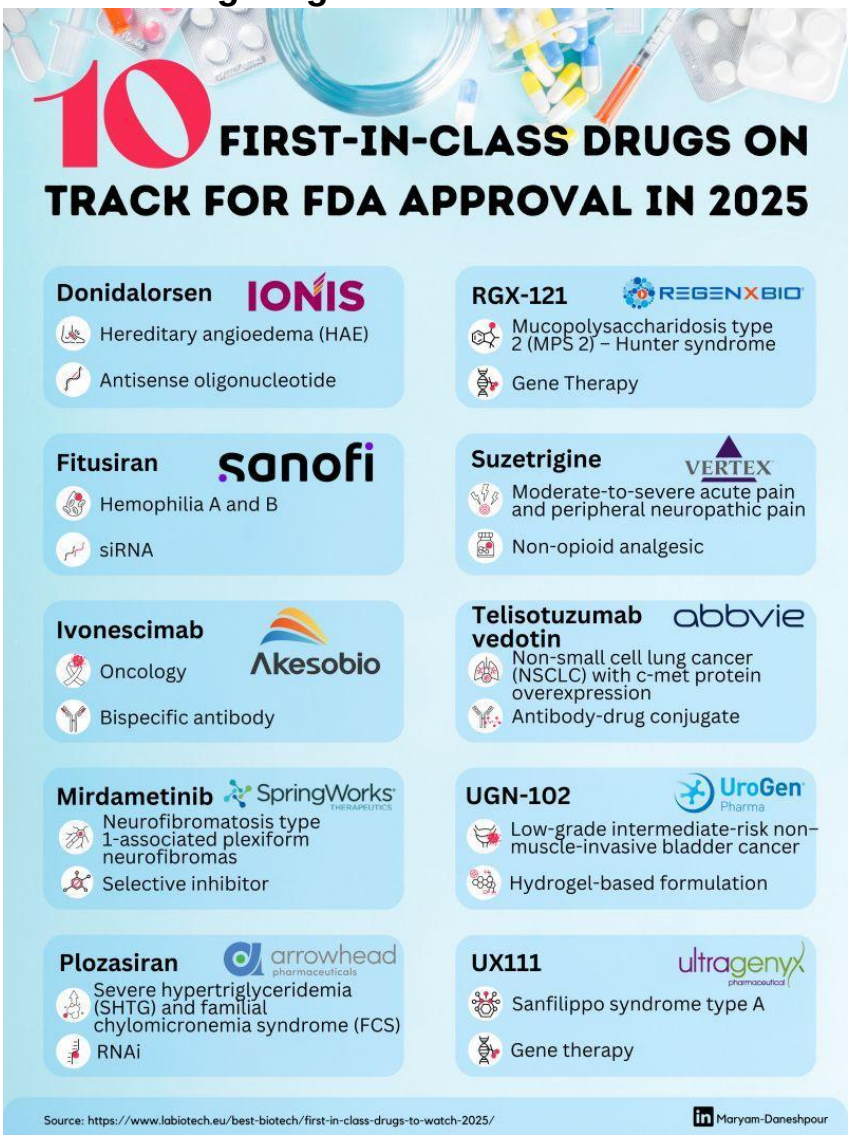
Patient Wellness First

BioSciTech biweekly NEWS

Issue: 1 February 2025

NEWS & COMMENTARIES

First-in-class therapies are revolutionizing medicine with innovative mechanisms of action targeting unmet needs.



In 2024, the FDA approved 50 new molecular entities, 24 of which were first-in-class!

by Maryam Daneshpour
https://www.linkedin.com/in/maryam-daneshpour/

In an insightful article by Labiotech.eu, a preview of transformative therapies expected this year is presented:

1. Donidalorsen (Ionis Pharmaceuticals, Inc.): A targeted treatment for hereditary angioedema, using antisense oligonucleotide technology.

2. Fitusiran (Sanofi): A subcutaneous siRNA therapy rebalancing clotting mechanisms in hemophilia patients.

3. Ivonescimab (Akeso Biopharma): A bispecific antibody for NSCLC, combining immune activation (PD-1 inhibition) with anti-angiogenesis (VEGF targeting).

4. RGX-121 (REGENXBIO): A gene therapy poised to become the first treatment for MPS 2, addressing neurological symptoms at their root.

5. Suzetrigine (Vertex Pharmaceuticals): A non-opioid NaV1.8 inhibitor offering a safer alternative for acute and neuropathic pain management.

6. Telisotuzumab Vedotin (AbbVie): An antibody-drug conjugate targeting c-Met protein overexpression in NSCLC, delivering precise tumor cell destruction.

7. Mirdametinib (SpringWorks Therapeutics): An oral MEK inhibitor reducing tumors associated with neurofibromatosis type 1 plexiform neurofibromas.

8. Plozasiran (Arrowhead Pharmaceuticals): An RNAi therapeutic tackling severe hypertriglyceridemia and familial chylomicronemia syndrome by silencing APOC3 production.

9. UGN-102 (UroGen Pharma): A bladder cancer treatment combining chemotherapy with innovative gel technology for localized, non-surgical tumor management.

10. UX111 (Ultragenyx): A gene therapy for Sanfilippo syndrome type A, addressing progressive neurodegeneration with a single-dose treatment.

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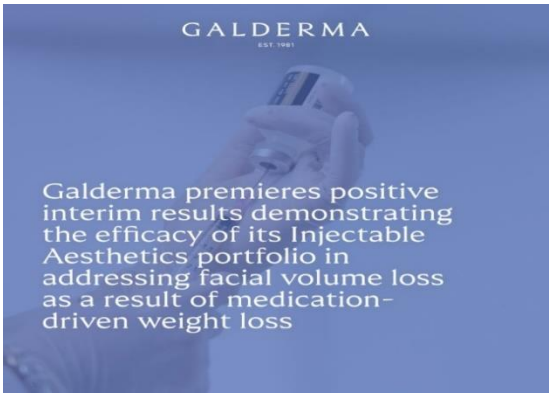


Galderma Positive Results are excited to present positive interim results demonstrating the efficacy of our Injectable Aesthetics portfolio in addressing facial volume loss from medication-driven weight loss, at the J.P. Morgan Healthcare Conference in San Francisco.

Facial volume loss is one of the major aesthetic concerns expressed by patients taking prescription weight loss medicines. The results of first of its kind phase IV clinical trial demonstrate that the combination of Sculptra® and Restylane® effectively improved the facial aesthetic appearance of these patients.

https://www.galderma.com/news/galderma-premieres-positive-interim-results-demonstrating-efficacy-its-injectable-aesthetics

Self-driving laboratories, advanced immunotherapies and five more technologies to watch in 2025

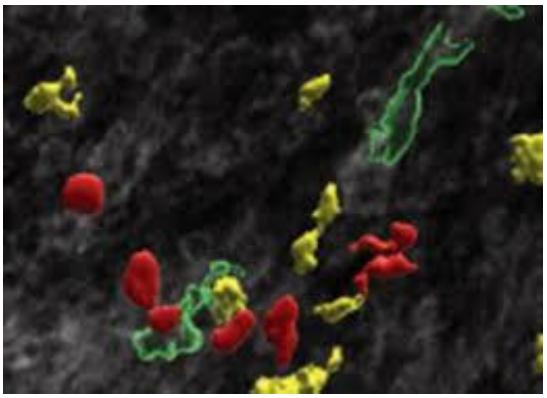
By Michael Eisenstein, 2025

https://www.nature.com/articles/d41586-025-00075-6

Sustainability and artificial intelligence dominate our seventh annual round-up of exciting innovations.

- Self-driving' laboratories
- Big opportunities for CAR T cells
- Bioremediation technologies
- Foundation models for biology
- Sustainable urban cooling
- Single-cell microbial analysis
- Photonic computing for AI

SELECTED PUBLICATIONS



A lipid made by tumour cells reprograms immune cells

By Anthony C. Buzzai & Thomas Tüting, 2025

https://www.nature.com/articles/d41586-024-03855-8

Cancer cells often develop resistance to multiple therapies. Recent findings reveal that these *'cross-resistant'* tumour cells release lipids that reprogram monocytes, a type of immune cell, preventing them from activating tumour-targeting T cells. Targeted cancer treatments, which inhibit proteins essential for tumour growth, can initially yield remarkable results but often fail as tumours adapt. Such resistance frequently extends to immunotherapies, a phenomenon known as *cross-resistance*. Researchers, led by Elewaut et al., used a mouse model to uncover a mechanism driving this resistance in melanoma, a type of skin cancer.

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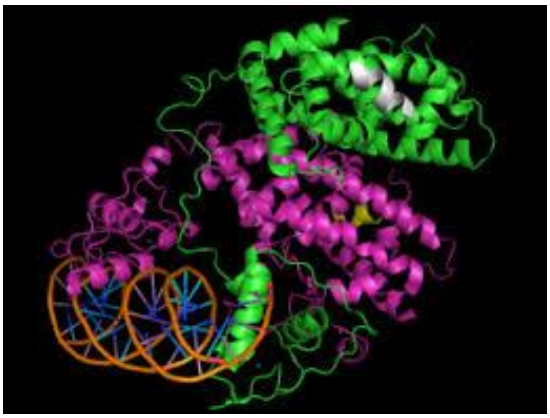

Discovery of PPAR Alpha Lipid Pathway Modulators That Do Not Bind Directly to the Receptor as Potential Anti-Cancer Compounds

Arwa Al Subait .... Mohamed Boudjelal, 2025

https://doi.org/10.3390/ijms26020736

Because of their role in fatty acid metabolism, which promotes cell proliferation, peroxisome proliferator-activated receptors (PPARs) are thought to be promising therapeutic targets for breast cancer. Al Sbait et al. employed the KAIMRC1 breast cancer cell line in this investigation. We demonstrated that when PPAR alpha is co-transfected, the PPARE-Luciferase reporter becomes highly activated without the need for an exogenous ligand, and that the activity can be inhibited by the antagonist GW6471. In order to find compounds that inhibit the PPARα-activated PPARE-Luciferase reporter in the KAIMRC1 cell, the study used this reporter system to screen 240 compounds that represented kinase inhibitors, epigenetic modulators, and stem cell differentiators. According to this research, these two substances affect the KAIMRC1 breast cancer cell line in opposite ways through fatty acid oxidation.

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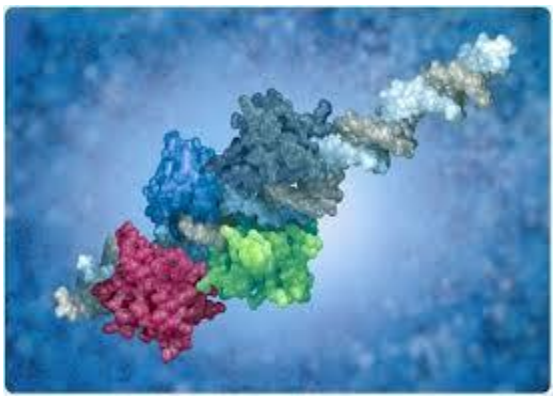
The new science of menopause: these emerging therapies could change women's health

By Lynne Peeples, 2025

https://www.nature.com/articles/d41586-025-00069-4

Researchers are pioneering new approaches to prolong ovarian health and revisiting hormone replacement therapy (*HRT*), a treatment that fell out of favour due to health concerns. In late 2022, Naomi Busch, a physician, found herself inundated with questions about menopause from her book group, as members grappled with symptoms like hot flushes, poor sleep, and mood swings. Busch's search for menopause specialists in Seattle revealed limited availability, highlighting a broader need for more informed care.



Ligand interaction landscape of transcription factors and essential enzymes in E. coli

Peng et al., 2025

https://doi.org/10.1016/j.cell.2025.01.003

Understanding protein-metabolite interactions is crucial for advancing biochemical research and drug discovery. Researchers have mapped the interactions of 296 small-molecule ligands with 69 essential enzymes and 45 transcription factors in *Escherichia coli* using a combination of rapid affinity purification, precision mass spectrometry, and molecular docking.

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Daily glucocorticoids promote glioblastoma growth and circadian synchrony to the host

Gonzalez-Aponte et al., 2025

https://doi.org/10.1016/j.ccell.2024.11.012

Glioblastoma (*GBM*), the most common malignant brain tumour in adults, exhibits poor prognosis despite aggressive treatments. Researchers have discovered that daily glucocorticoid signaling influences *GBM* growth and circadian rhythms, mediated by clock genes such as *Bmal1* and *Cry*. Blocking circadian signals, including glucocorticoids, significantly slows tumour progression. Data from *The Cancer Genome Atlas (TCGA)* revealed that elevated glucocorticoid receptor (*GR*) expression increases mortality risk. This study underscores the role of circadian signaling in tumour regulation and highlights potential therapeutic targets.

Calcineurin: An essential regulator of sleep revealed by biochemical, chemical biological, and genetic approaches

Jianjun Yu (余建军) et al., 2025

https://doi.org/10.1016/j.chembiol.2024.12.003

The molecular mechanisms underlying sleep remain elusive. Through biochemical and genetic approaches, researchers identified calcineurin (*CaN*) as a critical phosphatase in sleep regulation. *CaN* dephosphorylates the kinase *SIK3* at specific sites, influencing sleep duration. Reducing *CaN* activity led to a dramatic reduction of over five hours of sleep in mice. This breakthrough highlights a phosphatase-kinase pathway integral to sleep regulation and showcases the value of biochemical techniques in advancing brain research.

Site-saturation mutagenesis of 500 human protein domains

A.Beltran, X.Jiang, Y.Shen & B.Lehner, 2025

https://doi.org/10.1038/s41586-024-08370-4

A groundbreaking study analyzed over 500,000 human missense variants across 500 protein domains, revealing that 60% of pathogenic variants reduce protein stability. Protein stability was found to play a key role in recessive disorders and disease severity. Combining these findings with protein language models enabled functional site annotation and accurate stability predictions across protein families. This dataset offers a valuable resource for clinical variant interpretation and improving computational tools for genetic analysis.

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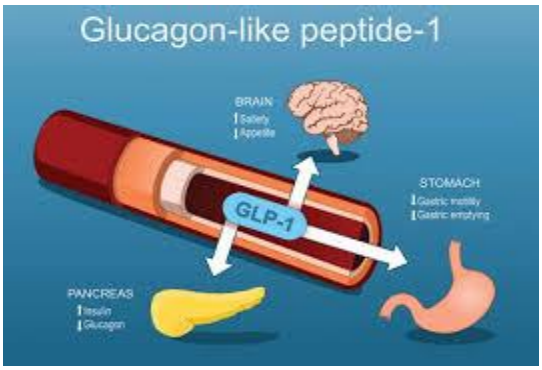
The androgen clock is an epigenetic predictor of long-term male hormone exposure

Sugrue et al., 2025

https://doi.org/10.1073/pnas.2420087121

Researchers have developed the "androgen clock," an epigenetic tool that measures long-term androgen exposure and tracks aging in male sheep and mice. Controlled by the androgen receptor, the clock's progression can be accelerated with dihydrotestosterone or halted by castration. This model provides a precise way to study age-related DNA methylation changes and offers potential applications in medicine, agriculture, and aging research.



Evaluating the benefits of the early use of GLP-1 receptor agonists

Peter-James H Zushin · Joseph C W, 2025

https://doi.org/10.1016/S0140-6736(24)02255-4

Initially developed for type 2 diabetes, GLP-1 receptor agonists have shown significant benefits in weight management and cardiovascular protection. Clinical trials like LEADER, SELECT, and SURPASS confirm their ability to reduce major adverse cardiovascular events (MACE), positioning them as transformative treatments for cardiovascular disease (CVD). By addressing obesity early, similar to statin use for primary prevention, GLP-1 receptor agonists could prevent obesity-related complications, improve health outcomes, and reduce the burden on healthcare systems.

Multidrug-resistant Gram-negative bacterial infections

Macesic et al., 2025

https://doi.org/10.1016/S0140-6736(24)02081-6

Multidrug-resistant Gram-negative bacteria, including carbapenem-resistant *Enterobacterales*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*, pose a global health threat. These pathogens rapidly acquire antimicrobial resistance (AMR), driving significant morbidity and mortality. Recent breakthroughs include advanced diagnostic technologies—biochemical, molecular, genomic, and proteomic tools—for rapid AMR detection, alongside newly licensed antibiotics that are transforming treatment approaches for these critical infections.

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

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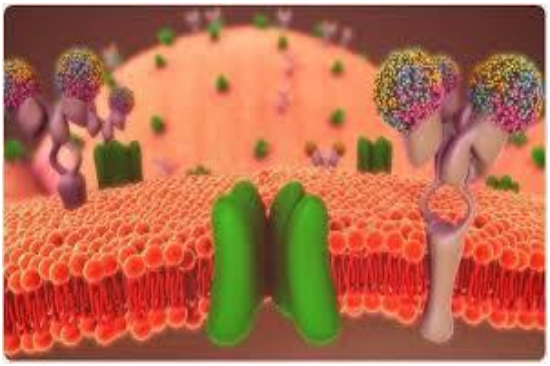
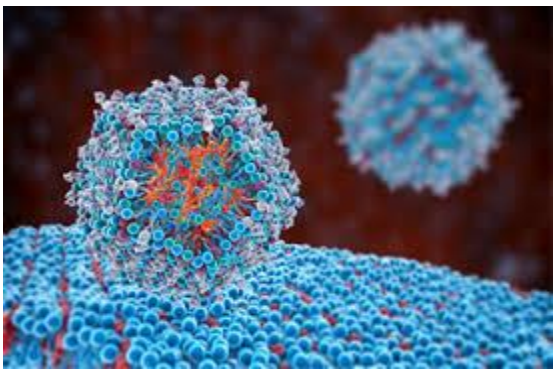


How to target membrane proteins for degradation: Bringing GPCRs into the TPD fold

Boguslawa Korona , Laura S. Itzhaki, 2025

https://doi.org/10.1016/j.jbc.2024.107926

Multispecific medicines are unlocking "undruggable" targets by inducing proximity between proteins, driving innovation in drug discovery. Targeted protein degradation (TPD) has shown great promise, especially for intracellular proteins, but membrane proteins—like GPCRs, which play key roles in many diseases—remain underexplored. This review highlights recent TPD advances and technologies aimed at degrading GPCRs, offering exciting opportunities to expand the therapeutic potential of this innovative approach.



Chemistry, manufacturing and controls strategies for using novel excipients in lipid nanoparticles

Laramy et al., 2025

https://doi.org/10.1038/s41565-024-01833-9

Lipid nanoparticles (LNPs) rely on novel lipid excipients to optimize nucleic acid delivery, but regulatory scrutiny comparable to active pharmaceutical ingredients creates economic and procedural challenges, slowing innovation. Despite their unique role in LNPs, global regulatory guidance remains limited, adding uncertainty to development. This Perspective highlights industry challenges in manufacturing and control of novel lipids and offers recommendations to clarify regulatory expectations and accelerate progress in LNP-based therapies.

Cancer cells impair monocyte-mediated T cell stimulation to evade immunity

Elewaut et al., 2025

https://www.nature.com/articles/s41586-024-08257-4

Cancer cells program the tumor microenvironment, which has a significant impact on anti-tumor immune responses. In specific niches within the tumor microenvironment, CD8+ T cells develop cytotoxic anti-tumor properties and go through full effector differentiation. Despite the fact that interactions with type 1 conventional dendritic cells have been linked to this process, little is known about the cellular actors and molecular mechanisms at play. This study by Elewaut et al., demonstrates how inflammatory monocytes can play a crucial part in stimulating intratumoral T cells. Collectively, this study by Elewaut et al., reveals that inflammatory monocytes play a crucial role in intratumoral T-cell stimulation, clarifies how oncogenic signaling impairs T-cell responses by counter-regulating PGE2 and IFN-I, and suggests logical combination treatments to improve immunotherapies.

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

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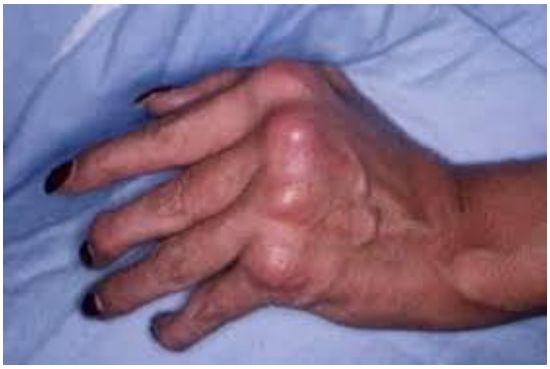
T cells in cardiac health and disease

Pilar Martín and Francisco Sánchez-Madrid, 2025

https://doi.org/10.1172/JCI185218.

Inflammation is a key factor in the pathophysiology of cardiovascular disease (CVD), which continues to be the world's leading cause of morbidity and mortality. Important elements of the adaptive immune system, T lymphocytes have been identified as important mediators in the development and progression of CVD as well as cardiac health. The various functions of T cell subsets, such as Th1, Th17, γδ T cells, and Tregs, in myocardial inflammatory processes like autoimmune myocarditis and myocardial infarction are examined in this review. In addition it provides an overview of recent developments in T cell-targeted treatments and their potential to alter immune responses and enhance clinical results for heart transplant recipients and patients with CVD.



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

Vats et al., 2025

https://doi.org/10.1172/JCI183219

Skin, lung, kidney, and gastrointestinal chronic inflammatory diseases are often the result of dysregulations of epithelial-immune interactions. However, little is known about the intraepithelial mechanisms that cause and maintain inflammation in these organs. In this study by Vats et al., used redox lipidomics to find ferroptosis-associated polyunsaturated phosphatidylethanolamine peroxidation in the epithelia of patients suffering from renal failure, psoriasis, asthma, and cystic fibrosis. Vats et al. proposes that methods aimed at ferroptosis or its causes could be useful in preventing or treating a range of chronic inflammatory diseases, since ferroptosis in certain epidermal keratinocytes initiates and maintains a pathological psoriatic multiorgan inflammatory circuit.

RECOMMENDED EVENTS & JOBS CORNER

Hall of Fame associated medal

The BMCS is pleased to announce the 2025 call for nominations for its Hall of Fame associated medal which recognises chemists for outstanding, significant contributions to any area of interest to the BMCS.

Independent nominations should be sent to the Conference Secretariat, Hg3 Conferences at events@hg3.co.uk

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

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ELRIG AWARD:

With Research & Innovation 2025 fast approaching we wanted to remind you of the Award opportunities at this conference!

ECP POSTER AWARD: A Poster Prize will be awarded for Best Early Career Professional Poster.

POSTER DEADLINES: To be considered for an oral Flash Poster Presentation in the Exhibition space please have your title & abstract submitted by 9th Feb. The deadline for all posters for general display abstract & title is 23rd Feb.

https://elrig.org/portfolio/research-innovation-2025-big-molecules-to-big-data-thinking-big-to-drive-innovative-research/#awards

Scientist, Cell Biology: **Curve Therapeutics Southampton, UK**

Curve Therapeutics is seeking an outstanding and ambitious scientist with experience in a range of cell biology techniques to join the dedicated team and you will be responsible for running the required assays as we develop our innovative therapeutics pipeline.

https://hr.breathehr.com/recruitment/vacancies/38864?identifier=curvetherapeuticslimited

Medical-Technical Specialist - Lab Manager Position Available

My Oncometabolism Laboratory is seeking to appoint a Medical-Technical Specialist to serve as Lab Manager.The lab focuses on the role of metabolism in cancer initiation, progression, and response to therapy

https://krebsforschung.meduniwien.ac.at/en/focus/tumor-biology/tardito-lab/

Altos Labs Scientist, Machine Learning

Our mission is to restore cell health and resilience through cell rejuvenation to reverse disease, injury, and the disabilities that can occur throughout life.

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