

Volume 2.32: August 24, 2020

Publications of the Week

A Switch in p53 Dynamics Marks Cells that Escape from Double-Strand Break-Induced Cell Cycle Arrest

First Author: Michael Tsabar (*pictured, top left*) | Senior Author: Galit Lahav (*center*) Cell Reports | Harvard Medical School



DNA damage induces a complex response that is largely orchestrated by the transcription factor p53, whose dynamics influence whether a damaged cell will arrest and repair the damage or will initiate cell death. How p53 responses and cellular outcomes evolve in the presence of continuous DNA damage remains unknown. The authors have found that a subset of cells switches from oscillating to sustained p53 dynamics several days after undergoing damage. Profile | Abstract

A Distinct Transcriptional Program in Human CAR T Cells Bearing the 4-1BB Signaling Domain Revealed by scRNA-Seq

First Author: Angela Boroughs | Senior Author: Marcela Maus *(pictured)* Molecular Therapy | Massachusetts General Hospital, Harvard Medical School, and the Broad Institute



The authors performed transcriptional profiling of bulk CAR T cell populations and single cells to characterize the transcriptional states of human T cells transduced with various co-stimulatory domains at rest and after activation by triggering their CAR or their endogenous T cell receptor. They identified a transcriptional signature common across CARs with the CD3 ζ signaling domain, as well as a distinct program associated with the 4-1BB co-stimulatory domain at rest and after activation. **Profile | Abstract**

Epigenetic Transcriptional Reprogramming by WT1 Mediates a Repair Response during Podocyte Injury

First Author: Sandrine Ettou (*pictured*, *right*) | Senior Author: Jordan Kreidberg (*left*) Science Advances | Boston Children's Hospital and Harvard Medical School



Wilms tumor-1 (WT1) is a master regulator of gene expression in podocytes, binding nearly all genes known to be crucial for maintenance of the glomerular filtration barrier. Using murine models and human kidney organoids, the authors investigated WT1-mediated transcriptional reprogramming during the course of podocyte injury. **Profile | Abstract**

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Awards

Michelson Prize for MIT's Dr. Michael Birnbaum

Human Vaccines Project



Dr. Michael Birnbaum *(pictured)* has received the 2020 Michelson Prize for Human Immunology and Vaccine Research for his project "Repertoire-Scale Determination of T Cell Recognition and Cross-Reactivity to HIV via pMHC Lentiviral Display". Dr. Birnbaum's research focuses on understanding and manipulating 'natural' adaptive immune responses in the context of cancer and infection by using a variety of strategies and techniques. **Read More**

Raouf A. Khalil, MD, PhD, Awarded a \$2.1M National Institutes of Health

Grant

Brigham and Women's Hospital Department of Surgery



Dr. Raouf Khalil *(pictured)* has been awarded a National Institutes of Health grant for his study "Vascular mechanisms of hypertension-in-pregnancy." One objective of Dr. Khalil's study is to understand how the release of placental factors could lead to endothelial cell dysfunction and reduction in vasodilator substances such as nitric oxide and prostacyclin. **Read More**

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Local News

Genetic Background Influences Disease Risk from Single-Gene Variants Broad Institute



Not everyone carrying high-risk variants of a single gene develops disease. Researchers at the Broad Institute, Massachusetts General Hospital, and Harvard Medical School, in partnership with IBM Research and health technology company Color, have discovered a possible reason why. The findings help explain why some genetically predisposed individuals do not develop disease, and also suggest ways to more accurately interpret patients' genetic risk of disease. **Read More**

Exercise Enhancement: Loss of a Specific Enzyme Increases Fat Metabolism and Exercise Endurance in Mice

Harvard Medical School



Harvard Medical School researchers have identified a critical role of the enzyme prolyl hydroxylase 3 (PHD3) in sensing nutrient availability and regulating the ability of muscle cells to break down fats. When nutrients are abundant, PHD3 acts as a brake that inhibits unnecessary fat metabolism. This brake is released when fuel is low and more energy is needed, such as during exercise. **Read More**

Bridging Research and Medicine: Whitehead Institute's Physician-Scientists

Whitehead Institute



Many Whitehead Institute researchers are motivated, at least in part, by the potential of their work to someday impact human health and disease, but for a small group, the connection between research and medicine is more immediate. Whitehead Institute's physician-scientists, researchers who also practice medicine, have a foot in both worlds, and they use that unusual position to act as conduits between lab and clinic, transferring expertise and insights in both directions. **Read More**

Dana-Farber Launches New Center for the Prevention and Treatment of BRCA-Related Cancers

Dana-Farber



Dana-Farber Cancer Institute is launching a new center of excellence – the Center for *BRCA* and Related Genes – dedicated to the care for, prevention of and research into *BRCA*-related cancers. The Center will be directed by Dr. Panos Konstantinopoulos (*pictured*), Director of Translational Research, Gynecologic Oncology at Dana-Farber. **Read More**

How a Biotech CEO Figured Out COVID-19 Surveillance Testing for Fifty Companies with Twelve-Hour Turnaround Times



Back in March, Dr. Sekar Kathiresan *(pictured)*, Chief Executive of Verve Therapeutics, felt he needed to ensure his company could catch any potential infections that might go undetected. So he tapped his connections. Kathiresan and a couple of biotech CEOs in the Kendall Square area got together to see if they could establish a testing infrastructure to keep their employees safe as they continued to work in labs developing potential medicines. **Read More**

 ${\rm MassBio}^{\rm @}$ Welcomes 18 Principal Investigators to its MassCONNECT PI Summer and COVID-19 Cycles

MassBio



The Massachusetts Biotechnology Council (MassBio[®]) recently kicked off the summer and COVID-19 cycles of its MassCONNECT Principal Investigators (PI) program, the only program in Massachusetts that is solely dedicated to serving the needs of PIs in life sciences. After a pilot program in 2019, MassCONNECT PI was officially launched in March 2020 to support academic and industry collaborations and reduce the time between drug discovery and development. **Read More**

New Gene Regulation Model Provides Insight into Brain Development



More often than not, Rbfox RNA-binding proteins bind to a very specific sequence, or motif, of nucleotide bases, "GCAUG." Now, a team of biologists from MIT has found that Rbfox proteins actually bind less tightly — but no less frequently — to a handful of other RNA nucleotide sequences besides GCAUG. These so-called "secondary motifs" could be key to normal brain development, and help neurons grow and assume specific roles. **Read More**

Study Reveals How Two Sex Chromosomes 'Talk' to Each Other to Make a Critical Decision during Development of the Female Embryo





Researchers at Massachusetts General Hospital (MGH) have solved a mystery that has long puzzled scientists: How do the bodies of female humans and all other mammals decide which of the two X chromosomes it carries in each cell should be active and which one should be silent? The MGH team discovered the role of a critical enzyme in the phenomenon known as X chromosome inactivation. **Read More**

COVID-19 Cytokine Storms May Prevent a Durable Immune Response Massachusetts General Hospital



Researchers at the Ragon Institute and Harvard Medical School have found that high levels of some cytokines seen in COVID-19 patients, as part of a cytokine storm, may prevent the development of long-term immunity to SARS-CoV-2, the virus that causes COVID-19. The team examined the spleens and lymph nodes of deceased COVID-19 patients and found a lack of germinal centers, an essential part of a durable immune response. **Read More**

Autism-Cholesterol Link

Harvard Medical School



Researchers at Harvard Medical School, MIT, and Northwestern University have identified a subtype of autism arising from a cluster of genes that regulate cholesterol metabolism and brain development. The researchers say their findings can inform both the design of precision-targeted therapies for this specific form of autism and enhance screening efforts to diagnose autism earlier. **Read More**

Putting a Crown on OMNIVAX

Wyss Institute



To confront the many challenges that infectious diseases pose to mankind head-on, a highly multi-disciplinary team of bioengineers, materials-scientists and

immunologists at Harvard's Wyss Institute has developed a broadly deployable biomaterials-based infection vaccine technology called "OMNIVAX." OMNIVAX was inspired by a fundamentally new cancer vaccine approach created by Dr. David Mooney's group. **Read More**

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Upcoming Events in Boston

August 25 12:00 PM	Community Forum on COVID-19 Research Online
August 25 8:00 PM	Virtual Film Screening and Q&A: From Controversy to Cure Online
August 26 12:00 PM	COVID-19: BioMaking Solutions – Dr. Brendan Manning, Sherlock Biosciences Online
August 26-27 8:00 AM	MassBio State of Possible Conference Online
September 3 12:00 PM	Dana Farber Targeted Protein Degradation Seminar Series Online

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iii Science Jobs in Boston

Scientist, *In Vivo* Biology Carmine Therapeutics

Preceptor, Stem Cell and Regenerative Biology Harvard Department of Stem Cell and Regenerative Biology

Senior Scientist, High Throughput Production Dragonfly Therapeutics

Project Manager, Genome Aggregation Database (gnomAD) Broad Institute

Associate Scientist II, Severe Genetic Disease Research Bluebird Bio

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