Patient Wellness First

BioSciTech biweekly NEWS

Issue: August 15th , 2024

NEWS & COMMENTARIES

FDA approves first telomerase inhibitor

Asher Mullard article cited below summarizes the US FDA approval of Geron's imetelstat (Rytelo) for adults with low- to intermediate-risk myelodysplastic syndromes (MDS) with transfusion-dependent anaemia who do not respond to erythropoiesis-stimulating agents (ESAs). The oligonucleotide-based drug is the first telomerase inhibitor to secure FDA approval. For further reading visit
https://www.nature.com/articles/d41573-024-00102-7

Blood Biomarkers to Detect Alzheimer Disease in Primary Care and Secondary Care.
Palmqvist et al.,2024
https://doi.org/10.1001/jama.2024.13855
The above paper reports that researchers from Lund University in Sweden have developed a groundbreaking blood test, known as the amyloid probability score 2 (APS2), which shows approximately 90 percent accuracy in diagnosing Alzheimer's disease. The test utilizes mass spectrometry to analyze two blood biomarkers related to Alzheimer's: The ratio of plasma phosphorylated tau 217 (p-tau217) relative to non-p-tau217, and the ratio of amyloid-β 42 to amyloid-β 40 in plasma outperforming traditional diagnostic methods that rely on clinical examinations and cognitive tests.

Slow convergence: Career impediments to interdisciplinary biomedical research

Berkes et al., 2024
https://doi.org/10.1073/pnas.2402646121
The paper describes that there are long-standing calls for more interdisciplinary/convergent research to address society's grand challenges. Despite these calls, there is no understanding of the impediments to interdisciplinary research. Berkes et al., 2024 study results that is based on researchers with PhDs in biomedical fields, are consistent with interdisciplinary researchers often falling through disciplinary divides, thus discouraging convergent research and reducing the pool of talent to train future generations of interdisciplinary researchers.

International Journal of Molecular Sciences

Special Call: "Noncoding RNAs' Functionality-Diagnosis and Therapy in Cancer and Other Indications" IJMS, MDPI, Due to a relatively high viewing and citations for the already published articles online, MDPI extended the deadline for submission to **January 20, 2025**.
https://www.mdpi.com/journal/ijms/special_issues/BYB9VZ31M7

Patient Wellness First

BioSciTech biweekly NEWS

Issue: August 15th , 2024

SELECTED PUBLICATIONS

Benefits for children with suspected cancer from routine whole-genome sequencing

Hodder et al., 2024

https://doi.org/10.1038/s41591-024-03056-w

The paper describes that the clinical whole-genome sequencing (WGS) has shown significant potential in benefiting pediatric cancer patients, especially by influencing treatment strategies for those at high risk. However, the effect of implementing WGS universally for children with suspected cancer on patient management is still not fully understood. In this study by Hodder et al., 2024 WGS variant data were examined alongside clinical and diagnostic information from 281 children (282 tumors) treated at two English centers (152 from a hematology unit and 130 from a solid tumor unit), where WGS had been adopted as a routine test. The findings indicated that WGS-specific variants altered the management of roughly 7% (20 out of 282) of the cases and provided additional disease-related insights in 108 instances involving 83 cases (29%), which were not detected by standard molecular tests. *For further reading, please refer to the paper cited above, Hodder et al., 2024*

Building genomic capacity for precision health in Africa

Olono et al., 2024

https://doi.org/10.1038/s41591-024-03081-9

This study describes that Africa is set to play a crucial role in the global population dynamics, with the United Nations predicting a population of 2.5 billion people (over 25% of the world's population) by 2050. As this demographic change unfolds, Africa confronts a distinctive healthcare challenge: managing a complex mix of infectious and non-communicable diseases. This situation calls for a shift away from traditional 'one-size-fits-all' medical models towards precision health approaches that are both effective and sustainable. *Please refer to Olono et al., 2024 review cited above for further reading.*

Identification and characterization of a small-molecule metallophore involved in lanthanide metabolism

Zytnick et al., 2024

https://doi.org/10.1073/pnas.2322096121

Zytnick et al., 2024 describes that the production of metallophores is crucial for microorganisms to thrive in environments where metals are scarce. Since the discovery of the first lanthanide-dependent enzyme, XoxF, just a decade ago, lanthanides have become recognized as essential life metals. In this study, Zytnick et al., 2024 examine methylolanthanin, a lanthanide chelator with a distinctive 4-hydroxy benzoate structure. The production of methylolanthanin is vital for maintaining wild-type levels of cellular lanthanides. As the demand for lanthanides—a resource limited by supply chains—continues to rise, there is growing interest in microbial methods for lanthanide extraction. *Please refer to Zytnick et al., 2024 review for further reading.*

Patient Wellness First

BioSciTech biweekly NEWS

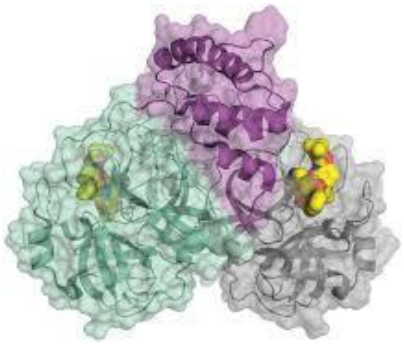
Issue: August 15th , 2024

Genomic insights into the 2022–2023Vibrio cholerae outbreak in Malawi

Chaguza et al., 2024

https://doi.org/10.1038/s41467-024-50484-w

This paper describes that Malawi faced its most severe outbreak of Vibrio cholerae (Vc) in the aftermath of devastating cyclones, resulting in over 58,000 cases and more than 1,700 deaths between March 2022 and May 2023. The research utilized population genomics to investigate the traits and origins of Vc isolates from the outbreak in Malawi. Chaguza et al. 2024 discovered that the outbreak was mainly driven by the ST69 clone, identified as part of the seventh cholera pandemic El Tor (7PET) lineage, with the O1 Ogawa serotype accounting for approximately 80% of cases, followed by the Inaba serotype at around 16%, and a smaller presence of non-O1/non-7PET serogroups (~4%). *Please refer to Chaguza et al. 2024 review.*

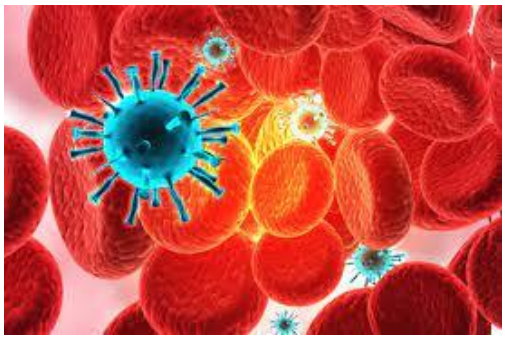


A Structural Comparison of Oral SARS-CoV-2 Drug Candidate Ibuzatrelvir Complexed with the Main Protease (Mpro) of SARS-CoV-2 and MERS-CoV

Chen et al., 2024

https://doi.org/10.1021/jacsau.4c00508

This study highlight that Ibuzatrelvir was recently introduced and patented by Pfizer as a potential treatment for SARS-CoV-2 infection. The drug has gained fast-track status from the FDA and is currently undergoing phase III clinical trials as a possible alternative to Paxlovid. Similar to nirmatrelvir, the active component of Paxlovid, ibuzatrelvir is an orally administered drug that targets the viral main proteases (Mpro) by forming a reversible covalent bond between its nitrile group and the active site thiol of the chymotrypsin-like cysteine protease protease (3CL protease). This inhibition of Mpro interferes with the processing of viral proteins necessary for replication within the host. However, unlike Paxlovid, ibuzatrelvir does not require coadministration with ritonavir, which in Paxlovid is used to inhibit human oxidative metabolism of nirmatrelvir. *Please consult Chen et al., 2024.*



Therapeutic potential of co-signaling receptor modulation in hepatitis B

Andreata et al., 2024

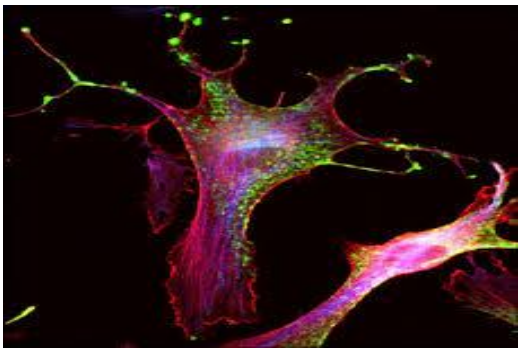
https://doi.org/10.1016/j.cell.2024.05.038

This paper highlight that reversing the dysfunction of CD8+ T cells is key to effectively treating chronic hepatitis B virus (HBV) infection, but the precise molecular targets for this remain unclear. In this study, the authors examined co-signaling receptors during the priming of hepatocellular T cells and tracked the progression and fate of dysfunctional HBV-specific $CD8^+$ T cells. Early in the infection, these cells increase the expression of several receptors, including PD-1, CTLA-4, LAG-3, OX40, 4-1BB, and ICOS. Although blocking co-inhibitory receptors had minimal impact, activating 4-1BB and OX40 was able to transform these cells into antiviral effectors. With continued stimulation, these cells developed into a self-renewing, long-lived, and heterogeneous population characterized by a distinct transcriptional profile. *Please consult Andreata et al., 2024 paper cited above.*

Patient Wellness First

BioSciTech biweekly NEWS

Issue: August 15th , 2024



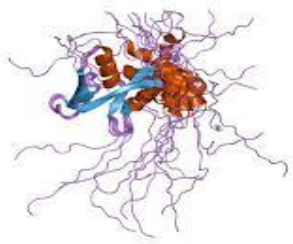
Recycled melanoma-secreted melanosomes regulate tumor-associated macrophage diversification

Parikh et al., 2024

https://doi.org/10.1038/s44318-024-00103-7

The paper mention that the extracellular vesicles (EVs) play a crucial role in cellular communication. In this study, the authors uncover a novel form of intercellular communication involving melanosomes, large EVs secreted by melanocytes for melanin transport. Unlike small EVs that are broken down within the recipient cell, melanosomes remain intact, acquire a unique protein profile, and can be passed on to another cell as "second-hand" EVs. The authors demonstrate that melanosomes secreted by melanoma cells and then processed through epidermal keratinocytes or dermal fibroblasts can subsequently be phagocyted by resident macrophages. This process results in macrophage polarization, leading to either pro-tumor or pro-immune cell infiltration phenotypes. Additionally, melanosomes transferred through fibroblasts can carry AKT1, which stimulates VEGF secretion from macrophages via an mTOR-dependent pathway, thereby promoting angiogenesis and metastasis in vivo. *Please consult Parikh et al., 2024 paper cited above.*

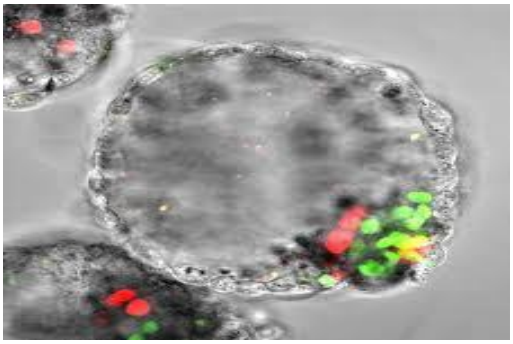
A ligand discovery toolbox for the WWE domain family of human E3 ligases



Münzker et al., 2024

https://doi.org/10.1038/s42003-024-06584-w

It is important to read in this paper that the tryptophan-tryptophan-glutamate (WWE) domain, though present in twelve human proteins, has not been extensively studied. Six of the proteins containing WWE domains also feature E3 ubiquitin ligase activity and the recognition of poly-ADP-ribosylated substrates by WWE domains suggests a potential application in the development of Proteolysis-Targeting Chimeras (PROTACs). In this work, the authors show new crystal structures of the WWE domains from HUWE1, TRIP12, and DTX1, which are bound to PAR building blocks and their analogs. These structures provide a comprehensive understanding of the structural diversity within PAR binding sites. *For further reading please consult Munzker et al., 2024 paper.*



Real-time assessment of mitochondrial DNA heteroplasmy dynamics at the single-cell level

Roussou et al., 2024

https://doi.org/10.1038/s44318-024-00183-5

Roussou et al., 2024 mention here that Mitochondrial DNA (mtDNA) is present in multiple copies within cells and is required for mitochondrial ATP generation. Even within individual cells, mtDNA copies can differ in their sequence, a state known as heteroplasmy. The principles underlying dynamic changes in the degree of heteroplasmy remain incompletely understood, due to the inability to monitor this phenomenon in real time. Here, Roussou et al (2024) employ mtDNA-based fluorescent markers, microfluidics, and automated cell tracking, to follow mtDNA variants in live heteroplasmic yeast populations at the single-cell level. *For further reading please consult Roussou et al., 2024 paper.*

Patient Wellness First

BioSciTech biweekly NEWS

Issue: August 15th , 2024

Immunological memory diversity in the human upper airway

Ramirez et al., 2024

https://doi.org/10.1038/s41586-024-07748-8

This study aims to enhance our understanding of immune memory at a critical mucosal barrier and demonstrated that nasal and nasopharyngeal swabs can be used to study immune memory in the upper airway by identifying distinct immune cell populations and exploring their stability, presence, and functionality over time, particularly in the context of SARS-CoV-2 breakthrough infections. The authors identified stable populations of tissue-resident memory T cells and B cells in the upper airway, with CD8-positive tissue-resident memory T cells marked by coexpression of CD69 and CD103, and CD4-positive tissue-resident memory T cells defined by CD69-positive non-naive cells. *For more details, please refer to the paper cited above.*

Proteomic aging clock predicts mortality and risk of common age-related diseases in diverse populations

Argentieri et al., 2024

https://doi.org/10.1038/s41591-024-03164-7

This study, conducted by Argentieri, et al., and published in Nature Medicine investigates the development and application of a proteomic aging clock to predict mortality and the risk of common age-related diseases across diverse populations. The proteomic age clock developed in this study presents a powerful tool for assessing biological aging and predicting the risk of age-related diseases and mortality across diverse populations. The findings suggest that proteomic aging, as measured by this clock, is a robust predictor of disease risk and functional decline, offering potential applications in personalized medicine for early intervention and management of age-related health risks. In summary, authors demonstrated that a higher ProtAgeGap was associated with poorer biological, physical, and cognitive functions, such as reduced telomere length, increased frailty index, slower reaction times, and lower grip strength. *Please refer to the paper cited above for more information.*

A high-light therapy restores the circadian clock and corrects the pathological syndrome generated in restricted-fed mice

Damara et al., 2024

https://doi.org/10.1073/pnas.2403770121

This study, conducted by Damaraa et al., and published in PNAS, in 2024, investigates the impact of high-light therapy on circadian misalignment and the associated pathological syndromes in restricted-fed (RF) mice. The researchers hypothesized that a specific "high-light" therapy could shift the misaligned central circadian clock (SCNCC) in RF mice to realign it with the peripheral clocks (PCCs), thereby correcting the metabolic syndrome and other associated pathologies. this study highlights the potential of high-light therapy as a non-invasive, effective treatment for circadian-related disorders. *For more information , please refer to the paper cited above.*

Patient Wellness First

BioSciTech biweekly NEWS

Issue: August 15th , 2024

RECOMMENDED EVENTS

Meta-omics approaches for studying the human gut microbiome in health and disease

Speakers: Hear Jordan Bisanz (Pennsylvania State University), Jean Macklaim (Diversigen), and Ivan Vujkovic-Cvijin (Cedars-Sinai), who will share advances on the use of meta-omics approaches to study the gut microbiome in the context of human health and disease.

Available On Demand @ https://x.com/cellhostmicrobe/status/1816835992025706707

Event: Beyond the Lab: Innovation Skills to Boost Your Career

Are you an early career professional looking to enhance your career? Whether you're an undergraduate, postgraduate, post-doc, you're invited to join our free Early Career Professional networking event. Focused on empowering you with the innovative skills to thrive in drug discovery and life science.

Date: 10th September

Time: 3:00pm - 7:30pm

Register for free now!

https://elrig.org/portfolio/beyond-the-lab-innovation-skills-to-boost-your-career/

Join the Chemical Probes Portal and Merck for the 4th Probe Hackathon.

Are you a PhD student or second year Masters student from surrounding areas studying Chemistry, Pharmacy or sciences?
Work with experts to review chemical probes in a race to find the best and worst compounds for use in biological research.

In person: Merck KGaA, Darmstadt, Germany, Monday 23rd September (09.00-17.30)

https://www.chemicalprobes.org/hackathons/merck2

JOBS CORNER

Post-Doc Position

Reservoir Surrogate Modeling with Knowledge-based Graph Neural Networks

Open postdoc position at Sorbonne University Abu Dhabi!

The candidate will work on hot topics (PINNs, GNNs, etc.) applied to real-world use case (geoscience) and will interact with research scientists from SCAI (Sorbonne center for Artificial Intelligence) and Geoscientists from Total Energies. A competitive salary will be provided.

Interested? Send your application including: a CV, a cover letter, PhD diploma and one representative publication related to the position

to abdenour.hadid@sorbonne.ae and Daniel.busby@totalenergies.com

The Senior/Principal Scientist will play a critical role in our drug discovery efforts, leveraging their expertise in both synthetic and medicinal chemistry. With a PhD and 5-10 years of experience in small molecule drug discovery, the ideal candidate will run projects within the Augustine Therapeutics pipeline. Familiarity with CNS drug design, structure-based drug design, PET tracer development, patent drafting, grant application writing and working with external parties is a plus. The therapeutic area of expertise will be in the neuroscience, cardiology, or metabolic disease space. The candidate must demonstrate a proven track record of leadership within a medicinal chemistry team, the ability to learn fast and adapt in a dynamic environment, a hands-on and can-do attitude.

https://www.augustinetx.com/careers/senior-principal-scientist-medicinal-chemistry