Patient Wellness First

BioSciTech biweekly NEWS

Issue: 15 December 2024

## NEWS & COMMENTARIES


### Cepheid Tuberculosis Assay Receives WHO Prequalification

The World Health Organization on Thursday announced that it has granted prequalification to a molecular diagnostic test for tuberculosis made by Danaher subsidiary Cepheid.

The Xpert MTB/RIF Ultra test is the first assay for tuberculosis diagnosis and antibiotic susceptibility testing that meets WHO's prequalification standards, the organization said in a statement.

**https://www.who.int/news/item/05-12-2024-who-announces-first-prequalification-of-a-tuberculosis-diagnostic-test**

### Old Story Revisited: Honeybee venom kills cancer cells

Researchers in the Perkins Cancer Epigenetics team are continuing their groundbreaking work into the use of honeybee venom as a powerful anti-cancer treatment. Perkins researchers had uncovered that honeybee venom could kill breast cancer cells, while leaving normal healthy cells essentially unaffected. This remarkable discovery showed that a specific concentration of honeybee venom can completely destroy cancer cell membranes within 60 minutes and induce 100% cancer cell death with minimal effect on normal cells.

**https://perkins.org.au/honeybee-venom-as-an-anti-cancer-treatment-continues/**

## SELECTED PUBLICATIONS

### Chocolate intake and risk of type 2 diabetes: prospective cohort studies

**Liu et al., 2024**

**https://doi.org/10.1136/bmj-2023-078386 (Published 04 December 2024)**

A large prospective study across three US cohorts found that consuming dark chocolate (≥5 servings/week) is associated with a 21% lower risk of type 2 diabetes (T2D), while milk chocolate showed no protective effect. Each weekly serving of dark chocolate reduced T2D risk by 3%. However, milk chocolate intake was linked to weight gain. These findings highlight the potential health benefits of dark chocolate, warranting further investigation through randomized trials.

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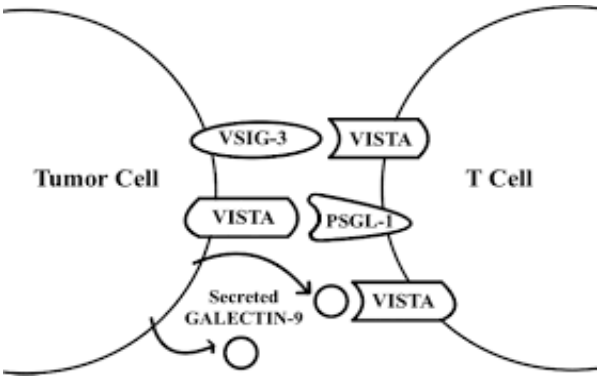
## Could ChatGPT get an engineering degree? Evaluating higher education vulnerability to AI assistants

**Borges et al., 2024**

**https://doi.org/10.1073/pnas.2414955121**

A study examining AI assistants' performance on STEM assessment questions from 50 courses at EPFL revealed that GPT-4 answered 65.8% correctly on average, and 85.1% with at least one prompting strategy. These findings highlight the vulnerability of traditional assessments to generative AI, as such tools can already pass many core courses. The study underscores the need to rethink assessment design to ensure the integrity of learning outcomes in higher education.

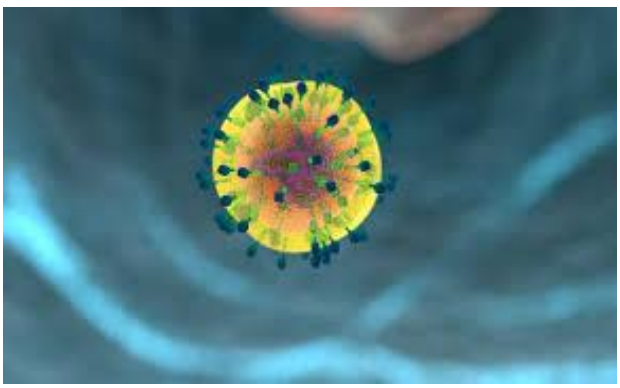



## Small molecule inhibitors targeting PD-L1, CTLA4, VISTA, TIM-3, and LAG3 for cancer immunotherapy (2020–2024)

**Cheng et al., 2024**

**https://doi.org/10.1016/j.ejmech.2024.117141**

Small-molecule immuno-oncology agents are emerging as a complement to antibody-based therapies, addressing challenges like tissue penetration, oral delivery, and high production costs. This review highlights advancements (2020–2024) in small molecules targeting key immune checkpoints (PD-1/PD-L1, CTLA4, VISTA, TIM-3, LAG3), their rational design, and potential limitations. These agents offer synergistic potential with antibodies, paving the way for improved cancer immunotherapy.



## Engineering synthetic suppressor T cells that execute locally targeted immunoprotective programs

**Reddy et al., 2024**

**https://doi.org/10.1126/science.adl4793**

Two new studies highlight the power of engineered T cells to treat diseases with precision. Reddy et al. designed T cells to combat autoimmune diseases and organ rejection by producing anti-inflammatory cytokines and absorbing proinflammatory ones, reducing systemic immunosuppression in mouse models. Simic et al. engineered T cells with synthetic receptors to target brain cancer cells, sparing healthy tissues elsewhere. These breakthroughs demonstrate how cell-based therapies can act locally and specifically, offering new hope for treating complex diseases.

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

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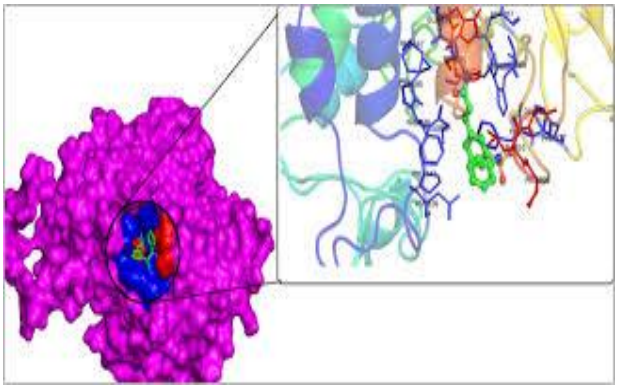


## Combined HDAC8 and checkpoint kinase inhibition induces tumor-selective synthetic lethality in preclinical models

**Chang et al., 2024**

**https://doi.org/10.1172/JCI165448**

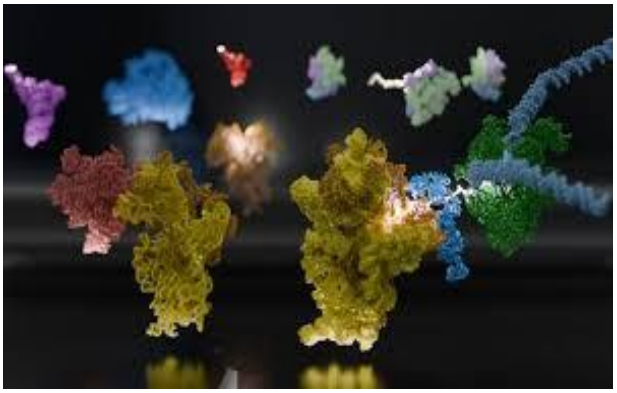
This study identifies histone deacetylase 8 (HDAC8) as a key target for cancer treatment, showing that its inhibition, combined with checkpoint kinase inhibitors, induces severe replication stress and genome instability selectively in cancer cells. This dual targeting causes replication fork collapse, irreversible cell-cycle arrest, and synergistic vulnerability, validated in patient-derived organoid and xenograft models. HDAC8 was found crucial for reducing acetylation of SMC3 and preventing R loop formation, ensuring genome stability during replication. These findings highlight a novel cancer-specific therapeutic strategy leveraging synthetic lethality between HDAC8 and checkpoint kinases.

## Ferroptosis of select skin epithelial cells initiates and maintains chronic systemic immune-mediated psoriatic disease

**Vats et al., 2024**

**https://doi.org/10.1172/JCI183219.**

Ferroptosis, a form of programmed cell death, plays a critical role in chronic inflammatory diseases affecting the skin, lungs, kidneys, and gastrointestinal tract. In psoriasis, ferroptosis-associated lipid peroxidation was observed in epithelial cells, particularly in keratin 14+ glutathione peroxidase 4 (Gpx4)-deficient keratinocytes. This process triggered a Th1/Th17-driven inflammatory response, sustaining the psoriatic phenotype. In a murine model, the anti-ferroptotic agent Liproxstatin-1 effectively reversed molecular, biochemical, and morphological features of psoriasis, matching the efficacy of targeted biologic therapies or T cell depletion. Targeting ferroptosis may provide a promising strategy for treating chronic inflammatory conditions.



## Molecular basis of mRNA delivery to the bacterial ribosome

**Webster et al., 2024**

**https://doi.org/10.1126/science.ado847**

In bacteria, transcription and translation occur simultaneously, allowing RNA polymerase and the ribosome to coordinate their activities. Using cryo-electron microscopy, Webster et al. captured the initial interaction between RNA polymerase and a ribosome as it begins translating a nascent mRNA. Supported by single-molecule experiments and in-cell cross-linking mass spectrometry, the study reveals how these molecular machineries work together to recruit the ribosome to the nascent mRNA, highlighting their cooperative dynamics.

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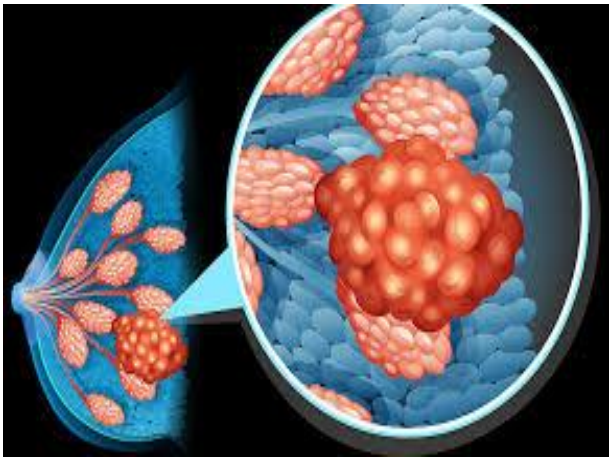
## Using artificial intelligence to document the hidden RNA virosphere

**Xin Hou et al., 2024**

**https://doi.org/10.1016/j.cell.2024.09.027**

Metagenomic tools often miss highly divergent RNA viruses. To address this, LucaProt, a deep learning algorithm, was developed to detect RNA-dependent RNA polymerase (RdRP) sequences in 10,487 metatranscriptomes from diverse ecosystems. By integrating sequence and predicted structural data, LucaProt identified 161,979 potential RNA virus species and 180 RNA virus supergroups, including exceptionally large and complex RNA virus genomes. A subset of these discoveries was validated through RT-PCR and sequencing. The newly identified RNA viruses were found across diverse environments, such as air, hot springs, and hydrothermal vents, with significant variation in virus diversity and abundance.



## A chemical screen identifies PRMT5 as a therapeutic vulnerability for paclitaxel-resistant triple-negative breast cancer

**Zhang et al., 2024**

**https://doi.org/10.1016/j.chembiol.2024.08.003**

Paclitaxel-resistant triple-negative breast cancer (TNBC) is difficult to treat, but a new study reveals an epigenetic vulnerability. Inhibiting PRMT5, an enzyme that stabilizes mitotic chromatin, leads to reduced expression of aurora kinase B (AURKB) and triggers mitotic catastrophe. The combination of PRMT5 inhibition with other type I PRMT inhibitors successfully suppresses tumor growth in resistant cells, with promising results validated in patient-derived models. This suggests a new therapeutic avenue for paclitaxel-resistant TNBC.

## Bioluminescence assay of lysine deacylase sirtuin activity

**Van Scoyk et al., 2024**

**https://doi.org/10.1016/j.chembiol.2024.10.006**

A novel assay, SIRTify, improves the measurement of sirtuin activity with higher sensitivity and specificity. Unlike traditional methods that can cause artifacts, SIRTify is homogenous and can detect a broader range of sirtuin activities, including decrotonylation and deglutarylation. This advancement offers a more comprehensive tool for studying the role of sirtuins in various biological processes.

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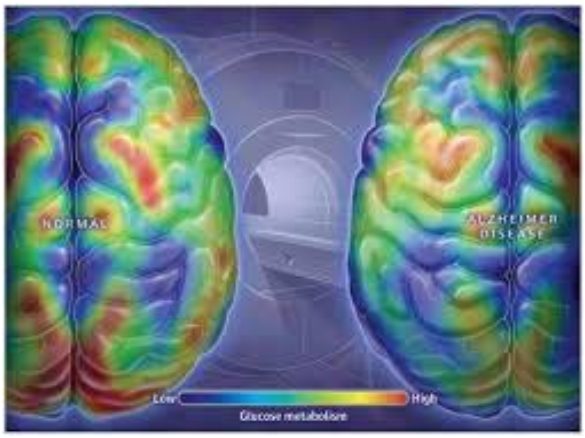


## β-hydroxybutyrate is a metabolic regulator of proteostasis in the aged and Alzheimer disease brain

**Madhavan et al., 2024**

**https://doi.org/10.1016/j.chembiol.2024.11.001**

This study uncovers how R-βHB, a ketone body, helps maintain proteostasis in aging and Alzheimer's disease. R-βHB facilitates the insolubilization of misfolded proteins, rescuing cellular health in models of amyloid-β toxicity. These findings open up new possibilities for using ketone bodies in therapeutic approaches to neurodegenerative diseases.

## Adipose tissue retains an epigenetic memory of obesity after weight loss

**Hinte et al., 2024**

**https://doi.org/10.1038/s41586-024-08165-7**

Even after significant weight loss, adipose tissue retains epigenetic changes induced by obesity, which contribute to rapid weight regain. These persistent alterations prime adipocytes for unhealthy responses when exposed to obesogenic environments. Understanding this "obesogenic memory" could lead to more effective strategies for long-term weight management and combating metabolic diseases.

## Spatial proteomics identifies JAKi as treatment for a lethal skin disease

**Nordmann et al., 2024**

**https://doi.org/10.1038/s41586-024-08061-0**

Toxic epidermal necrolysis (TEN) is a severe skin condition triggered by drug reactions, and this study identifies key molecular drivers. Using spatial proteomics, researchers reveal the involvement of JAK/STAT and interferon signaling in TEN. Targeted JAK inhibitors (JAKi) reduce cytotoxicity in skin cells and improve clinical outcomes in patients, providing a new therapeutic option for this life-threatening disease.

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# RECOMMENDED EVENTS

Mass General Brigham

**Postdoctoral Training Program in Precision and Genomic Medicine**

Call for applications for the NHGRI-funded MGB T32

**https://cgm.massgeneral.org/training-program-overview/**


**Bioinformatics**

Transform Extensive Data into Actionable Insights with Advanced Computational Tools for Pharma R&D

**April 3 - 4, 2025 ALL TIMES EDT**

**https://www.bio-itworldexpo.com/bioinformatics**

**Bright breakthroughs: Real stories of beating rare disease**

**Thursday, December 12, 2024**

**If you've already registered, to login to the webinar.**

**https://view6.workcast.net/register?cpak=1425594420065128&referrer=DL1&utm_campaign=webinars2024&et_rid=51389519&et_cid=5442563**

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## JOBS CORNER


### Senior Bioinformatician (f/m/d) R&D Computational Research

CureVac SE is a global biopharmaceutical company researching and developing novel drugs based on the natural molecule Messenger RNA (mRNA). Our focus is on prophylactic vaccines, innovative cancer immunotherapies and protein-based therapies. Currently, all RNA people are striving to achieve our main goal: To bring multiple best-in-class mRNA drugs to market.

**https://career.curevac.com/job/T%C3%BCbingen-%28Senior%29-Bioinformatician-%28fmd%29-R&D-Computational-Research/1137685055/**

### EIPOD-LinC Fellowship Programme

EIPOD-LinC is a Postdoctoral fellowship programme supporting promising researchers from around the world who are passionate about interdisciplinary research. The programme is designed to support the increasing diversity of career paths in Europe's research landscape providing researchers with the mentoring, training and career development support needed to become leaders in academia, industry and beyond.

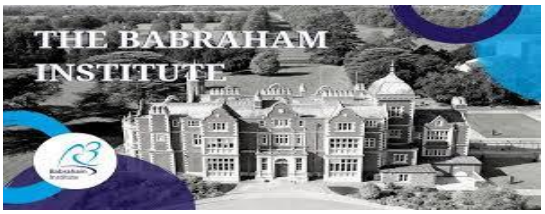
**https://www.embl.org/about/info/postdoctoral-programme/eipod-linc-exploring-life-in-context/?et_rid=51389519&et_cid=54397**

### 2025-26 GSK Scholarships for Future Health Leaders

Three scholarships are offered to support the training and development of the next generation of leaders in global health, and strengthen the capacity of health systems and health-related research in Africa.

**deadline on Wednesday 05 March 2025.**

**https://www.lshtm.ac.uk/study/fees-and-funding/funding-scholarships/2025-26-gsk-scholarships-future-health-leaders**




### Principal Investigators in Immunology

Particularly interested to hear from candidates who can strengthen and complement our expertise in RNA biology and/or in vivo studies of immunity across the life course.

**Closing date:Sunday 12th January 2025.**

**https://babrahaminstitute.livevacancies.co.uk/#/job/details/477?target=frame**

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DGRSDT البحث العلمي في خدمة المواطن https://dgrsdt.dz/en

ALGERIAN SCA Algerian Scholars & Competencies Abroad algeriansca-dz.org

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## Head of Biology (Oncology, Director or VP level) at CHARM Therapeutics

seeking an experienced Biology leader with a passion for scientific innovation. This key leadership role will be instrumental in driving our oncology-focussed drug discovery pipeline and leading a world-class team of drug discovery scientists.

https://charmtx.com/careers/head-of-biology-oncology-director-or-vp-level/?gh_jid=4486893101

## Senior Laboratory Research Scientist in Chemical Biology

Reports to: Head of Chemical Biology STP
This is a full-time, fixed term (three-year) position on Crick terms and conditions of employment
The program
https://www.crick.ac.uk/careers-study/vacancies/2024-12-03-senior-laboratory-research-scientist-in-chemical-biology

## Wellcome Sanger Institute
## Applications for the Sanger Prize 2025 are now open!

Are you an undergraduate student from a low or middle-income country with a passion for genomics? This is a great opportunity to join us for a fully funded 3-month internship in a world-class research environment.

**What's included?**

✅ Work in a lab of your choice with leading scientists.
✅ All travel, living, and training costs are covered.
📅 Apply now: https://ow.ly/unjW50UfK05
✉️ Questions? Email us: sangerprize@sanger.ac.uk

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