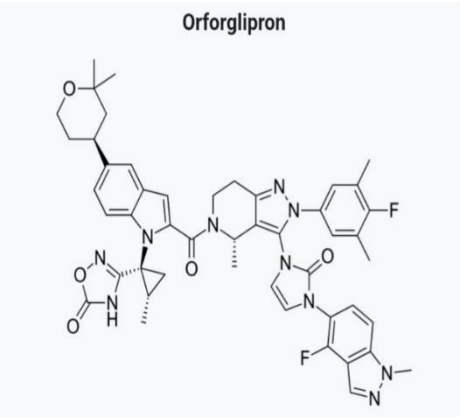
Patient Wellness First

Issue: 15 May 2025

BioSciTech biweekly NEWS

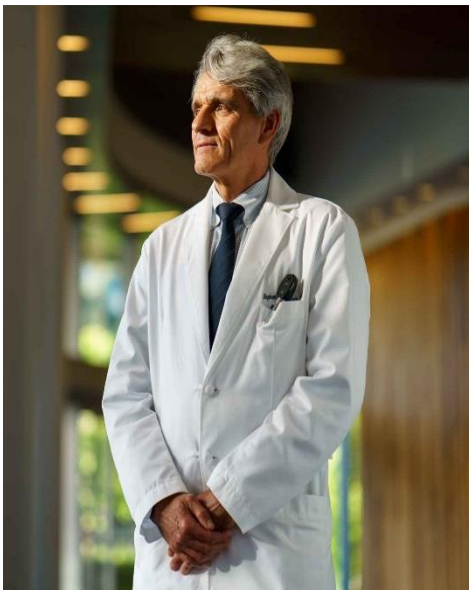
NEWS & COMMENTARIES



Lilly's oral GLP-1, orforglipron, demonstrated statistically significant efficacy results and a safety profile consistent with injectable GLP-1 medicines in successful Phase 3 trial. Orforglipron is the first small molecule GLP-1 to successfully complete a Phase 3 trial, lowering A1C by an average of 1.3% to 1.6% across doses

The investigational once-daily oral pill reduced weight by an average 16.0 lbs (7.9%) at the highest dose in a key secondary endpoint. The overall safety and tolerability profile of orforglipron in ACHIEVE-1 was consistent with injectable GLP-1 therapies

https://investor.lilly.com/node/52266/pdf

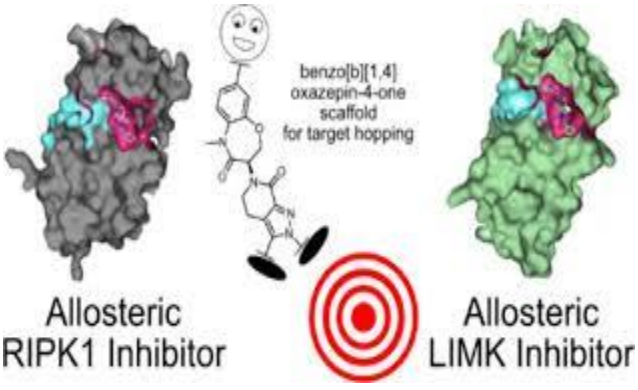


Stephen Hauser Wins Breakthrough Prize for Role in Redefining MS

UCSF luminary has played a pivotal part in identifying the cause of multiple sclerosis, leading to a new generation of game-changing therapies.Neuro-immunologist Stephen Hauser, MD, whose maverick thinking transformed the treatment landscape for patients with multiple sclerosis (MS), has received the 2025 Breakthrough Prize in Life Sciences. Hauser, a UCSF professor of neurology and director of the Weill Institute for Neurosciences, was recognized April 5 for overturning "the scientific consensus on the mechanism of MS, identifying the immune system's B cells as the primary driver of damage to nerve cells." The award also cited his instrumental role in developing therapies that have "revolutionized modern treatment of the disease."

https://www.ucsf.edu/news/2025/04/429746/stephen-hauser-wins-breakthrough-prize-role-redefining-ms

SELECTED PUBLICATIONS



Repurposing of the RIPK1-Selective Benzo[1,4]oxazepin-4-one Scaffold for the Development of a Type III LIMK1/2 InhibitorClick to copy article link

Sebastian Mandel et al., 2025

DOI:10.1021/acschembio.5c00097

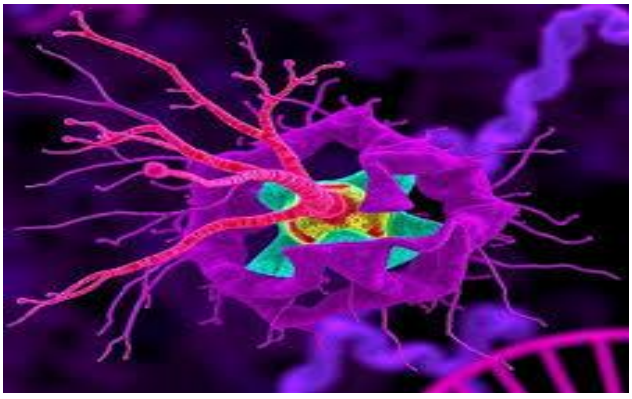
In a rare example of allosteric scaffold hopping, researchers repurposed the benzoxazepinone scaffold, known for RIPK1 inhibition, to develop a selective LIMK1/2 inhibitor. Exploiting a shared inactive kinase conformation, the new compound (10) demonstrated low nanomolar potency and high selectivity, with minimal off-target effects. This study expands the potential of allosteric inhibitor design, offering a novel strategy for targeting kinases beyond traditional orthosteric approaches.

Gastric cancer genomics study using reference human pangenomes

Du Jiao, Xiaorui Dong, 2025

DOI: 10.26508/lsa.202402977

Pangenomes are reshaping genomics, but their use in disease research remains limited. In a new study, researchers developed a graph-based gastric cancer pangenome (GGCPan) from 185 patients and compared it to linear and standard reference genomes. While small variant detection showed minimal differences, GGCPan significantly improved structural variant identification and revealed unique cancer driver genes. The findings underscore the potential of disease-specific pangenomes and the need for new tools tailored to this emerging reference framework.

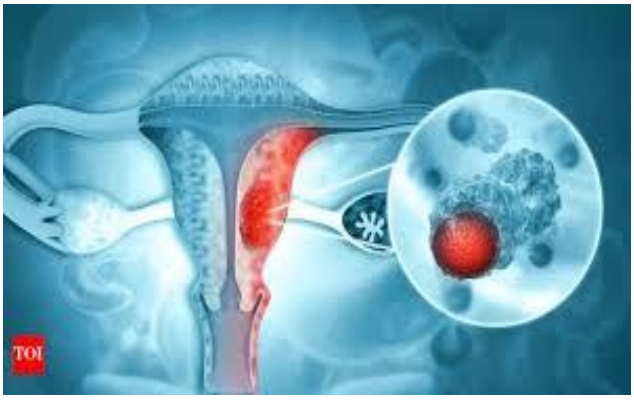


An ISWI-related chromatin remodeller regulates stage-specific gene expression in Toxoplasma gondii

Belen Pachano et al., 2025

https://doi.org/10.1038/s41564-025-01980-2

In *Toxoplasma gondii*, ATP-dependent chromatin remodellers are poorly understood. This study uncovers a specialized ISWI complex involving TgSNF2h, AP2VIII-2, and TgRFTS that regulates genome accessibility and transcription. TgSNF2h insulates active genes from neighboring silenced regions, ensuring precise stage-specific expression. It also modulates access for key regulators like MORC, influencing parasite development. These findings highlight the critical role of chromatin architecture in *T. gondii* life cycle control.



First evidence of microplastics in human ovarian follicular fluid: An emerging threat to female fertility

Luigi Montano et al., 2025

DOI:10.1016/j.ecoenv.2025.117868

In a groundbreaking study, researchers have detected microplastics (MPs) in the ovarian follicular fluid of women undergoing IVF, marking the first such discovery in humans. Using SEM-EDX, MPs under 10 µm were found in 14 of 18 samples, with an average of 2,191 particles/mL. A significant correlation was observed between MP concentration and FSH levels, suggesting potential reproductive implications. While no direct link to IVF outcomes was found, these results raise important concerns about the presence of MPs in reproductive tissues and their impact on human fertility and health.

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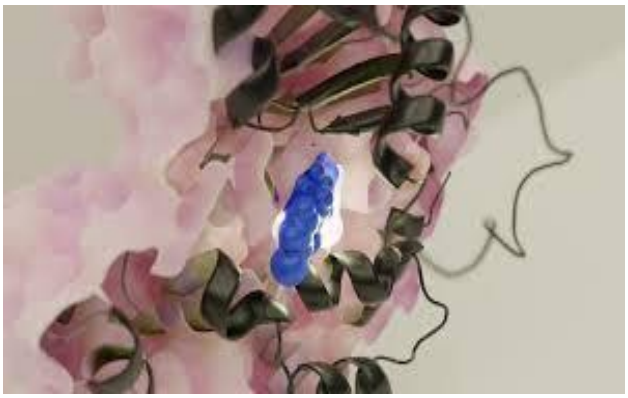
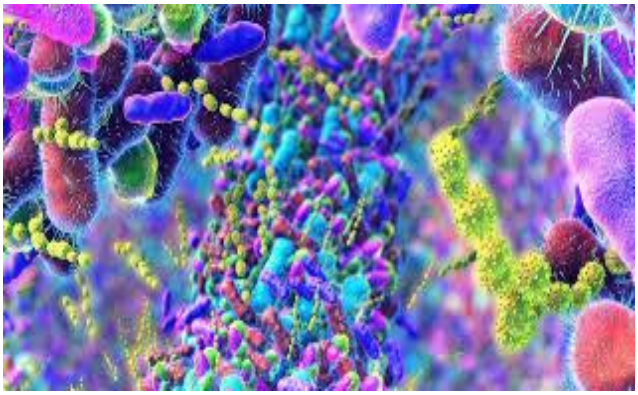


Discovery of synthetic small molecules targeting the central regulator of Salmonella pathogenicity

Abdelhakim Boudrioua et al., 2025

DOI: 10.1126/sciadv.adr5235

Researchers have identified a promising antivirulence compound, C26, that inhibits *Salmonella Typhimurium* by targeting HilD, the master regulator of its secretion systems. By suppressing effector protein secretion, C26 prevents bacterial invasion of host cells. Unlike natural ligands, C26 binds HilD with a distinct mechanism and shows activity inside macrophages. Potent analogs of C26 offer a new path for developing antivirulence therapies to combat *Salmonella*infections in humans and animals without promoting antibiotic resistance.



Microbiota-derived bile acids antagonize the host androgen receptor and drive anti-tumor immunity

Wen-Bing Jin et al., 2025

DOI: 10.1016/j.cell.2025.02.029

A new study reveals that previously uncharacterized bile acids (BAs) produced by gut microbes can act as potent antagonists of the human androgen receptor (hAR). Using integrated BA metabolomics and microbial genetics, researchers identified 56 lesser-known BAs—some capable of suppressing AR activity and slowing tumor progression. One such BA also enhanced anti-PD-1 immunotherapy in an AR-dependent manner. These findings uncover a novel microbiota–host interaction and highlight the therapeutic potential of microbiota-derived metabolites in cancer and hormone signaling.

A chemical radar allows bacteria to detect and kill predators

Shuaibing Zhang et al., 2025

DOI: 10.1016/j.cell.2025.02.033

Amoebal predation has shaped bacterial evolution, though the molecular defences remain poorly understood. This study shows that Pseudomonas syringae detects and kills Polysphondylium pallidum via a chemical radar. It secretes syringafactin, which the amoeba modifies; CraR senses this and triggers pyrofactin production. This mechanism is common in P. syringae and boosts A. thaliana infection in the presence of amoebae. The findings advance understanding of bacterial sensing and natural product discovery.

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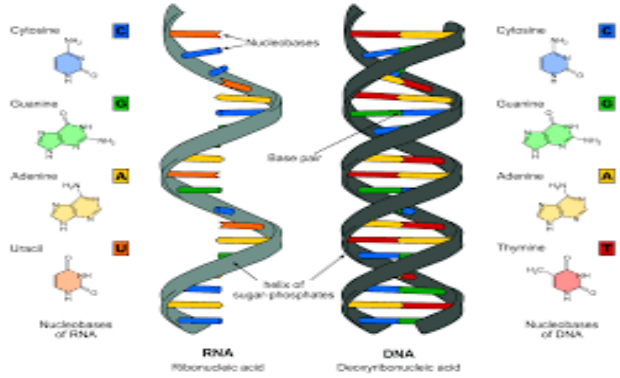
Natural products chlorotonils exert a complex antibacterial mechanism and address multiple targets

Felix Deschner et al., 2025

DOI: 10.1016/j.chembiol.2025.03.005

Amoebal predation has driven bacterial defences, though the molecular details remain unclear. This study shows that Pseudomonas syringae uses a “chemical radar” to detect and kill Polysphondylium pallidum. It secretes syringafactin, which the amoeba modifies; the altered molecule is sensed by CraR, triggering pyrofactin production. This mechanism is widespread in P. syringae and aids infection of A. thaliana in the presence of amoebae. These findings shed light on bacterial sensing and natural product discovery.

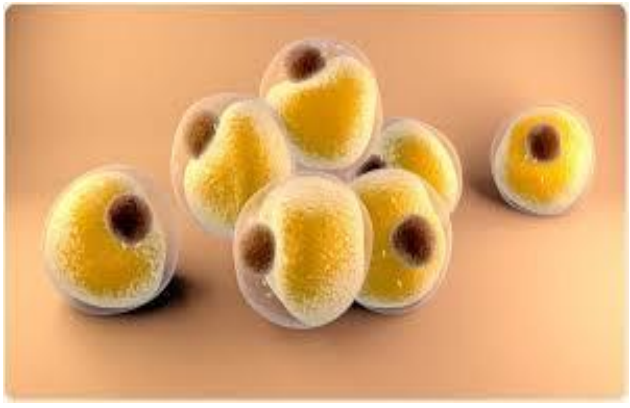


Ligand-binding pockets in RNA and where to find them

Seth D. Veenbaas et al., 2025

DOI:10.1073/pnas.2422346122

RNA regulates genes through complex structures, some of which bind small molecules to influence biology. Identifying RNA regions that bind “drug-like” ligands has been challenging. This study introduces fpocketR, a computational tool for finding such RNA pockets. Using their cell-based Frag-MaP method, the authors validated several new ligand-binding sites. The findings expand druggable RNA targets and support therapeutic exploration of RNA-ligand interactions.

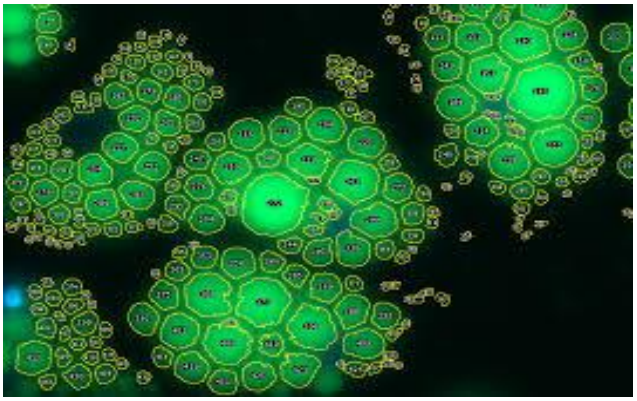


MOB1 deletion in murine mature adipocytes ameliorates obesity and diabetes

Miki Nishio et al., 2025

DOI:10.1073/pnas.2424741122

Obesity-linked disorders like type 2 diabetes are influenced by lifestyle, genes, and pathways like Hippo-YAP1. While YAP1/TAZ blocks fat cell maturation in vitro, its role in mature adipocytes was unclear. Researchers created mice lacking MOB1 in fat cells and found they resisted weight gain, burned more fat, and had better insulin sensitivity on a high-fat diet. These benefits depended on YAP1 and its target FGF21, a lipid metabolism hormone. The study reveals a YAP1–FGF21 axis as a potential target for treating metabolic disease.

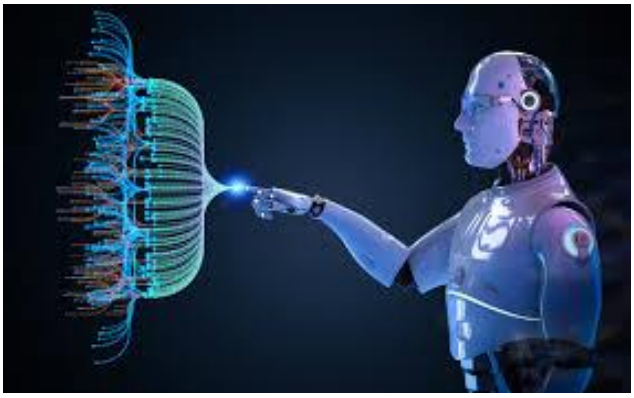


PPARα regulates ER–lipid droplet protein Calsyntenin-3β to promote ketogenesis in hepatocytes

Lauren F. Uchiyama et al., 2025

DOI:10.1073/pnas.2426338122

Ketone production relies on fatty acid release, but the role of organelle contacts is not well understood. CLSTN3β, found at ER–lipid droplet junctions, is shown here to be upregulated by PPARα during fasting or ketogenic diets. Liver-specific loss of CLSTN3β reduces ketogenesis, while its overexpression boosts ketone production. CLSTN3β promotes lipid droplet–mitochondria communication, aiding fat breakdown and mitochondrial stress responses. This underscores the importance of membrane contact sites in regulating ketogenesis.



GenAI synthetic data create ethical challenges for scientists. Here's how to address them.

David B. Resnik et a., 2025

DOI:10.1073/pnas.2409182122

Generative AI has expanded the use of synthetic data in science, helping fill gaps, correct biases, and reduce reliance on human or animal subjects. It's now used across fields, including drug discovery. However, growing use raises ethical concerns around validity, misuse, and public trust. The paper outlines strategies to address these risks. Its aim is to ensure synthetic data benefits science while minimising harm.

RECOMMENDED EVENTS

The application for the Fulbright Foreign Student Program for the Middle East and North Africa is open. Apply here for the upcoming 2026-2027 academic

Interested applicants should review the award requirements promptly, as some deadlines are in early to mid-May. Application deadlines vary by location.

https://www.amideast.org/our-work/find-a-scholarship/graduate-study/fulbright/how-to-apply/how-to-apply

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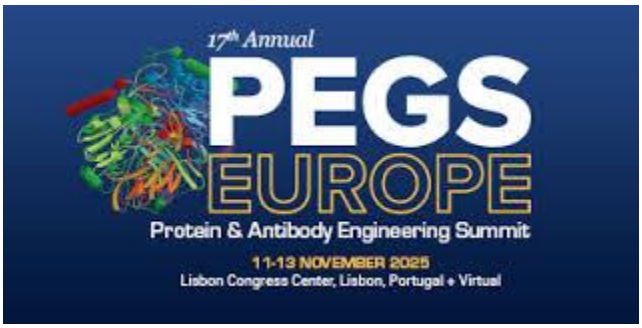

Preliminary Agenda for our 17th Annual PEGS Europe is now available. This year's event will take place in Lisbon, Portugal from 11-13 November 2025 and will feature expanded coverage of ML/AI applications in protein engineering, multispecific antibodies, ADCs, emerging targets, oncology, expression, and analytical characterisation.
https://www.pegsummiteurope.com/

Registration is now OPEN for Drug Discovery 2025 – ELRIG's flagship event!
ACC Liverpool | 🗓 21–22 October 2025
Join over 3,000 global delegates, connect with 200+ exhibitors, and explore 14 tracks of cutting-edge science — from Chemical Biology and Omics to Translating Ideas into Therapies.
https://elrig.eventsair.com/drug-discovery-2025/delegate-registration/Site/Register

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