E. coli	N-GST
F66-30G	FOS Protein	Human	FOS	Baculovirus-Insect Cells	N-GST

Conclusions

TF therapeutics have progressed from concept to clinical reality, with multiple compounds entering late-stage trials and receiving regulatory approval.[32] Advances in precision delivery, drug discovery, and personalized medicine now facilitate highly specific targeting of disease-driving mechanisms.[48]

As these therapies demonstrate safety and efficacy in autoimmune, oncology, and genetic diseases, they are set to redefine treatment paradigms and offer new hope to patients facing previously untreatable conditions.

References and further reading

1. Lambert, S.A., *et al.* (2018). The Human Transcription Factors. *Cell*, (online) 172(4), pp.650–665. https://doi.org/10.1016/j.cell.2018.01.029.
2. Huilgol, D., *et al.* (2019). Transcription Factors That Govern Development and Disease: An Achilles Heel in Cancer. *Genes*, (online) 10(10). https://doi.org/10.3390/genes10100794.
3. Lee, T. and Young, Richard A. (2013). Transcriptional Regulation and Its Misregulation in Disease. *Cell*, 152(6), pp.1237–1251. https://doi.org/10.1016/j.cell.2013.02.014.
4. Shiah, J.V., Johnson, D.E. and Grandis, J.R. (2023). Transcription Factors and Cancer. *The Cancer Journal*, (online) 29(1), pp.38–46. https://doi.org/10.1097/ppo.0000000000000639.
5. Vishnoi, K., *et al.* (2020). Transcription Factors in Cancer Development and Therapy. *Cancers*, (online) 12(8). https://doi.org/10.3390/cancers12082296.
6. Hasan, A., *et al.* (2024). Deregulated transcription factors in the emerging cancer hallmarks. *Seminars in Cancer Biology*, (online) 98, pp.31–50. https://doi.org/10.1016/j.semcancer.2023.12.001.
7. Shan, Q., *et al.* (2021). Tcf1 and Lef1 provide constant supervision to mature CD8+ T cell identity and function by organizing genomic architecture. *Nature Communications*, (online) 12(1). https://doi.org/10.1038/s41467-021-26159-1.
8. Békés, M., Langley, D.R. and Crews, C.M. (2022). PROTAC targeted protein degraders: the past is prologue. *Nature Reviews Drug Discovery*, (online) 21(3), pp.1–20. https://doi.org/10.1038/s41573-021-00371-6.
9. Park, M. and Hong, J. (2016). Roles of NF-κB in Cancer and Inflammatory Diseases and Their Therapeutic Approaches. *Cells*, 5(2), p.15. https://doi.org/10.3390/cells5020015.
10. Sun, S.-C., Chang, J.-H. and Jin, J. (2013). Regulation of nuclear factor-κB in autoimmunity. *Trends in Immunology*, (online) 34(6), pp.282–289. https://doi.org/10.1016/j.it.2013.01.004.
11. Aud, D. and Peng, S.L. (2006). Mechanisms of Disease: transcription factors in

inflammatory arthritis. *Nature Clinical Practice Rheumatology*, 2(8), pp.434–442. https://doi.org/10.1038/ncprheum0222.

12. Pearl, J.R., *et al.* (2019). Genome-Scale Transcriptional Regulatory Network Models of Psychiatric and Neurodegenerative Disorders. 8(2), pp.122-135.e7. https://doi.org/10.1016/j.cels.2019.01.002.
13. Santos, B.F., *et al.* (2023). FOXO family isoforms. *Cell Death & Disease*, (online) 14(10), pp.1–16. https://doi.org/10.1038/s41419-023-06177-1.
14. Rai, S.N., *et al.* (2021). Therapeutic Potential of Vital Transcription Factors in Alzheimer's and Parkinson's Disease With Particular Emphasis on Transcription Factor EB Mediated Autophagy. *Frontiers in Neuroscience*, (online) 15. https://doi.org/10.3389/fnins.2021.777347.
15. Boj, S.F., *et al.* (2001). A transcription factor regulatory circuit in differentiated pancreatic cells. 98(25), pp.14481–14486. https://doi.org/10.1073/pnas.241349398.
16. Parrillo, L., *et al.* (2023). The Transcription Factor HOXA5: Novel Insights into Metabolic Diseases and Adipose Tissue Dysfunction. *Cells*, (online) 12(16), p.2090. https://doi.org/10.3390/cells12162090.
17. Zhao, B., *et al.* (2023). Role of transcription factor FOXM1 in diabetes and its complications (Review). *International Journal of Molecular Medicine*, (online) 52(5), p.101. https://doi.org/10.3892/ijmm.2023.5304.
18. Mao, S., *et al.* (2024). Role of transcriptional cofactors in cardiovascular diseases. *Biochemical and Biophysical Research Communications*, pp.149757–149757. https://doi.org/10.1016/j.bbrc.2024.149757.
19. Lee, Y., *et al.* (2025). Advances in transcription factor delivery: Target selection, engineering strategies, and delivery platforms. *Journal of Controlled Release*, (online) 384, p.113885. https://doi.org/10.1016/j.jconrel.2025.113885.
20. Moyer, C.L. and Brown, P.H. (2023). Targeting nuclear hormone receptors for the prevention of breast cancer. *Frontiers in Medicine*, (online) 10. https://doi.org/10.3389/fmed.2023.1200947.
21. Shah, M., *et al.* (2024). US Food and Drug Administration Approval Summary: Elacestrant for Estrogen Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative, *ESR1*-Mutated Advanced or Metastatic Breast Cancer. *Journal of clinical oncology*. https://doi.org/10.1200/jco.23.02112.
22. Shirai, Y., *et al.* (2021). An Overview of the Recent Development of Anticancer Agents Targeting the HIF-1 Transcription Factor. *Cancers*, 13(11), p.2813. https://doi.org/10.3390/cancers13112813.
23. Stephen, Cidlowski, J.A., *et al.* (2023). The Concise Guide to PHARMACOLOGY 2023/24: Nuclear hormone receptors. *British Journal of Pharmacology*, 180(S2). https://doi.org/10.1111/bph.16179.
24. Toledo, R.A., *et al.* (2022). Hypoxia-Inducible Factor 2 Alpha (HIF2α) Inhibitors: Targeting

Genetically Driven Tumor Hypoxia. 44(2), pp.312–322. https://doi.org/10.1210/endrev/bnac025.

25. Wu, X., *et al*. (2025). Belzutifan for the treatment of renal cell carcinoma. *Therapeutic Advances in Medical Oncology*, (online) 17. https://doi.org/10.1177/17588359251317846.
26. Raynor, J.W., Minor, W. and Chruszcz, M. (2007). Dexamethasone at 119 K. *Acta Crystallographica Section E Structure Reports Online*, 63(6), pp.o2791–o2793. https://doi.org/10.1107/s1600536807020806.
27. FDA. (2025). *Drug Approval Package: Coreg (Carvedilol) NDA #20-297/S9*. (online) Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2003/20-297s009_Coreg.cfm.
28. FDA. (2024). *Drug Approval Package: Brand Name (Generic Name) NDA #*. (online) Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/204063Orig1s000TOC.cfm.
29. FDA. (2025). *Drug Approval Package: Azulfidine (Sulfasalazine) NDA #21-243*. (online) Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2000/21243_Azulfidine.cfm (Accessed 20 Aug. 2025).
30. Ehrlich, L.A., *et al*. (2017). U.S. Food and Drug Administration approval summary: Eltrombopag for the treatment of pediatric patients with chronic immune (idiopathic) thrombocytopenia. *Pediatric Blood & Cancer*, 64(12). https://doi.org/10.1002/pbc.26657.
31. Research, C. for D.E. and (2023). FDA approves elacestrant for ER-positive, HER2-negative, ESR1-mutated advanced or metastatic breast cancer. *FDA*. (online) Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-elacestrant-er-positive-her2-negative-esr1-mutated-advanced-or-metastatic-breast-cancer.
32. Jung, H. and Lee, Y. (2025). Targeting the Undruggable: Recent Progress in PROTAC-Induced Transcription Factor Degradation. *Cancers*, 17(11), p.1871. https://doi.org/10.3390/cancers17111871.
33. Sakamoto, K.M., *et al*. (2001). Protacs: Chimeric molecules that target proteins to the Skp1-Cullin-F box complex for ubiquitination and degradation. *Proceedings of the National Academy of Sciences*, 98(15), pp.8554–8559. https://doi.org/10.1073/pnas.141230798.
34. Liu, J., *et al*. (2021). TF-PROTACs Enable Targeted Degradation of Transcription Factors. *Journal of the American Chemical Society*, 143(23), pp.8902–8910. https://doi.org/10.1021/jacs.1c03852.
35. PROTAC Clinical Progress Search Results - Global Drug Intelligence Database. Available from: *Global landscape of PROTAC: Perspectives from patents, drug pipelines, clinical trials, and licensing transactions - ScienceDirect*
36. Wang, X., *et al*. (2024). Annual review of PROTAC degraders as anticancer agents in 2022. *European Journal of Medicinal Chemistry*, (online) 267, p.116166. https://doi.org/10.1

016/j.ejmech.2024.116166.

37. Pfizer (2024). *Arvinas and Pfizer's Vepdegestrant (ARV-471) Receives FDA Fast Track Designation for the Treatment of Patients with ER+/HER2- Metastatic Breast Cancer | Pfizer*. (online) *Pfizer*. Available at: https://www.pfizer.com/news/announcements/arvinas-and-pfizers-vepdegestrant-arv-471-receives-fda-fast-track-designation.
38. Lapidot, M., *et al*. (2020). Inhibitors of the Transcription Factor STAT3 Decrease Growth and Induce Immune Response Genes in Models of Malignant Pleural Mesothelioma (MPM). *Cancers*, (online) 13(1), p.7. https://doi.org/10.3390/cancers13010007.
39. Tsimberidou, A.M., *et al*. (2025). Phase I Trial of TTI-101, a First-in-Class Oral Inhibitor of STAT3, in Patients with Advanced Solid Tumors. *Clinical Cancer Research*, (online) 31(6), pp.965–974. https://doi.org/10.1158/1078-0432.ccr-24-2920.
40. Vontz, G., *et al*. (2023). Abstract 1659: Development of HJC0152, its analogs and protein degraders to modulate STAT3 for triple-negative breast cancer therapy. *Cancer Research*, (online) 83(7_Supplement), pp.1659–1659. https://doi.org/10.1158/1538-7445.am2023-1659.
41. Ramadass, V., Vaiyapuri, T. and Tergaonkar, V. (2020). Small Molecule NF-κB Pathway Inhibitors in Clinic. *International Journal of Molecular Sciences*, (online) 21(14). https://doi.org/10.3390/ijms21145164.
42. Yu, Z. and Zhang, Y. (2024). Foundation model for modeling and understanding transcription regulation from genome. *National Science Review*, (online) 11(11). https://doi.org/10.1093/nsr/nwae355.
43. Abid, D. and Brent, M.R. (2023). NetProphet 3: a machine learning framework for transcription factor network mapping and multi-omics integration. *Bioinformatics*, 39(2). https://doi.org/10.1093/bioinformatics/btad038.
44. Frömel, R., *et al*. (2025). Design principles of cell-state-specific enhancers in hematopoiesis. *Cell*. (online) https://doi.org/10.1016/j.cell.2025.04.017.
45. Li, T., *et al*. (2023). CRISPR/Cas9 therapeutics: Progress and Prospects. *Signal Transduction and Targeted Therapy*, (online) 8(1), pp.1–23. https://doi.org/10.1038/s41392-023-01309-7.
46. Hao, L., *et al*. (2024). Targeting and monitoring ovarian cancer invasion with an RNAi and peptide delivery system. *Proceedings of the National Academy of Sciences of the United States of America*, 121(11). https://doi.org/10.1073/pnas.2307802121.
47. Sang, Y., Xu, L. and Bao, Z. (2024). Artificial transcription factors: technology development and applications in cell reprogramming, genetic screen, and disease treatment. *Molecular Therapy*. (online) https://doi.org/10.1016/j.ymthe.2024.10.029.
48. Pandelakis, M., Delgado, E. and Ebrahimkhani, M.R. (2020). CRISPR-Based Synthetic Transcription Factors In Vivo: The Future of Therapeutic Cellular Programming. *Cell Systems*, 10(1), pp.1–14. https://doi.org/10.1016/j.cels.2019.10.003.

About Sino Biological Inc.

Sino Biological is an international reagent supplier and service provider. The company specializes in recombinant protein production and antibody development. All of Sino Biological's products are independently developed and produced, including recombinant proteins, antibodies and cDNA clones. Sino Biological is the researchers' one-stop technical services shop for the advanced technology platforms they need to make advancements. In addition, Sino Biological offer pharmaceutical companies and biotechnology firms pre-clinical production technology services for hundreds of monoclonal antibody drug candidates.

Sino Biological's core business

Sino Biological is committed to providing high-quality recombinant protein and antibody reagents and to being a one-stop technical services shop for life science researchers around the world. All of our products are independently developed and produced. In addition, we offer pharmaceutical companies and biotechnology firms pre-clinical production technology services for hundreds of monoclonal antibody drug candidates. Our product quality control indicators meet rigorous requirements for clinical use samples. It takes only a few weeks for us to produce 1 to 30 grams of purified monoclonal antibody from gene sequencing.

Drug combination shows promise for treating aggressive T-cell lymphomas

Relapsed/refractory peripheral and cutaneous T-cell lymphomas (R/R PTCL and CTCL) are aggressive blood cancers that often resist standard therapy. Patients with these lymphomas may require stem cell transplants, but the disease needs to be brought under control before patients can undergo this treatment. A new study by investigators from PETAL Consortium at Mass General Brigham found the combination of duvelisib and romidepsin to be effective, tolerable and safe for patients with R/R PTCL and CTCL. Their findings suggest that this drug combination offers a novel strategy to help these patients control the disease in order to be eligible for stem cell transplants. The results are published in *Blood Advances*.

> *This real-world study builds upon prior clinical trials by providing a more comprehensive view of using the drug combination in clinical practice, including variations in clinical setting, prescribing patterns, and adverse event management within a diverse, higher-risk population. Despite dose modifications and interruptions, high response rates were observed in patients."*
>
> *Josie Ford, BS, first author, clinical research coordinator at Massachusetts General Hospital*

Clinicians administered the treatment to 38 patients, tracking treatment effectiveness, how long the patient lived and side effects. Study outcomes showed that the drug combination helped shrink or eliminate cancer in 61% of patients, with 47% having no detectable cancer. Eleven patients went on to receive stem cell transplants. Additionally, in patients with the nodal T-follicular helper cell subtype of lymphoma, 82% of patients responded well. The drug combination had manageable side effects, but one patient died from treatment-related complications.

"These findings support duvelisib and romidepsin's efficacy, safety and tolerability, and we hope the study facilitates improved access to the treatment through insurance coverage and regulatory agency approvals," said senior author Salvia Jain, MD, a founding member of the PETAL consortium and a hematologist and medical oncologist at MGH. "Future direction would lie in determining markers of response or resistance, ideally through non-invasive monitoring so the treatment can be personalized."

Source:

Mass General Brigham

Journal reference:

Ford, J., *et al*. (2025). Real-world Evidence of Duvelisib and Romidepsin in Relapsed/Refractory Peripheral and Cutaneous T-cell Lymphomas. *Blood Advances*. doi.org/10.1182/bloodadvances.2025016347.

Plant-based fitness supplements for reversing metabolic syndrome

A new study reveals that while exercise is key, specific plant-based mineral nutrients may offer an added metabolic boost and enhance your workouts and diet.

Study: Effects of 12 Weeks of Chromium, Phyllanthus emblica Fruit Extract, and Shilajit Supplementation on Markers of Cardiometabolic Health, Fitness, and Weight Loss in Men and Women with Risk Factors to Metabolic Syndrome Initiating an Exercise and Diet Intervention: A Randomized Double-Blind, Placebo-Controlled Trial. Image credit: Supitcha McAdam/Shutterstock.com

Exercise is fundamental to a healthy life, but its effects depend on a fitness-promoting diet. Lifestyle changes that integrate these aspects are often advised to help manage metabolic syndrome and its complications. A recent experimental trial published in ***Nutrients*** examined the effect of chromium supplements and plant-based extracts that enhance its bioavailability and improve cardiometabolic markers.

Introduction

People often become more sedentary as they age, with increased fat mass and impaired glucose and lipid metabolism. This elevates the risk of metabolic syndrome, which is defined

by the presence of at least three out of several key health conditions. These include abdominal obesity, hypertension, glucose intolerance, high triglycerides, and low high-density lipoproteins (HDL, 'good' cholesterol).

While exercise and dietary changes help reduce this risk, their impact must be carefully assessed while making recommendations. The current study aimed to obtain evidence of how three nutrients popularly associated with cardiometabolic risk affect the outcomes of an integrated weight loss program in a high-risk group.

The three test nutrients include trivalent chromium (Cr), *Phyllanthus emblica* (PE), and Shilajit (SJ).

Phyllanthus emblica, also known as the Indian gooseberry or emblic, is rich in multiple phytochemicals with antioxidant, anti-inflammatory, and cardioprotective attributes. It may also improve endothelial health and function, reduce platelet aggregation, and lower blood glucose levels.

Shilajit, also known as mum, mumie, or mumlayi, is a mineral found in mountain rock crevices in Central Asia. It enhances stress adaptation and has added antioxidant and anti-inflammatory properties. In traditional Indian medicine, it is used to manage hypertension, diabetes mellitus, high blood lipids, and inflammation.

Chromium is reported to improve blood glucose control, restoring impaired insulin sensitivity. It may also improve body composition by reducing fat mass.

The current study aimed to identify whether combining these three might enhance their individual effects.

About the study

The study included 166 people with a sedentary lifestyle and two or more markers of metabolic syndrome. Their average age was 48.6 years, and their mean body mass index was 34.2 kg/m^2.

Candidates participated in a 12-week exercise program incorporating endurance and resistance exercises performed three days a week under supervision, with 10,000 steps on the intervening days. They were also asked to cut their energy intake by 5%.

The participants were divided into five groups, matched for age and sex, BMI, and body mass. One group received a placebo. The other four received *Phyllanthus emblica* (PE), trivalent chromium (Cr), and the herb shilajit (SJ) in various combinations once a day for 12 weeks:

- 500 mg PE (PE-500)

- 1000 mg/d of PE (PE-1000)
- 400 µg of Cr with 6 mg each of PE and SJ (Cr-400)
- 800 µg of Cr with 12 mg each of PE and SJ (Cr-800)

Study findings

Compared to placebo, all intervention groups showed modest improvements in cardiometabolic markers, particularly at six weeks, although not all changes reached statistical significance. The effects were generally less significant by 12 weeks.

Training adaptation

Training adaptations were observed in all groups. Lifting volume nearly doubled during resistance training over 12 weeks. Resting energy expenditure also increased, with higher fat and carbohydrate oxidation at rest. Resting heart rate and diastolic blood pressure went down in most groups.

All groups had an increased aerobic capacity and could go longer before muscle fatigue set in. These effects were most prominent with Cr-400. However, the improvements in these areas were not statistically different from those in the placebo group, indicating that the effects were primarily due to exercise.

Muscular strength and endurance increased in all groups, but the PE-1000 showed higher gains, suggesting its superior effect. Fat was lost in all groups, but lean mass increased in the Cr-800 group over the PE-1000 or Cr-400 groups at 12 weeks. The Cr-800 group showed significantly greater fat loss and lean muscle gain at six weeks compared to placebo, but this advantage was not sustained at 12 weeks. The overall effect of these changes was small.

Cardiometabolic changes

The changes in lipid levels were comparable to those in the placebo group, attributable to the effect of exercise. However, glucose metabolism and insulin sensitivity markers improved with Cr-400 and PE-1000 compared to placebo. Some of these differences reached statistical significance, while others only approached it. Notably, changes in glucose and insulin markers were generally modest.

PE appears to have an anti-inflammatory effect irrespective of Cr when used alongside a combined exercise and dietary intervention.

Platelet function improved with Cr-800 and PE-1000 supplementation compared to the placebo, and hemodynamic markers like flow-mediated dilation diameter were better. However, the increase in platelet aggregation, used in the study to infer improved platelet function, should be interpreted with caution, as it may be misunderstood without context.

No adverse effects were observed on blood cells, mood, quality of life, or side effects, indicating that these supplements were well-tolerated. A slight increase in reported dizziness was noted in the PE-1000 group, though this was not statistically significant. In all groups, exercise and a healthy diet promoted mood stability, improved energy, and the ability to do vigorous activities.

Prior research corroborates these findings, showing that PE is as effective as atorvastatin at higher doses in improving endothelial function and reducing oxidative stress and inflammation. Chromium was also reported to have some similar effects. However, past research has shown inconsistent outcomes, and bioavailability challenges for chromium remain a concern.

Conclusions

In overweight people at risk for metabolic syndrome, "*the results suggest that PE and Cr with PE and SJ supplementation may enhance some exercise- and diet-induced changes in markers of health*." The higher doses (PE-1000 and Cr-800) had greater benefits, though all dosages were associated with some beneficial effects.

However, many improvements were also seen in the placebo group, emphasizing that exercise and dietary modification were the primary drivers of change. The reported differences between supplement and placebo groups were generally small and sometimes short-lived.

Additional validation is required to reproduce these exploratory efforts in a more diverse population before they can be accepted as definitive.

Future research could extend the scope of the study to younger people, those in training, and those without risk factors for metabolic syndrome. Additionally, it is unclear whether these benefits persist without exercise training and with other types of diet modifications. The study also highlights the need to differentiate statistically significant findings from trends and to consider clinical relevance when evaluating supplement efficacy.

Journal reference:

- Martinez, V., McAngus, K., Dickerson, B. L., et al. (2025). Effects of 12 Weeks of Chromium, Phyllanthus emblica Fruit Extract, and Shilajit Supplementation on Markers of Cardiometabolic Health, Fitness, and Weight Loss in Men and Women with Risk Factors to Metabolic Syndrome Initiating an Exercise and Diet Intervention: A Randomized Double-Blind, Placebo-Controlled Trial. *Nutrients*. Doi: https://doi.org/10.3390/nu17122042. https://www.mdpi.com/2072-6643/17/12/2042