Patient Wellness First

BioSciTech biweekly NEWS

Issue: 1 December 2024

NEWS & COMMENTARIES

Are GLP-1 drugs really for everybody?

Nature Medicine Editorial, 2024

https://www.nature.com/articles/s41591-024-03382-z

As GLP-1 receptor agonists emerge as treatment options for conditions beyond diabetes and obesity, it becomes critical to understand how genetic, clinical and sociodemographic differences impact their effects on weight loss.

Two for one: candidate obesity drug boosts energy use and curbs calorie intake

By Ardanaz & Steculorum

https://www.nature.com/articles/d41586-024-03548-2

The discovery of a pathway that controls appetite and calorie burning has led to the development of a drug that modulates both by targeting one receptor, offering a promising strategy for weight loss and improved metabolic health.

What does a scientist look like?

By Katie Langin

Children are drawing women more than ever before. Study is based on 20,860 sketches drawn by children over 5 decades
When asked to draw a scientist, school-age kids in the United States are increasingly sketching women. That's the main conclusion of a new study that compiled information about 20,860 pictures drawn by students age 5 to 18 over 5 decades.

https://www.science.org/content/article/what-does-scientist-look-children-are-drawing-women-more-ever?utm_campaign=Science+Magazine&utm_medium=ownedSocial&utm_source=linkedin

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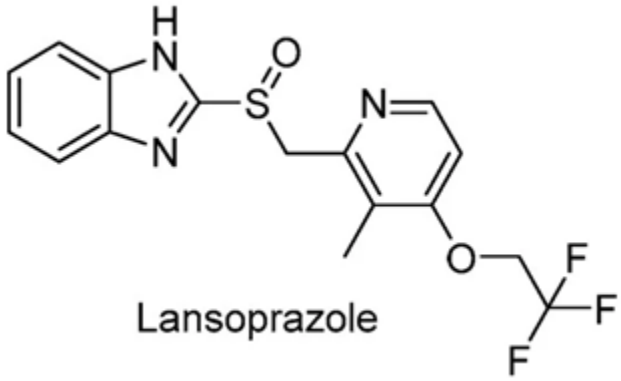
SELECTED PUBLICATIONS

A time-stratified, case–crossover study of heat exposure and perinatal mortality from 16 hospitals in sub-Saharan Africa

Hanson et al., 2024

https://doi.org/10.1038/s41591-024-03245-7

Extreme heat events may increase perinatal mortality risks in sub-Saharan Africa, particularly for intrapartum stillbirths. Analyzing 138,015 births across four countries, researchers found a 34% higher odds of perinatal death associated with a rise in mean temperature from the 75th to 99th percentile one week before birth. Stronger associations were observed during the hottest seasons, emphasizing the need for improved intrapartum care.



Lansoprazole

Inhibition mechanism of potential antituberculosis compound lansoprazole sulfide

Kovalova et al., 2024

https://doi.org/10.1073/pnas.2412780121

Tuberculosis remains a leading global cause of death, with rising multi-drug resistance highlighting the need for new treatments. Lansoprazole and its metabolite, lansoprazole sulfide (LPZS), show promise as antituberculosis agents. Using structural, biochemical, and computational approaches, researchers found that LPZS inhibits the respiratory chain supercomplex III2IV2 in Mycobacterium smegmatis by binding to the Qo cavity, blocking quinol oxidation.

Gliocidin is a nicotinamide-mimetic prodrug that targets glioblastoma

Chen et al., 2024

https://doi.org/10.1038/s41586-024-08224-z

Glioblastoma is incurable, requiring better treatments. Researchers identified gliocidin, a prodrug that selectively kills glioblastoma cells by targeting a vulnerability in purine synthesis through indirect inhibition of IMPDH2, causing replication stress and tumor cell death. Gliocidin is converted by NMNAT1 into a tumoricidal metabolite, GAD, which blocks the NAD+ pocket of IMPDH2. Gliocidin crosses the blood-brain barrier and extends survival in glioblastoma mouse models. Combined with temozolomide, it enhances tumor cell killing and further prolongs survival, showing promise as a therapeutic option for glioblastoma patients.

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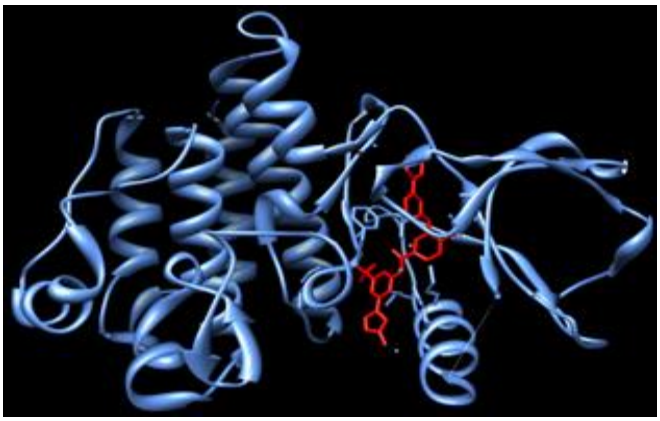
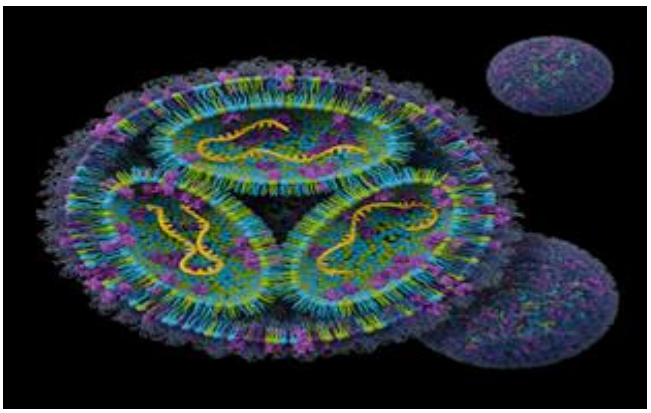


Overcoming tyrosine kinase inhibitor resistance in lung cancer brain metastasis with CTLA4 blockade

Fu et al., 2024

https://doi.org/10.1016/j.ccell.2024.09.012

Lung cancer brain metastases (LCBM) often develop resistance to tyrosine kinase inhibitors (TKIs). Single-cell RNA sequencing of LCBM samples revealed that TKI treatment increases CTLA4 expression in T cells, creating an immune-suppressive environment driven by tumor-derived HMGB1. In murine LCBM models, combining CTLA4 blockade with TKIs proved more effective than TKI monotherapy or TKIs with PD1 blockade. This study identifies CTLA4 as a key player in TKI resistance and highlights its blockade as a promising strategy to improve LCBM treatment outcomes.



Lipid Nanoparticle Delivery of TALEN mRNA Targeting LPA Causes Gene Disruption and Plasma Lipoprotein(a) Reduction in Transgenic Mice.

Garcia et al., 2024

https://doi.org/10.1016/j.ymthe.2024.11.020

Lipoprotein(a) (Lp(a)) is a genetic risk factor for cardiovascular disease, unresponsive to standard lipid-lowering treatments. This study explores a gene-editing approach using TALEN mRNAs to target the LPA gene for permanent Lp(a) reduction. TALEN mRNAs, delivered via LUNAR® lipid nanoparticles, achieved over 80% reduction in plasma Lp(a) levels in transgenic mice with human LPA, sustained for at least five weeks. Gene-inactivating deletions were confirmed through sequencing.

Small molecule modulator of neuronal lysosome positioning and function resolves Alzheimer's Disease-linked pathologies in cultured human neurons

Snead et al., 2024

https://doi.org/10.1101/2024.11.04.621986

An abnormal increase in axonal lysosomes is linked to neurodegenerative diseases like Alzheimer's. Researchers identified RH1115, a small molecule that modulates the autophagy-lysosomal pathway, restoring proper lysosome distribution in neurons. RH1115 reduced axonal lysosome buildup and secreted Aβ42 levels in human iPSC-derived neurons lacking JIP3, demonstrating its anti-amyloidogenic potential. The molecule also enhanced lysosomal degradation, required JIP4 to correct lysosome pathology, and increased TMEM55B levels.

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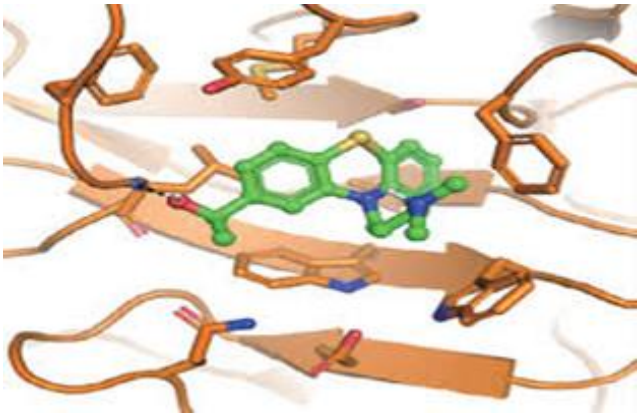
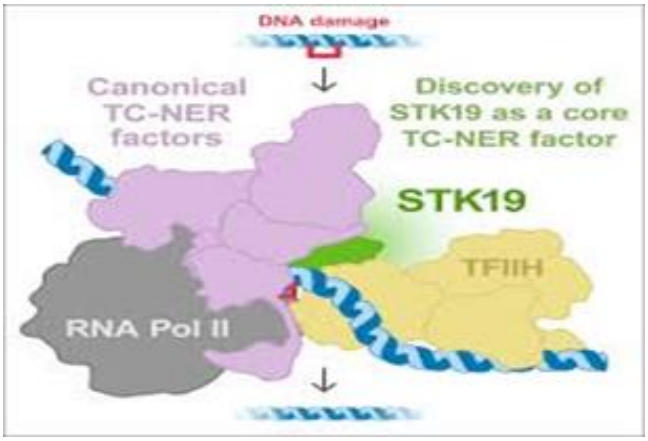


Selective degradation of multimeric proteins by TRIM21-based molecular glue and PROTAC degraders

Lu et al., 2024

https://doi.org/10.1016/j.cell.2024.10.015

A metabolite of the antipsychotic acepromazine, (S)-ACE-OH, has been identified as a molecular glue that induces TRIM21-mediated degradation of nuclear pore proteins, disrupting nucleocytoplasmic trafficking. Functionalized into proteolysis-targeting chimeras (PROTACs), it selectively degrades multimeric proteins while sparing monomeric ones, offering precision for treating diseases driven by aberrant protein assemblies, such as cancer, neurodegeneration, and autoimmunity.

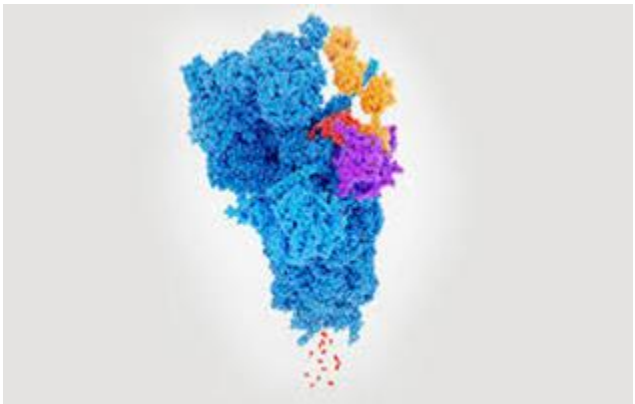


STK19 positions TFIIH for cell-free transcription-coupled DNA repair

Mevissen et al., 2024

https://doi.org/10.1016/j.cell.2024.10.020

New insights into transcription-coupled nucleotide excision repair (TC-NER) reveal that STK19 links stalled RNA polymerase II to downstream repair processes. Using in vitro systems and cryo-EM, researchers showed that STK19 interacts with the TC-NER complex, positioning TFIIH for lesion verification. Disruption of this interface impairs repair, highlighting STK19's critical role in ensuring error-free DNA repair after transcription stalling.



Development of PROTACs using computational approaches

Ge et al., 2024

https://doi.org/10.1016/j.tips.2024.10.006

The development of PROTACs, drugs that degrade proteins via the ubiquitin-proteasome system, is being revolutionized by computational biology and AI-driven drug design (CADD/AIDD). In silico tools now model PROTAC structures, predict activity, and optimize molecule design. Despite challenges like limited training data and deviations from small-molecule druggability, recent advances highlight the transformative potential of these technologies in designing next-generation PROTAC therapeutics.

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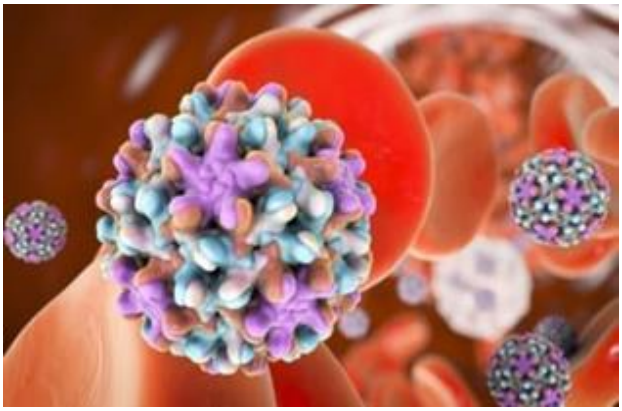
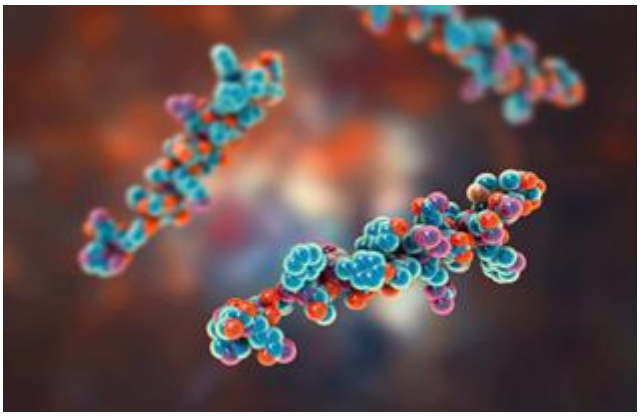


m6A mRNA methylation by METTL14 regulates early pancreatic cell differentiation

Dario F De Jesus et al., 2024

https://doi.org/10.1038/s44318-024-00213-2

New research highlights the role of N6-methyladenosine (m6A), a key mRNA modification, in pancreas development and β-cell differentiation. The study shows that METTL14, an m6A writer protein, is crucial for early pancreatic cell differentiation in both humans and mice. Temporal changes in METTL14 levels and m6A landscapes regulate genes essential for pancreas and β-cell development, offering insights into glucose homeostasis and diabetes.



Intestinal NUCB2/nesfatin-1 regulates hepatic glucose production via the MC4R-cAMP-GLP-1 pathway

Geng et al., 2024

https://doi.org/10.1038/s44318-024-00300-4

A groundbreaking study reveals that nesfatin-1, a gut hormone encoded by NUCB2, senses nutrients like glucose and lipids to regulate liver glucose production via a gut-brain-liver circuit. Nesfatin-1 interacts with melanocortin 4 receptor (MC4R), boosting cAMP and GLP-1 secretion in the gut, which inhibits hepatic glucose output. These findings uncover a novel gut-brain communication pathway essential for maintaining systemic glucose homeostasis.

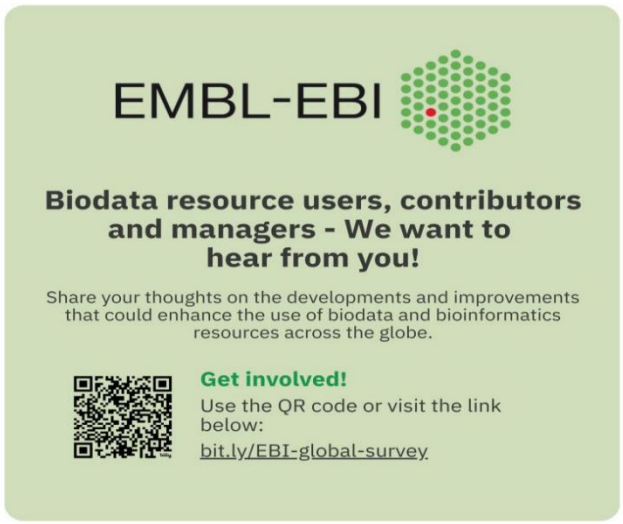
Towards routine proteome profiling of FFPE tissue: insights from a 1,220-case pan-cancer study

Tüshaus et al., 2024

https://doi.org/10.1038/s44318-024-00289-w

Researchers have created the first large-scale pan-cancer proteome resource by analyzing 1,220 FFPE tumor samples across six cancer types using advanced mass spectrometry. The study introduces a novel normalization method for consistent sample loading and identifies 11,000 proteins, uncovering tissue-specific and cancer-entity protein fingerprints. This resource, accessible via an interactive web platform, offers a powerful tool for biomarker discovery and cancer research.

RECOMMENDED EVENTS & FELLOWSHIPS



SURVERY

Current use and future needs of biodata and bioinformatics resources in low-resource geographical regions

The EMBL-European Bioinformatics Institute (EMBL-EBI) is interested in exploring how biodata could create greater global impact, including in low-resource geographical regions. Our questions focus on ways to improve how life scientists in a range of settings use, contribute to and deliver digital infrastructure. Your feedback will lead to the preparation of a public-facing summary report, as well as helping EMBL-EBI to improve its resources and services.

https://docs.google.com/forms/d/e/1FAIpQLSdXczGyZ9AUF5rVwDVq_6rOC-mlkU7gNDu-JFBh5pfCkJAJCA/viewform

Cell Symposia: Hallmarks of cancer

In partnership with Sun Yat-sen University Cancer Center and Guangdong Provincial Anticancer Association

November 7–9, 2024, Guangzhou, China

https://www.cell-symposia.com/hallmarksofcancer-2024/index.html

Lancement du Prix Gustave Roussy pour récompenser l'innovation scientifique en cancérologie

À l'occasion du 150e anniversaire de la naissance de son fondateur et à l'aube des 100 ans de l'Institut qui porte aujourd'hui son nom, Gustave Roussy est fier d'annoncer le lancement du **Prix Gustave Roussy**. Cette distinction annuelle exceptionnelle vise à récompenser un chercheur ou une chercheuse dont les découvertes scientifiques ont un impact majeur sur la prise en charge des patients atteints de cancer.

https://forms.office.com/e/rBSaqphxwG

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Future Africa at the University of Pretoria is pleased to invite early-career researchers across Africa to apply for the Future Africa Research Leadership Fellowship (FAR-LeaF II).

This two-year fellowship programme, supported by the Carnegie Corporation of New York, focuses on future-looking science leadership and developing the next generation of African scientists and academics.

Applications open on Monday, 11 November 2024.

https://www.futureafrica.science/farleaf/uncategorized/call/

SWBio DTP PhD studentship!

An exciting PhD studentship with Helen Waller Evans, Emyr Lloyd-Evans, and myself focused on understanding the role of cholesterol and its metabolites in brain development.

Application deadline: Wednesday, 11 December 2024

https://bpb-eu-w2.wpmucdn.com/blogs.bristol.ac.uk/dist/f/373/files/2024/11/swbio-25-project-3.pdf

12 WEEKS INTERNSHIP FULLY PAID

Department Summary

The CryoEM Group in the Department of Structural Biology is dedicated to providing high-resolution structural insights into biological macromolecules involved in health and disease.

This internship position is located in South San Francisco, on-site.

https://careers.gene.com/us/en/job/GENEUS202411129173EXTERNALENUS/2025-Summer-Intern-Department-of-Structural-Biology?utm_source=linkedin&utm_medium=phenom-feeds

We only ask you to co-sponsor scientific event for the emerging countries contact us: admin@algeriansca-dz.org