Patient Wellness First

BioSciTech biweekly NEWS

Issue: July 1st, 2024

NEWS & COMMENTARIES

What steps to take when funding starts to run out

By Neil Savage, 2004

https://www.nature.com/articles/d41586-024-01570-y

Summary: As the grant funding for Zhen Jiang's research in molecular regulation of insulin signaling and glucose transport came to an end after five years, he faced the challenge of securing new funds. Despite encountering setbacks when his grant application was scored too low to qualify for funding, Jiang, a biochemist at Boston University's Chobanian and Avedisian School of Medicine in Massachusetts, sought alternative ways to sustain his research on inflammation in obesity and its correlation with tissue damage. This experience highlights the struggles researchers often face when existing grants expire with no immediate replacement in sight. "We depend on grant support, and if you don't have money, a school can let you go." A stressful situation to be in, he says.

Biomedical paper retractions have quadrupled in 20 years — why?

By Holle Else, 2024

https://doi.org/10.1038/d41586-024-01609-0

The article addresses the rate of retractions for European biomedical-science papers that has skyrocketed over the past two decades, with a fourfold increase between 2000 and 2021, according to a comprehensive study of thousands of retractions. The study discovered that two-thirds of these retractions were due to research misconduct, which included issues such as data and image manipulation or authorship fraud. This analysis suggests that research misconduct has become increasingly prevalent in Europe. Alberto Ruano-Ravina, a public-health researcher at the University of Santiago de Compostela in Spain, led the research.

Cheaper versions of blockbuster obesity drugs are being created in India and China

https://doi.org/10.1038/d41586-024-02044-x

Companies in India and China are vying to produce less expensive versions of various weight-loss medications as the patents on those medications are about to expire, expanding access to such treatments. Thanks to Chinese and Indian pharmaceutical companies, popular weight-loss medications like Wegovy could soon be more affordable and accessible to a wider audience. A long line of organizations is creating duplicates of the complex natural medications, and some are hustling to make changed or further developed forms to contend in the worldwide market.

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SELECTED PUBLICATIONS

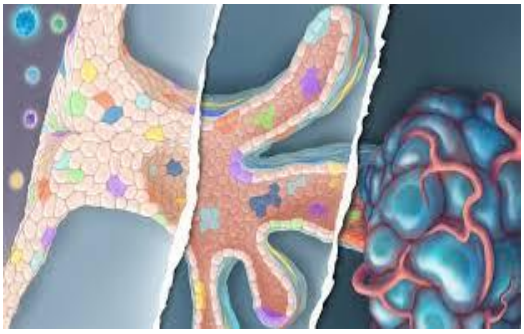
AstraZeneca's CAPItello-290 phase III trial of Truqap plus chemotherapy in advanced or metastatic TNBC fails to meet dual primary endpoints. The CAPItello-290 phase III trial for Truqap (capivasertib) in combination with paclitaxel in patients with locally advanced (inoperable) or metastatic triple-negative breast cancer (TNBC) did not meet the dual primary endpoints of improvement in overall survival (OS) versus paclitaxel in combination with placebo in either the overall trial population or in a subgroup of patients with tumours harbouring specific biomarker alterations (PIK3CA, AKT1 or PTEN). **https://www.pharmabiz.com/NewsDetails.aspx?aid=169803&sid=2**

How the brain regulates inflammation

Alexandra Flemming

https://doi.org/10.1038/s41577-024-01045-1

Summary: The study conducted by Jin, H. et al., 2024 *"A body–brain circuit that regulates body inflammatory responses"*. **https://doi.org/10.1038/s41586-024-07469-y**", demonstrates that infections have the ability to trigger neural circuits responsible for bodily responses like fever and malaise. They identified a neural pathway that communicates emerging inflammatory responses from the body to the brain. By administering lipopolysaccharide (LPS) or other immune insults to mice, they observed the activation of specific neurons in the caudal nucleus of the solitary tract (cNST) in the brainstem. Silencing these neurons led to uncontrolled inflammatory responses, while their activation reduced levels of pro-inflammatory cytokines and stimulated anti-inflammatory responses.



Tracing unknown tumor origins with a biological-pathway-based transformer model

Xie et al., 2024

https://doi.org/10.1016/j.crmeth.2024.100797

The Cancer of Unknown Primary (CUP) is a type of metastatic cancer where the primary site cannot be identified using standard diagnostic procedures. In an effort to address this challenge, Xie et al., 2024 has developed BPformer, which is a deep learning method that integrates the transformer model with prior knowledge of biological pathways. By training on transcriptomes from 10,410 primary tumors across 32 cancer types, BPformer has achieved impressive accuracy rates of 94%, 92%, and 89% in identifying primary tumors, primary sites of metastatic tumors, and metastatic sites of metastatic tumors, respectively, surpassing existing methods. In a retrospective study, BPformer was validated and demonstrated consistency with tumor sites diagnosed through immunohistochemistry and histopathology.

By Dr. M.Boudjelal (KAIMRC), Dr. M. Aid-Boudries (Harvard), Dr. M. Belhocine (UAE), Dr. F. Amokrane Nait Mohamed (Harvard)

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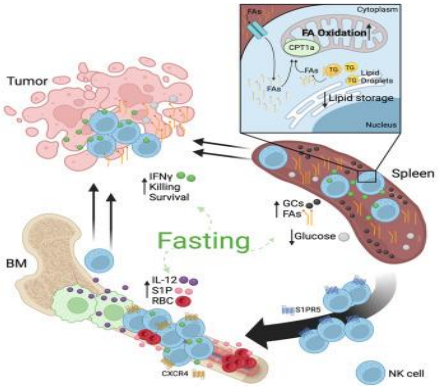
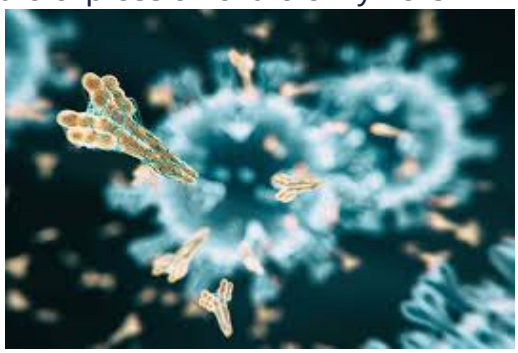


Fasting reshapes tissue-specific niches to improve NK cell-mediated anti-tumor immunity

Delco et al., 2024

https://doi.org/10.1016/j.immuni.2024.05.021

Based on recent research, fasting has been associated with positive impacts on cancer outcomes. The study delved into the effects of fasting on the body's natural killer (NK) cell anti-tumor immunity. The findings revealed that intermittent fasting bolstered the body's defense against both solid and metastatic tumors, and this improvement was reliant on NK cells. Notably, fasting prompted the movement of NK cells from peripheral tissues to the bone marrow. Moreover, human subjects undergoing fasting displayed reduced levels of circulating NK cells. In fasted mice, NK cells in the spleen underwent metabolic changes due to increased concentrations of fatty acids and glucocorticoids, which enhanced fatty acid metabolism by upregulating the expression of the enzyme CPT1A.



Multiparatopic antibodies induce targeted downregulation of programmed death-ligand 1

Ludwig et al., 2024

https://doi.org/10.1016/j.chembiol.2024.02.014

PD-L1 inhibits antigen-specific T cell responses by binding to PD-1 on activated T cells. Targeted antibodies disrupting this interaction have been developed due to high levels of these proteins in the tumor microenvironment. Despite some success, response rates are low, prompting the need for new strategies. Ludwig et al., 2024 study introduces antibody fusion proteins that block immune checkpoint pathways by targeting molecular trafficking. These engineered multiparatopic antibodies engage multiple receptor epitopes on PD-L1, leading to rapid clustering, internalization, and degradation in a manner dependent on epitope and topology. By combining ligand blockade and receptor downregulation, they enhance immune cell activation and reduce PD-L1 availability in mouse tumors.

Successful use of anti-CD19 CAR T cells in severe treatment-refractory stiff-person syndrome

Faissner et al., 2024

https://doi.org/10.1073/pnas.2403227121

The use of autologous chimeric antigen receptor (CAR) T cells has proven to be highly effective in treating neuroimmunological disorders like myasthenia gravis. The authors present a case where anti-CD19 CAR T cells were successfully used to treat stiff-person syndrome (SPS) that was not responding to other treatments. A 69-year-old woman with a 9-year history of treatment-resistant SPS experienced significant improvements after receiving an infusion of autologous anti-CD19 CAR T cells (KYV-101). Following the infusion, she showed reduced leg stiffness, remarkable enhancement in gait, more than a 100% increase in walking speed, and an improvement in daily walking distance from less than 50 meters to over 6 kilometers within 3 months.

By Dr. M.Boudjelal (KAIMRC), Dr. M. Aid-Boudries (Harvard), Dr. M. Belhocine (UAE), Dr. F. Amokrane Nait Mohamed (Harvard)

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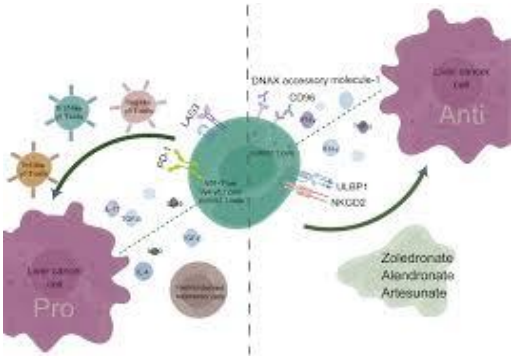
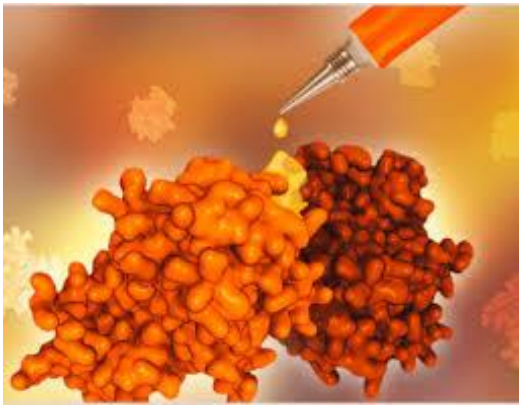


Immunotherapy-activated T cells recruit and skew late-stage activated M1-like macrophages that are critical for therapeutic efficacy

van Elsas et al., 2024

https://doi.org/10.1016/j.ccell.2024.04.011

Limited knowledge exists regarding the specific contribution of each immune cell subset to total tumor clearance through immunotherapy. However, our research demonstrates that therapy-induced intratumoral CD8+ T cells play a crucial role in recruiting and influencing late-stage activated M1-like macrophages. These macrophages are essential for effectively controlling tumors in two different murine models of cancer immunotherapy. The CD8+ T cells activate CCR5 signaling, which summons the macrophages into the tumor and its surrounding area. In vitro experiments reveal that exposing non-polarized macrophages to activated T cell supernatant and tumor lysate replicates the late-stage activated and tumoricidal phenotype. Furthermore, the transcriptomic signature of these macrophages is also found in a similar macrophage population present in human tumors, and it correlates with the clinical response to immune checkpoint inhibitors. This highlights the necessity of functional cooperation between CD8+ T cells and effector macrophages for effective immunotherapy and cautions against combining immunotherapy with broad macrophage-targeting strategies.



MOLECULAR GLUES

Molecular glues and bifunctional compounds: Therapeutic modalities based on induced proximity

Stuart L. Schreibe 2024

https://doi.org/10.1016/j.chembiol.2024.05.004

This Perspective delves into molecular adhesives and dual-purpose compounds—proximity-inducing compounds—and provides a framework for comprehending and leveraging their resemblance to hotspots, missense mutations, and posttranslational modifications (PTMs). This perspective also demonstrates its relevance to intramolecular adhesives, where compounds facilitate interactions between distinct domains of the same protein. A historical overview of these compounds is presented, illustrating how the field has evolved from molecular adhesives targeting native proteins, to dual-purpose compounds targeting fusion proteins, and back to molecular adhesives and dual-purpose compounds targeting native proteins. Modern screening techniques and data analyses involving pre-selected target proteins are shown to result in either synergistic molecular adhesives or dual-purpose compounds that induce proximity, thereby enabling innovative functional outcomes.

- **Molecular glues for protein-protein interactions: Progressing toward a new dream**
  Konstantinidou and Ark, 2024
  https://doi.org/10.1016/j.chembiol.2024.04.002

- **Molecular glues and induced proximity: An evolution of tools and discovery**
  Stephanie Anne Robinson, Jennifer Anne Co, Steven Mark Bani, 2024
  https://doi.org/10.1016/j.chembiol.2024.04.001

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Focus on China

https://www.nature.com/collections/efchdhgeci

China's status at the summit of the Nature Index remains unrivalled as the gap between it and the United States grows. The key question is where Chinese research will go next. As the nation seeks international recognition for its scientific achievements, betting big on large-scale experiments, it is also carving its own path in publishing and partnerships. Time will tell how these strategies will shift the status quo of the global research landscape.

- **China seeks global impact and recognition**
- **China's research clout leads to growth in homegrown science publishing**
- **China's big-science bet**
- **Chinese research collaborations shift to the Belt and Road**
- **Why China has been a growing study destination for African students**
- **Chinese science still has room to grow**

RECOMMENDED EVENTS

Ph.D. Scholarship

An opportunity for top students to apply for a PhD scholarship at the University of Sydney! One category of scholarships (see below) is only fort students from the MENA region.

Applicants can be considered for multiple scholarships including:

- RTP and USYDIS
- Middle East, North Africa

Deadlines:

- Expressions of Interest - **18 August 2024**

https://sydney.au1.qualtrics.com/jfe/form/SV_dnz8K0AIg2BVvPU

A WEBINAR – MANAGING YOUR MENTAL WELLBEING THROUGH YOUR CAREER AND PROFESSIONAL DEVELOPMENT

Discover practical strategies and expert insights from our recent webinar on managing your mental wellbeing through proactive career planning and professional development, where we delved into topics such as coping with career precarity, loneliness, and psychological safety.

https://elrig.org/beyond-the-lab-managing-your-mental-wellbeing-through-your-career-and-professional-development/

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African BioGenome Project

Genomics for the future of biological diversity across Africa

African Plant Genome Assembly and Annotation Fellowship

Call for Applications

African Plant Genome Assembly and Annotation Fellowship 2024

November, 2024 | IITA, Ibadan, Nigeria

The International Institute of Tropical Agriculture (IITA), Nigeria, Inqaba Biotec, West Africa, and the African BioGenome Project (AfricaBP) Open Institute are partnering on a short-term training fellowship program on Plant Genome Assembly and Annotation. This 8 weeks (virtual) and 10-day on-site intensive training program will empower African scientists with advanced skills in plant genomics, specifically focusing on genome assembly and annotation strategies.

https://redcap.africanbiogenome.org/surveys/?s=3FXRFYAKKKD3FPWK

Open Challenge Innovation

Angelini Pharma launches new crowd-sourcing challenge to fund innovative solutions to drug adherence and management of epilepsy

The task is challenging but essential: to identify new innovative Drug Delivery Systems (DDS) and Treatment Approaches to significantly improve the lives of people with epilepsy. Approximately one-third of people living with hashtag#epilepsy face difficulties with anti-seizure medicine adherence, a challenge particularly acute for elderly and pediatric populations. This low adherence highlights the urgent need for more effective treatments that better address the diverse needs of patients with epilepsy.

Visit the Link

https://angelinipharma.community.wazoku.com/challenge/14a2d7cbd74447cc8f380cd8688157ca?entities=idea&sort=-relevancy&page=1&pageSize=15&include_descendants&filters=%7B%22show_archived%22:true%7D&parentType=challenge&parentId=14a2d7cbd74447cc8f380cd8688157ca&communityId=02763ac3a84d4911b7ffb36c4b7ab354