

NEWS & COMMENTARIES



David Baltimore, one of modern biology's most influential scientists, passed away at his home in Woods Hole, Massachusetts, on September 6, 2025 at the age of 87, leaving legions of former trainees and the scientific community to contemplate the significance of a career that spanned the era of molecular biology from its infancy to the advent of cellular engineering and genome editing. A powerful intellectual force who defied categorization as a virologist, immunologist, or cancer biologist—his work indeed spanned a wide swath of biomedicine—David will

long be remembered for his many seminal contributions and for building and leading some of the world's most consequential scientific institutions.

[https://www.cell.com/cell/fulltext/S0092-8674\(25\)01180-8](https://www.cell.com/cell/fulltext/S0092-8674(25)01180-8)



Top 10 countries by active drug pipelines (2025)

- United States – 11,455 drugs | 💰 \$673B
- China – 7,032 | 💰 \$256.8B
- South Korea – 3,386 | 💰 \$28.8B
- United Kingdom – 3,214 | 💰 \$52.8B
- Australia – 2,615 | 💰 \$24.2B
- Germany – 2,545 | 💰 \$68.6B
- France – 2,485 | 💰 \$50.6B
- Canada – 2,446 | 💰 \$34.8B
- Spain – 2,381 | 💰 \$30.7B
- Japan – 2,160 | 💰 \$98.8B

[https://www.linkedin.com/posts/nigelajones1964\\_top-10-countries-by-active-drug-pipelines-activity-7396100546585333760-OSve](https://www.linkedin.com/posts/nigelajones1964_top-10-countries-by-active-drug-pipelines-activity-7396100546585333760-OSve)



African Drug Regulatory Agency

By Mwila Mulubwa, Leon Mutesa & Kelly Chibale, 2025

Africa finally has its own drug-regulation agency — and it could transform the continent's health. If it gets things right, the first major regulator of medicines to launch for 30 years could empower Africa to tackle African challenges around health and disease. After more than a decade of planning, the launch of the African Medicines Agency (AMA) is being celebrated in Mombasa, Kenya, this week at the Seventh Biennial Scientific Conference on Medical

Products Regulation in Africa.

<https://www.nature.com/articles/d41586-025-03637-w>

## WATCH: Phases of Clinical Research Explained: Understanding Phase I, II, III & IV Clinical Trials

Are you ready to understand how new medicines move from the lab to real patients? In this detailed tutorial, you'll discover the phases of clinical research explained step-by-step – from the first-in-human studies to real-world post-marketing surveillance. Clinical research is at the heart of every medical breakthrough. Before a drug reaches patients, it passes through four critical phases of clinical trials, each designed to answer a specific question about safety, efficacy, and long-term performance.

<https://www.youtube.com/watch?v=qjkl9nY7djc>



### Phases of Clinical Research

1

#### Phase I – “Is it Safe?”

- Small number of healthy volunteers (20–100)
- Tests safety, tolerability, and dose levels
- Identifies how the body absorbs, distributes, and eliminates the drug

2

#### Phase II – “Does it Work?”

- Patients with the disease (100–300)
- Evaluates effectiveness and side effects
- Helps define dosing guidelines and treatment response

3

#### Phase III – “Is it Better?”

- Large patient groups (300–3,000+)
- Compares the new treatment to the current standard of care
- Provides the critical evidence needed for regulatory approval

4

#### Phase IV – “What Happens in Real Life?”

- Conducted after approval and market launch
- Monitors long-term safety, real-world effectiveness, rare side effects
- Helps refine treatment guidelines and usage patterns

*Clinical research progresses step by step, ensuring that every new medical therapy is scientifically sound, effective, and safe before reaching patients.*

[www.skyhealthacademy.net](http://www.skyhealthacademy.net)

## SELECTED PUBLICATIONS



### Research integrity is undoubtedly in crisis

**Andrew Greya , Alison Avenellb Mark J Bolland**

**DOI: 10.1016/S0140-6736(25)02122-1**

Richard Horton argues against the existence of a research integrity crisis, which contrasts with the Lancet Commission's assertion of an urgent crisis. Horton's focus on researcher misconduct overlooks more prevalent issues affecting publication integrity. This approach diverts attention from the crucial question of research reliability to the less significant inquiry into its unreliability.

Emphasizing research reliability could enhance the responsiveness to publication integrity concerns. Furthermore, contrary to Horton's claim, evidence suggests that publisher responses to integrity issues are often slow, opaque, incomplete, and inconsistent.



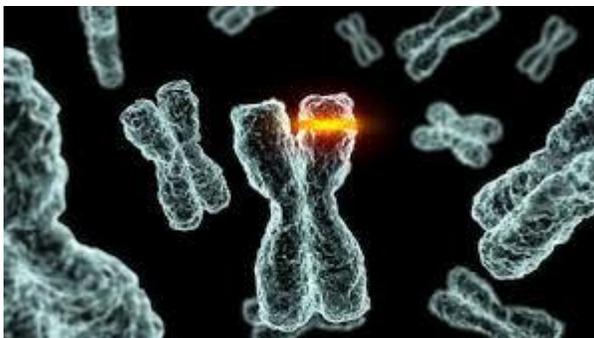
### Africa's Health Security and Sovereignty agenda: a new way forward

**Jean Kaseya, 2025**

**DOI: 10.1016/S0140-6736(25)02315-3**

In the aftermath of the COVID-19 pandemic, Africa articulated the ambitious the New Public Health Order (NPHO) to strengthen institutions, the workforce, manufacturing, domestic financing, and partnerships for health security.<sup>1</sup> This vision, endorsed by African Heads of

State in 2022, guided the continent's public health rebuilding process from the vulnerabilities exposed by the pandemic.



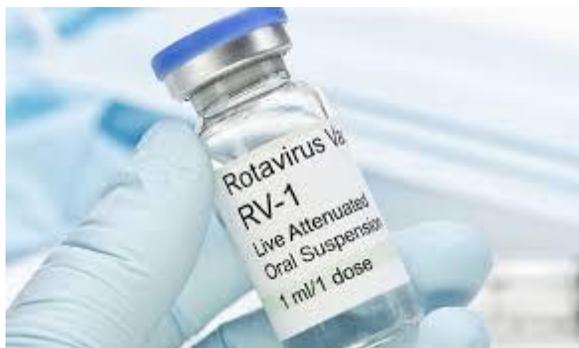
### Proteome-wide model for human disease genetics

**Rose Orenbuch et al., 2025**

**<https://doi.org/10.1038/s41588-025-02400-1>**

Missense variants are difficult to interpret due to their subtle effects. Current prediction models work well for known disease genes but lack general applicability. To improve this, popEVE was created, combining evolutionary and human population data to evaluate

variant harmfulness across the proteome. It identifies variants in 442 genes related to severe developmental disorders, including 123 new candidates, and can prioritize causal variants using only child exomes. This offers a valuable method for interpreting rare disease variants, particularly in single cases.

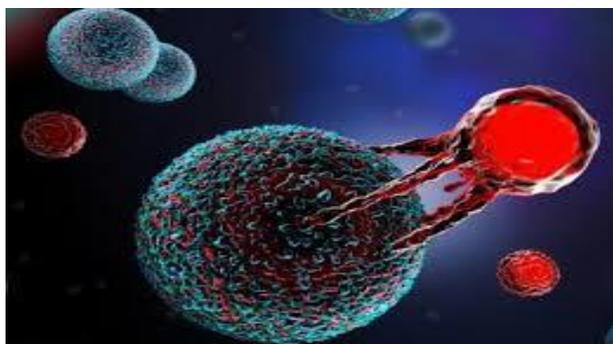


## Mechanisms of maternal antibody interference with rotavirus vaccination

**Tawny L Chandler et al., 2025**

<https://doi.org/10.1038/s44318-025-00582-2>

Maternal antibodies are passed to fetuses and infants to protect them while their immune systems are still developing. However, these antibodies can also hinder infants' responses to vaccines, making them vulnerable to diseases like rotavirus. Current rotavirus vaccines are given orally to infants at 6-8 weeks. The presence of maternal antibodies leads to lower antibody production after vaccination, but the reasons for this are unclear. A mouse model study shows that maternal antibodies block vaccine replication and affect immune responses, highlighting their role in reducing the effectiveness of oral rotavirus vaccines.

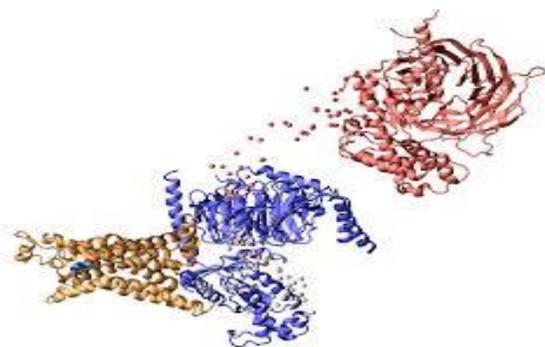


## Physiologically based pharmacokinetic model for CAR-T cell delivery and efficacy in solid tumors

**Hadjigeorgiou et al., 2025**

**DOI:10.1073/pnas.2522634122**

Preclinical studies show promise for CAR-T therapy in treating glioblastoma, diffuse midline gliomas, and neuroblastoma, but challenges remain for solid tumors. A mathematical model was developed to improve CAR-T therapy by optimizing vascular normalization and reducing CAR-T doses. It suggests combining therapies and direct delivery to enhance effectiveness.

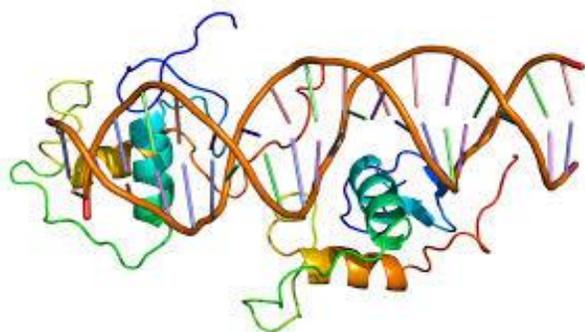


## Dissociation kinetics of G proteins from G protein-coupled receptors and effects of allosteric modulation

**Jinan Wang et al., 2025**

**DOI :10.1073/pnas.2512423122**

Protein-protein interactions (PPIs) are important for cellular signaling but are difficult to simulate due to slow dynamics. This study used a new PPI-Gaussian accelerated MD (PPI-GaMD) method to explore how G proteins dissociate from G protein-coupled receptors (GPCRs). The findings matched experimental data and showed that positive allosteric modulators slowed down this dissociation, aiding future drug discovery for GPCRs.



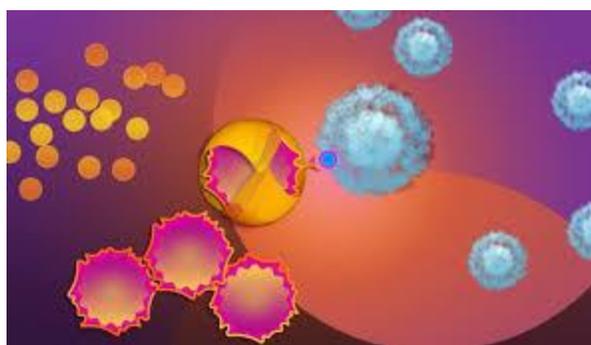
target for treating drug-resistant tumors.

### **Circadian regulator REV-ERBa is a master regulator of tumor lineage plasticity and an effective therapeutic target**

**Xiong Zhang et al., 2025**

**DOI :10.1073/pnas.2513468122**

Tumor lineage plasticity (LP) is a key factor in therapy resistance and metastasis in prostate cancer. Understanding this process is essential for better treatment. The study shows that targeting the androgen receptor can shift REV-ERBa's role, making it a potential



### **Selective HLA knockdown and PD-L1 expression prevent allogeneic CAR-NK cell rejection and enhance safety and anti-tumor responses in xenograft mice**

**Fuguo Liu et al., 2025**

**DOI: 10.1038/s41467-025-63863-8**

Allogeneic cellular immunotherapy is a potential cancer treatment but faces the problem of donor cell rejection. This study evaluates HLA and immune checkpoints in the rejection of allogeneic NK cells and finds CD8+ T cells lead this process. A new gene construct can create CAR-NK cells that avoid host rejection and effectively kill tumor cells while maintaining safety by reducing inflammatory cytokines. This method could improve allogeneic immunotherapies.



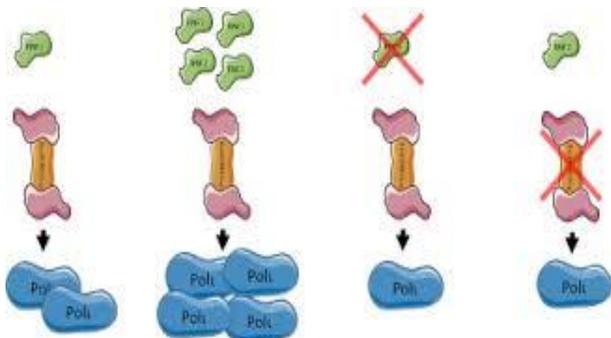
### **The limitations of small molecule and genetic screening in phenotypic drug discovery**

**Fabien Vincent and Davide Gianni**

**DOI: 10.1016/j.chembiol.2025.10.008**

Phenotypic screens using functional genomics or small molecules offer new biological insights and potential drug targets but have significant limitations. This perspective discusses these limitations and suggests

strategies for effective use of phenotypic screening.



## The E3 ligase RNF32 controls the IκB kinase complex and NF-κB signaling in intestinal stem cells

**Angela Lauriola et al., 2025**

DOI: [10.1016/j.molcel.2025.10.005](https://doi.org/10.1016/j.molcel.2025.10.005)

Nuclear factor κB (NF-κB) signaling is crucial for various cell functions. RNF32, a RING E3 ubiquitin ligase found in mouse intestinal stem cells, regulates the IκB kinase (IKK) complex, which activates NF-κB. RNF32's activity relies on calmodulin, reacting to increased calcium ion levels. This leads to RNF32 activation, NEMO recruitment, and IKK activation, showing how NF-κB signaling is controlled in the intestinal epithelium.

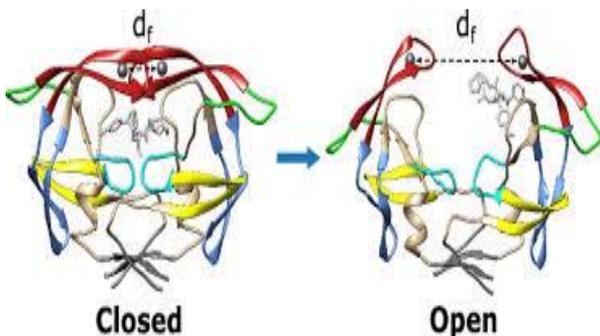


## Repurposing the antihistamine cyproheptadine for osteoarthritis: nothing to sneeze at

**Richard F. Loeser, and Philip R. Coryell**

DOI: [10.1172/JCI197144](https://doi.org/10.1172/JCI197144)

Osteoarthritis (OA) is a common and painful joint disease that requires new treatments. A study found that the antihistamine cyproheptadine can activate FOXO3, which may help in OA by reducing joint damage and pain in mice, indicating its potential as a treatment.

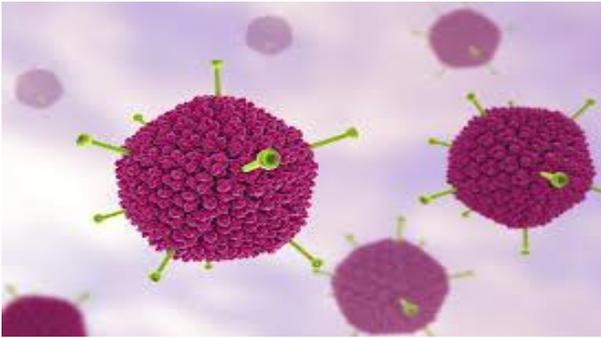


## Modeling protein–small molecule conformational ensembles with PLACER

**Ivan Anishchenko et al., 2025**

DOI: [10.1073/pnas.2427161122](https://doi.org/10.1073/pnas.2427161122)

Modeling the different shapes of protein–small molecule interactions is important for understanding and designing biological systems but is challenging. The researchers created a graph neural network named PLACER, which works at an atomic level to enhance the speed and generality of these interactions. PLACER can generate accurate structures of small molecules based on their atomic makeup and helps in protein–small molecule docking. The tool is quick and can produce many predictions to show different shapes.



## Comparative analysis of adenovirus, mRNA, and protein vaccines reveals context-dependent immunogenicity and efficacy

**Bakare Awakoaiye et al., 2025**

**DOI:10.1172/jci.insight.198069**

Despite the extensive use of adenovirus, mRNA, and protein vaccines during the COVID-19 pandemic, their immunological profiles and efficacy are not fully understood. In a study comparing these vaccines in mice, Ad5 showed the most prolonged antigen expression, while mRNA vaccines elicited stronger IFN responses and better antigen presentation. Ad5's effectiveness was reduced by preexisting immunity, whereas mRNA vaccines stayed effective after multiple uses.

## RECOMMENDED EVENTS & JOB CORNER



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fait notre fierté mais, surtout, nous permet de servir pleinement notre vocation : « Engagés pour le progrès thérapeutique au bénéfice des patients ».

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UK Human Functional  
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### Functional Genomics and AI Summer School (1st – 3rd Sept 2026, Exeter U.K)

In partnership with Google DeepMind and the U.K. Human Functional Genomics Initiative, the University of Exeter is offering a (2/3) day workshop covering a range of genome-sequencing topics, where students will get expert-led hands-on experience with the newly developed AlphaGenome

<https://www.ukfunctionalgenomics.com/events/functional-genomics-and-ai-summer-school/>

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