Patient Wellness First

BioSciTech biweekly NEWS

Issue: 15 January 2025

NEWS & COMMENTARIES

Insilico Medicine licenses 2nd AI-generated cancer drug candidate to Menarini's Stemline in $550M deal. Another new year, another half-billion-biobuck transaction between Insilico Medicine and the Italian drugmaker Menarini Group. Following a licensing agreement last January—which saw Menarini's Stemline Therapeutics subsidiary pick up an artificial intelligence-designed breast cancer therapy candidate from Insilico for $12 million upfront and more than $500 million tied to its future successes—the two companies are at it again with a similar deal.

https://www.fiercebiotech.com/medtech/insilico-medicine-licenses-2nd-ai-generated-cancer-drug-candidate-menarinis-stemline-550m

2025 Predicted Most Impactful Clinical Trials Nature Medicine invited top researchers to highlight the most impactful clinical trials anticipated for 2025. These trials span groundbreaking advancements, including gene therapies for prion and sickle-cell diseases, as well as innovative digital tools addressing cancer and mental health.

Gene therapy for prion disease. ...
Precision nutrition in a diverse cohort. ...
CBD to prevent psychosis. ...
Base editing for sickle-cell disease. ...
Cool roofs to prevent heat-related disease. ...
Radiopharmaceuticals for prostate cancer. ...
Chatbot to aid cervical cancer screening.

https://www.nature.com/articles/s41591-024-03383-y

How I turned seemingly 'failed' experiments into a successful Ph.D.

By SHREYA PRAMANIK 2024

I sat alone in our microscopy room, staring at the blank wall. "It doesn't work no matter what I do!" I thought despairingly. I had spent the past 10 months repeating an experiment with various tweaks to the protocol, and still I saw nothing—the synthetic vesicles that were supposed to divide weren't dividing at all. A progress report about my Ph.D. project was due in a month, and I felt I had nothing to write about.

https://www.science.org/content/article/how-i-turned-seemingly-failed-experiments-into-a-successful-phd

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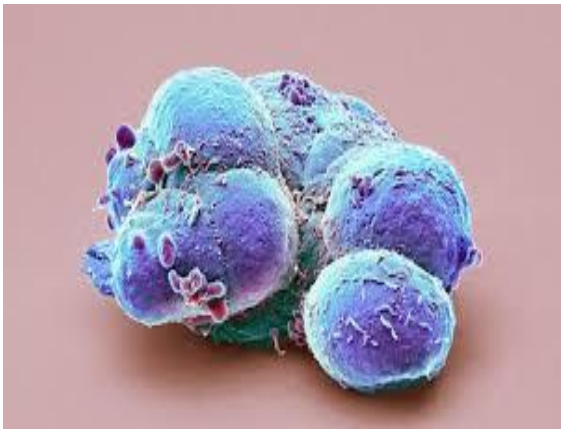
Breaking boundaries: Bacteria act as architects of host T cell modulators using bile acids

LINA YAO 2024

https://doi.org/10.1126/science.adq2341

Bile acids, long hailed for their crucial role in food digestion and absorption, are not mere passengers in the gut journey. These molecules originate from cholesterol in the liver and undergo further chemical modification by trillions of gut-resident microbiota to generate a vibrant array of secondary bile acids (1, 2). Recent research shines a spotlight on secondary bile acids as nature's messengers, which wield direct influence over host physiology. From their antimicrobial properties to their pivotal role in colon and liver cancers through nuclear receptor engagement, these molecules are modulating host metabolism and energy expenditures.



U.K. publishes first guidelines for human embryo models grown from stem cells

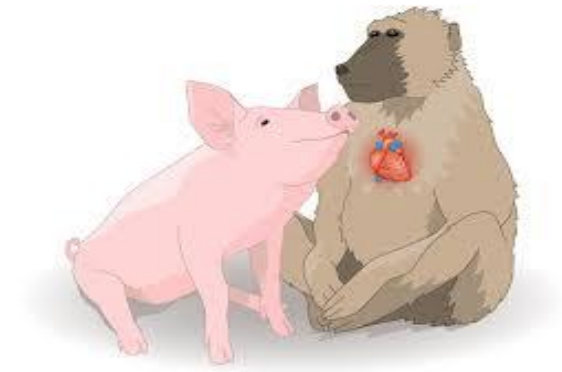
ETBYALEX EPSHTEIN

New code of practice aims to provide clarity about the ethical and legal boundaries of a rapidly developing research field. The United Kingdom should set up a specialized committee to oversee all studies using embryo models grown from stem cells, according to the country's first guidelines for such research.

The code of practice, published yesterday by a working group led by University of Cambridge researchers, aims to remove long-standing ethical and legal ambiguities that have left scientists unsure about the acceptable boundaries of their work.

https://www.science.org/content/article/uk-publishes-first-guidelines-for-embryo-models-grown-from-stem-cells

SELECTED PUBLICATIONS



Genetically engineered pig heart transplantation in non-human primates

Singh et al., 2025

https://doi.org/10.1038/s43856-025-00731-y

A study of 10-gene-edited (10-GE) pig hearts transplanted into baboons showed life-supporting function for up to 225 days (average 128 days), marking progress in cardiac xenotransplantation. Using continuous perfusion preservation and anti-CD40 immunosuppression, researchers observed variable outcomes influenced by chronic vasculopathy, thrombosis, and acute rejection. These results suggest 10-GE organs may be suitable for clinical use, with two cases already approved for compassionate human transplants.

By Dr. M.Boudjelal (KAIMRC), Dr. M. Belhocine (AGU), Dr. F. Amokrane Nait Mohamed (Harvard), Dr. Bilal Djeghout (Quadram Institute)

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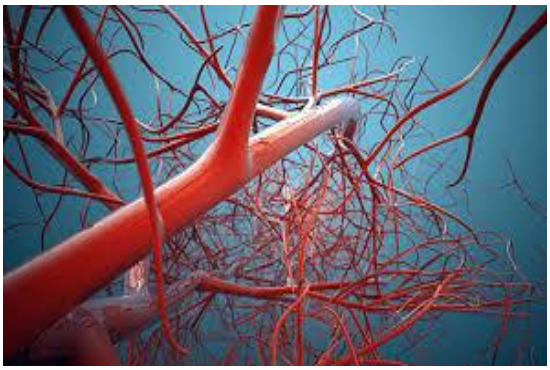
Predicting gene sequences with AI to study codon usage patterns

Tomer Sidi et al., 2024

https://doi.org/10.1073/pnas.2410003121

Researchers used AI to predict codon usage in eukaryotes and bacteria, uncovering evolutionary-selected patterns. The models outperformed frequency-based methods, with higher accuracy for highly expressed genes and bacteria, aligning with selective pressure theories. Results suggest links between codon usage, protein length, and cotranslational folding. This deep-learning tool offers insights for optimizing codon usage in natural and engineered proteins, advancing genetic and evolutionary research.



An organotypic atlas of human vascular cells

Barnett et al., 2024

https://doi.org/10.1038/s41591-024-03376-x

A comprehensive single-cell transcriptomics study of 67,000 vascular cells from 19 human tissues has revealed 42 unique vascular cell states and detailed angiodiversity across the body. Key findings include transitional arterial signatures, organ-specific endothelial populations, and pathways mediating endothelial–mural cell communication. Tissue-specific transcriptional regulators, such as FOXF1 in lung vasculature, were identified, alongside potential vascular drug targets. This open-access resource offers valuable insights into vascular biology and therapeutic strategies for vascular diseases

Targeting Smurf1 to block PDK1–Akt signaling in KRAS-mutated colorectal cancer

Peng et al., 2024

https://doi.org/10.1038/s41589-024-01683-5

Researchers uncovered a critical role for Smurf1-mediated neddylation of PDK1 in activating the PI3K–Akt signaling pathway, a key driver of KRAS-mutated colorectal cancer (CRC). The Smurf1-PDK1 complex facilitates Akt activation, promoting tumor growth. A novel Smurf1 degrader, Smurf1-antagonizing repressor of tumor 1, effectively blocks PDK1–Akt signaling and suppresses tumors, either alone or with a PDK1 inhibitor. These findings reveal a promising new approach for targeting PI3K–Akt and treating KRAS-mutant cancers

By Dr. M.Boudjelal (KAIMRC), Dr. M. Belhocine (AGU), Dr. F. Amokrane Nait Mohamed (Harvard), Dr. Bilal Djeghout (Quadram Institute)

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A foundation model for clinician-centered drug repurposing

Huang et al., 2024

https://doi.org/10.1038/s41591-024-03233-x

Drug repurposing expands the use of approved drugs for new diseases, but AI models often focus on diseases with existing treatments. TxGNN, a graph foundation model, enables zero-shot drug repurposing for 17,080 diseases, even those with limited treatment options, using a medical knowledge graph and neural networks. It improves prediction accuracy by 49.2% for indications and 35.1% for contraindications compared to other methods. TxGNN also provides interpretable predictions that align with off-label prescriptions, offering valuable insights for human experts.

Reconciling heterogeneous dengue virus infection risk estimates from different study designs

Huang et al., 2024

https://doi.org/10.1073/pnas.2411768121

Understanding who, where, and how many people are at risk of infection is key to effective protection strategies. This study compares three approaches (two using blood samples and one using case counts) to estimate dengue infection risk, revealing significant differences in their estimates. By addressing factors like antibody fluctuations, measurement noise, and age-related risk variability, the methods were reconciled. These findings highlight the importance of integrating blood sample and case count data to improve risk assessments for infectious diseases beyond dengue.

A β-hydroxybutyrate shunt pathway generates anti-obesity ketone metabolites

Maria Dolores Moya-Garzon et al., 2024

https://doi.org/10.1016/j.cell.2024.10.032

β-Hydroxybutyrate (BHB), a key ketone body, undergoes a newly discovered secondary metabolic pathway involving CNDP2-dependent conjugation with amino acids. This pathway produces anti-obesity metabolites, BHB-amino acids, including ketosis-inducible BHB-Phe, which suppresses feeding by activating hypothalamic and brainstem neurons. CNDP2 knockout (KO) mice lack BHB-amino acids, show increased food intake, and gain weight on ketogenic diets. This pathway, conserved in humans, links BHB metabolism to energy balance and feeding regulation.

By Dr. M.Boudjelal (KAIMRC), Dr. M. Belhocine (AGU), Dr. F. Amokrane Nait Mohamed (Harvard), Dr. Bilal Djeghout (Quadram Institute)

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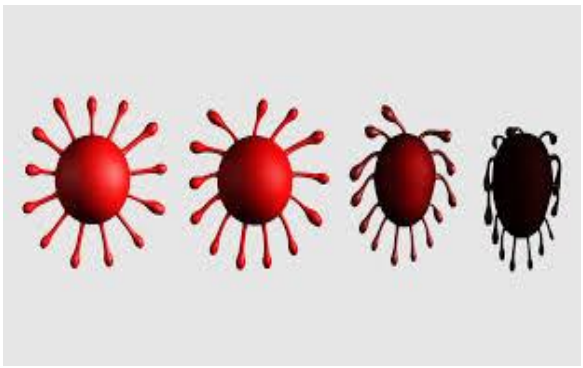
Identification of two repurposed drugs targeting GSDMD oligomerization interface I to block pyroptosis

Hu et al., 2024

https://doi.org/10.1016/j.chembiol.2024.10.002

Gasdermin D (GSDMD), a key executor of pyroptosis, is a critical drug target for inflammatory diseases and cancer. While existing inhibitors like necrosulfonamide and disulfiram modify cysteine residues to prevent pyroptosis, this approach risks adverse reactions by disrupting protein function. Instead, this study targeted the oligomerization interface of GSDMD's pore-forming structure. Using high-throughput screening, two repurposed drugs were identified as safe and potent GSDMD inhibitors, demonstrating synergistic therapeutic effects in murine models of sepsis and cancer. These findings offer promising candidates for anti-inflammatory and anti-cancer immunotherapies.

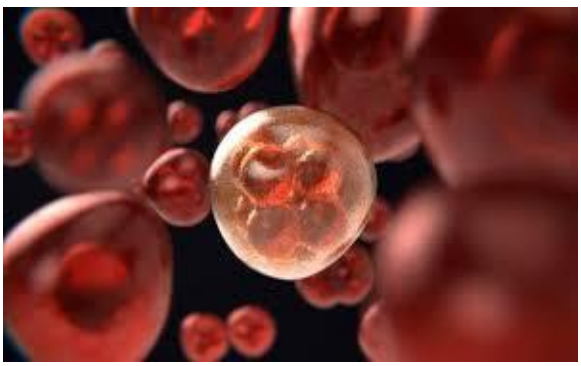


Senescence as a therapeutic target in cancer and age-related diseases

Domhnall McHugh, Imanol Durán & Jesús Gil, 2024

https://doi.org/10.1038/s41573-024-01074-4

This review explores cellular senescence as a key factor in ageing, tissue maintenance, and cancer prevention, while highlighting its detrimental role in chronic inflammation and age-related diseases through the senescence-associated secretory phenotype (SASP). The authors discuss emerging senotherapies, including senolytics and senomorphics, as well as strategies to harness the immune system for clearing senescent cells. They evaluate the integration of these therapies with cancer treatments and their potential to revolutionize clinical approaches to ageing and multimorbidity.



Dysfunctional natural killer cells can be reprogrammed to regain anti-tumor activity

Sabag et al., 2024

https://doi.org/10.1038/s44318-024-00094-5

This study investigates the dysfunction of natural killer (NK) cells, which play a crucial role in immune surveillance and cancer control. The authors reveal that anergic NK cells share functional and transcriptional similarities with exhausted NK cells found in tumor microenvironments. Through identifying key regulatory molecules, Egr2 and DGKα, they demonstrate that a nanoparticle-based delivery system can reprogram dysfunctional NK cells. This innovative strategy offers promise for developing advanced immunotherapeutic treatments targeting cancer.

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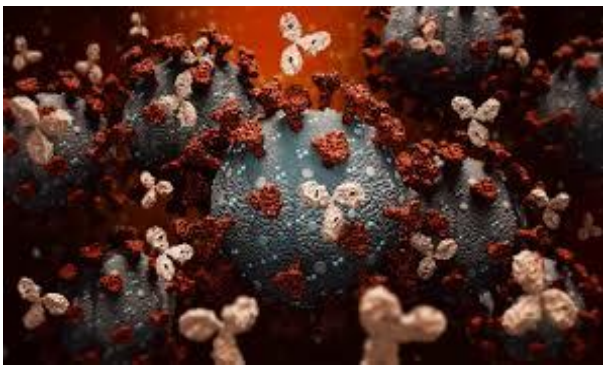

A metabolic inhibitor blocks cellular fucosylation and enables production of afucosylated antibodies

Pierre-André Gilormini et al., 2024

https://doi.org/10.1073/pnas.2314026121

This research introduces a fucose mimetic that effectively blocks cellular fucosylation, enabling the production of afucosylated antibodies with enhanced anti-cancer efficacy. Unlike previous methods, this inhibitor prevents fucosylation without being incorporated into cellular processes, offering a simple, scalable solution for academic and industrial applications. The approach has significant implications for antibody therapeutics and glycoprotein engineering.

A molecular glue degrader of the WIZ transcription factor for fetal hemoglobin induction

TING et al., 2024

https://doi.org/10.1126/science.adk6129

Addressing the challenges of sickle cell disease (SCD), this study identifies dWIZ-1 and dWIZ-2, molecular glue degraders targeting the WIZ transcription factor, a newly identified repressor of fetal hemoglobin (HbF). These compounds robustly induce HbF in preclinical models, demonstrating tolerability and efficacy. By unveiling the structural mechanism of WIZ degradation, the authors propose a transformative therapeutic approach to SCD treatment, accessible globally.

RECOMMENDED EVENTS

BII | Prize for Science | Innovation

The BII & Science Prize for Innovation.

To encourage more scientists to translate their research, BioInnovation Institute (BII) and Science award the BII & Science Prize for Innovation.

Behind every life-changing solution is an entrepreneurial scientist – a creative mind who proved an idea in the lab and dared to carry it out in the world.

https://www.science.org/content/page/bioinnovation-institute-science-prize-innovation

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NCI Immunotherapy Fellowship

Co-sponsored by the National Cancer Institute (NCI) and the Society for Immunotherapy of Cancer (SITC) and made possible in part by an educational grant from EMD Serono.

One Year at the NCI's Center for Cancer Research **Begins July 2025**

Application Period: July 8–Aug. 19, 2024

https://www.sitcancer.org/professional-development/nci-immunotherapy-fellowship?utm_source=email&utm_medium=realmagnate&utm_campaign=NCI24

5th AfroBioTech Conference

February 16-18, 2025 | John Lewis Student Center at Georgia Tech, Atlanta, Georgia, USA

Registration Information for the 5th AfroBiotech Conference

Funding Opportunities Available: Thanks to the generous support of the AIChE® Foundation, we are pleased to announce that student and post-doc attendees have the opportunity to apply for financial support to attend the 5th AfroBiotech Conference!

https://www.aiche.org/conferences/afrobiotech-conference/2025/registration-information

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