The Bench & Beyond

SAN DIEGO BIOMED NEWS

Publications, Publications! A Snapshot

EXCLUSIVE BEHIND THE SCENES

HYPOXIA, REPLICATION TIMING, HIV VS DOPAMINE, NK CELLS, AND MORE

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The Big Picture

OUR MISSION:

Giving every patient a fighting chance.

San Diego BioMed pledges world-class biomedical research that targets many disease areas -- Diabetes, Cancer, Aging, Alzheimer's, Asthma, Lupus, Multiple Sclerosis, Dementia and Drug Use Disorder, HIV Vaccines, and Parkinson's Disease. We are committed to accelerating medical advances that maintain health and improve quality of life.

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San Diego BioMed News Link

Publications

SEE THE LATEST PUBLICATIONS FROM LABS AT SAN DIEGO BIOMED

While new discoveries are the grand indicator of success at San Diego BioMed, the impact truly occurs when these discoveries are published in international scientific journals and made accessible to the community. This information can then be used by scientists to advance therapies or cures. This is why paper publications are pivotal to the job.

“CD16a pairs form the basal molecular subunit for the NK-cell ADCC lytic synapse,” published in *The Journal of Immunology*

Link to Read

TANIA CID FROM THE MURIN LAB

Congratulations to the Murin Lab for the publication of their first paper! The Journal of Immunology is a well-established international scientific journal.
Dr. Daniel Murin is San Diego BioMed’s youngest PI and his work is a testament to determination, a network of support, and state of the art innovative science.

In this study, researchers Daniel Murin and Tania Cid investigated the complex molecular structure formed between white blood cells, called natural killer (NK) cells, and another target cell. Their experiments show, for the first time, how a region that responds to stimuli (CD16a) is uniquely arranged on the surface of these NK cells. They used novel cutting-edge technology and techniques from MINFLUX nanoscopy to isolate and pinpoint the exact location of CD16a with incredible precision—down to just 2.5 billionths of a meter. Through this they discovered that pairs of CD16a are likely the default (resting) state of the NK cells. This discovery is significant as it can help explain why certain antibody-based treatments work better for some people than others. Dr. Murin comments, “we are so excited to make our mark in academia and are looking forward to building on this work in the future!”

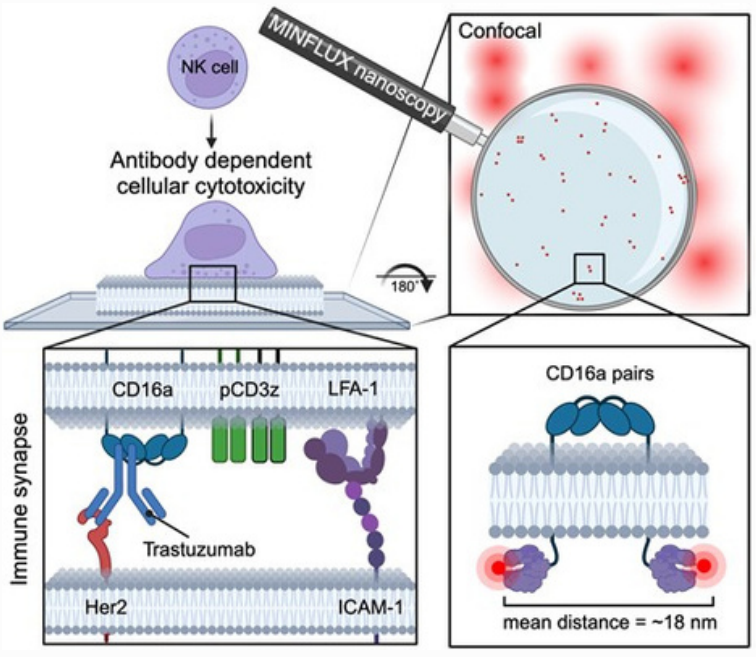


Figure. The figure above shows a conceptualized visual representation of the magnifying process used with MINFLUX nanoscopy that revealed the CD16a pairs.

“Defining the hypoxic thresholds that trigger blood-brain barrier disruption: the effect of age,” published in *Aging-US*

Link to Read

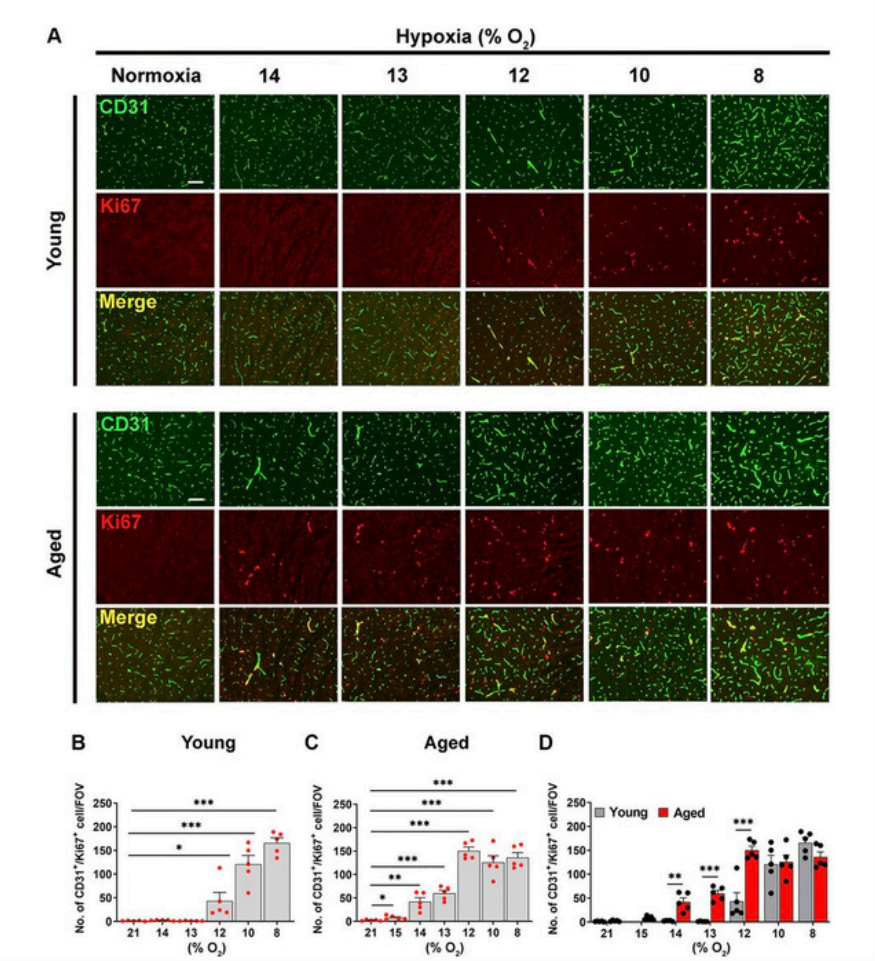


Figure. In the figure above, images of the midbrain under different levels of Hypoxia are captured through colored “stains,” green to mark the targeted cell and red for it’s proliferation. At the top are samples from a younger age group, which shows much less proliferation than the older age group displayed on the bottom. This shows the age-related differences in response to Hypoxia.

In this study, researchers Dr. Richard Milner, Sebok Halder, and Arjun Sapkota investigated how aging affects the brain's vulnerability to low oxygen, known as Hypoxia.

They studied the Blood Brain Barrier (BBB) which is an intricate network of really tight blood vessels that act like a security system for your brain. It protects your brain by controlling what can pass into it from your blood, letting good stuff in like oxygen and nutrients, while keeping bad stuff out, like bacteria and toxins. The Milner Lab identified the specific oxygen levels that disrupt the BBB, with higher disruption evident in older age groups. These findings are important for understanding age-related cognitive decline and the potential risks faced by individuals with chronic oxygen-limiting conditions including Asthma, Sleep Apnea, Emphysema, and heart disease.

The Milner lab additionally looked at the effects of Hypoxia on specialized immune cells called microglia. Microglia activation is a sign of brain inflammation. Preclinical experiments exhibited a spike in microglial activation across all age groups when affected by Hypoxia, but the older group showed a much greater increase. The persistent microglial activation observed here reflects a broader concern in aging: low-grade, chronic inflammation that quietly drives disease over time. Overall, this reinforces their prior findings in age-related cognitive decline and suggests that repair mechanisms may weaken over time.

“Timing is Everything.” - Dave Gilbert

“MASTER TRANSCRIPTION-FACTOR BINDING SITES CONSTITUTE THE CORE OF EARLY REPLICATION CONTROL ELEMENTS,”
PUBLISHED IN *THE EMBO JOURNAL*

Link to Read

DNA has become a household term to define the “being” of any living thing, and is even clumsily used to refer to inanimate objects. Most of us are familiar with DNA’s 4 letter alphabet, which encodes the blueprint for life. Today, we can chemically synthesize any DNA code, we can create billions of copies of that code in a test tube, and we can even cure diseases by correcting mistakes in the code. It must come as quite a surprise then, that we still do not know the genetic code that tells cells how to replicate DNA. This is a major mystery in molecular biology and is the motivation for research in the Gilbert lab at San Diego BioMed.

The Gilbert lab believes that the secret to understanding how DNA replicates lies in understanding why it bothers to replicate the code in any particular order; after all, it is commonly thought that the sole purpose of DNA replication is to make one complete copy of the DNA before the cell divides into two. The Gilbert lab likes to remind people that, in a living cell, it’s not just DNA that replicates. Rather, the entire structure of chromosomes, including all of their associated components, must be dismantled, the DNA copied, and all the infrastructure rebuilt. This rebuilding process imparts flexibility to change the infrastructure and Mother Nature is too resourceful to squander this opportunity.

The Gilbert lab has spent over 30 years compiling evidence that chromosomes are replicated in segments or “domains” and that the temporal order in which domains are replicated dictates what type of chromosomal infrastructure they assemble. Indeed, the Gilbert lab has shown that different types of cells replicate chromosome domains in a different order and cells from diseased tissues have unique alterations in this replication timing program. In 2019, by systematically removing parts of chromosomes, the Gilbert lab discovered specific control centers that determine this temporal order. However, they were not able to sufficiently pinpoint where these control centers are in order to understand how they work.

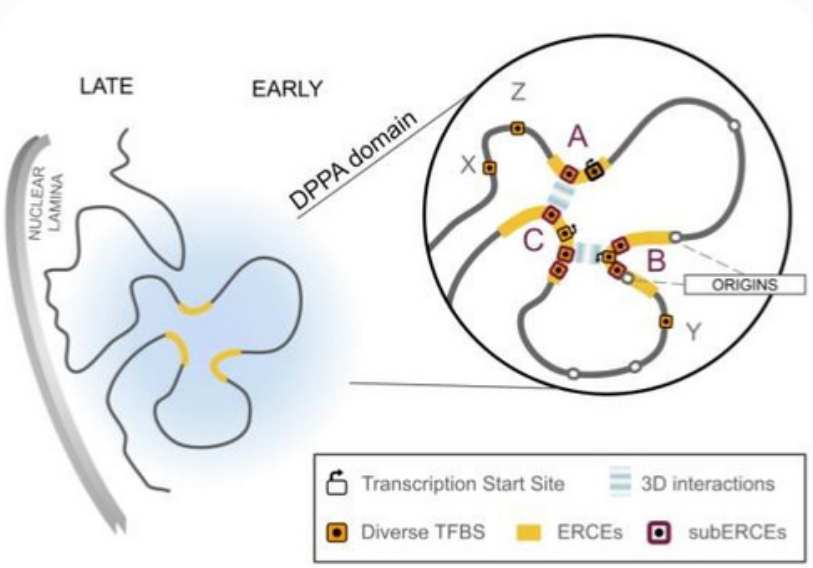


Figure. While paying close attention to the icon guide, you can trace the figure above and see that the component that plays into DNA replication timing can be dissected into subparts with many roles. Understanding these roles may help in discovering ways to alter the cell’s fate.

In the current work, published by The European Molecular Biology Organization (EMBO J.), researchers Dr. Dave Gilbert, Takayo Sasaki, and Satoshi Uchino have shown that these control centers contain numerous binding sites in the DNA for multiple proteins known as “master transcription factors”, whose job is to turn individual genes on and off to alter the identity of cells. This work unveils a simple but elegant means by which cells coordinate changes in gene regulation with changes in replication timing. And the purpose is quite sensible; it is known that turning genes on and off can be a fleeting event that fades away as cells experiment with new fates and revert back to their old ways. But, if the master transcription factors are diverse and abundant enough to bind all the sites in the replication control centers, they can trigger changes in replication timing that could alter the infrastructure of chromosomes and make the switch to the new cell type irreversible, whether it be a normal or diseased cell type. What is still not known is whether these switches are encoded in the alphabet of the DNA and what that code might be. Understanding that code could allow us to alter the fates of cells or switch diseased cells back to normal. Stay tuned for the Gilbert lab’s subsequent studies!

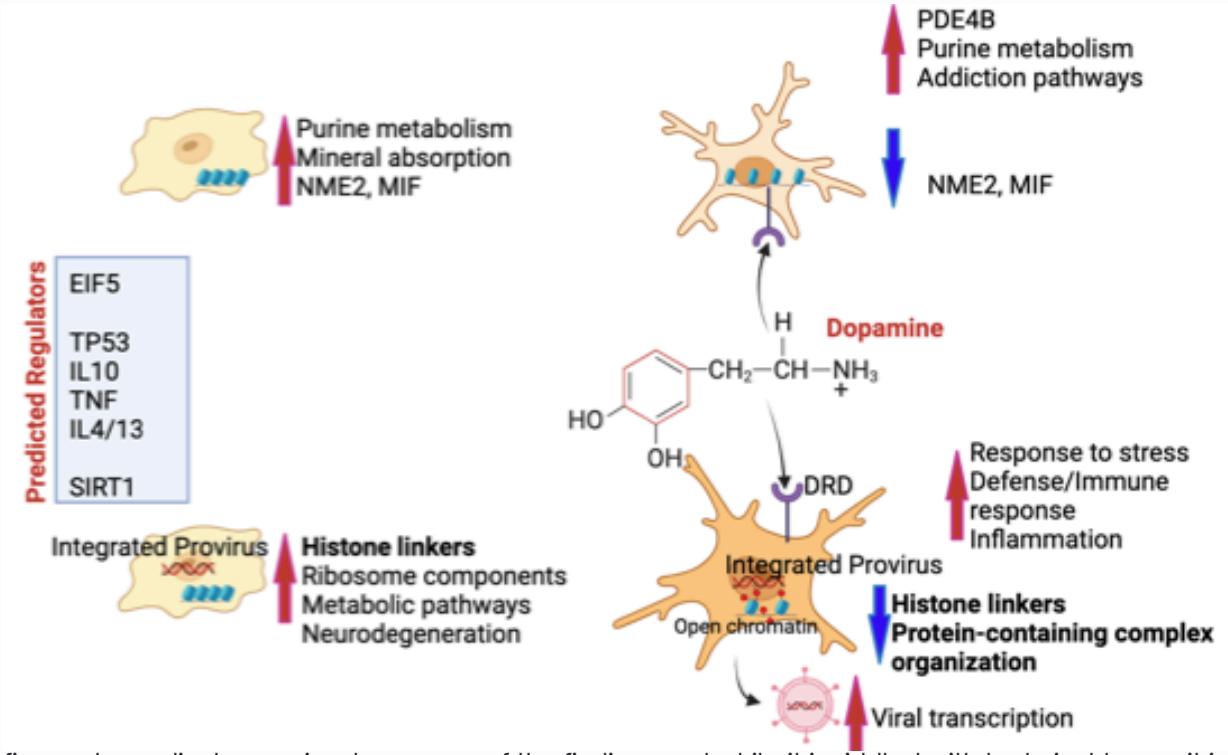
Link to Read

"A Single-Cell Perspective on the Effects of Dopamine in the Regulation of HIV Latency Phenotypes in a Myeloid Cell Model"

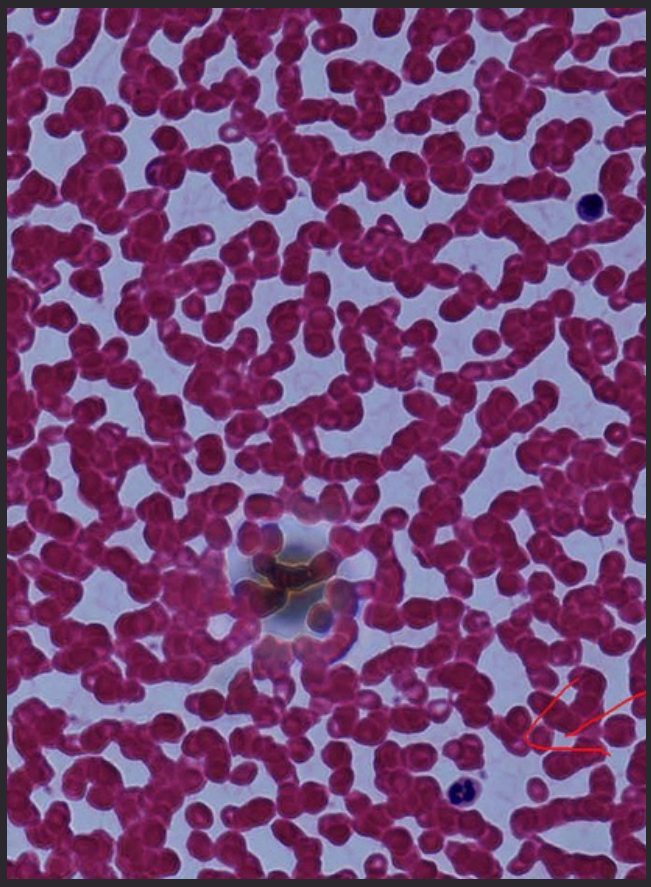
PUBLISHED IN *MULTIDISCIPLINARY DIGITAL PUBLISHING INSTITUTE (MDPI)*

The main challenge in treating HIV is that some infected cells hide in parts of the body, like the brain, where they can't be reached by the immune system or treatments. Another issue is that people at high risk for HIV infection, like those who use drugs, often have a harder time controlling the virus. This is because substances like dopamine, which are at high levels in the bodies of people who use drugs, can "wake up" the hidden virus and cause inflammation.

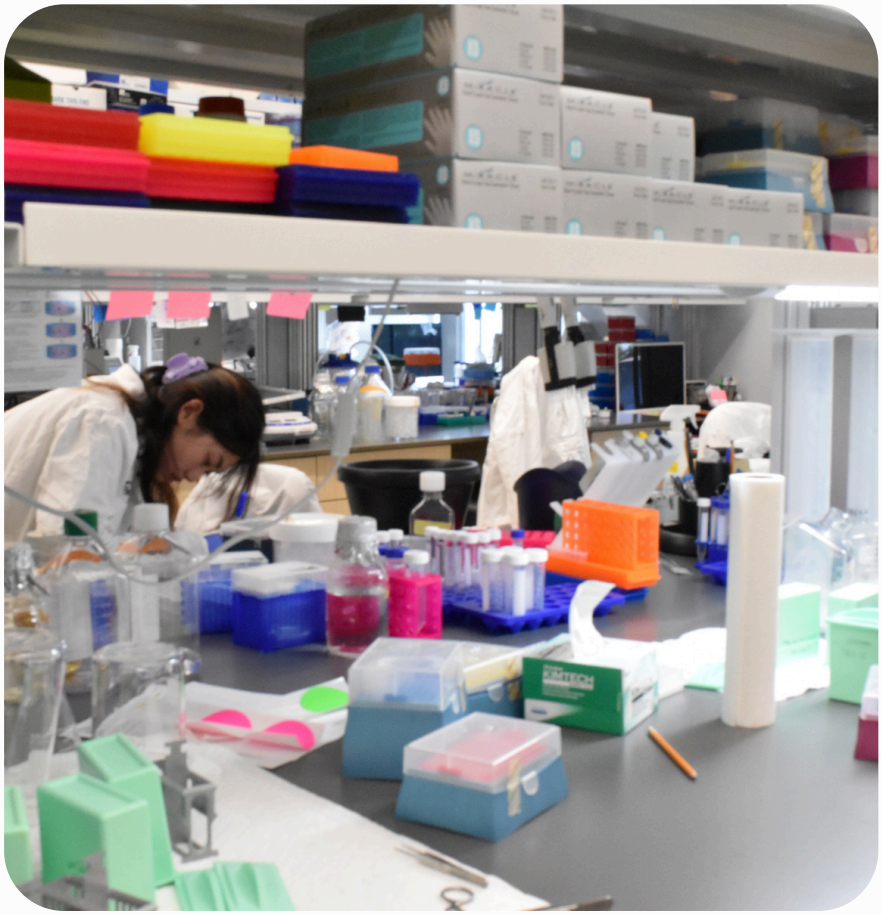
In this study, researchers in the Marcondes Lab looked at different types of cells in the body that could be affected by HIV. They focused on two groups: the cells that are silently infected (but not producing the virus) and the cells that are actively making the virus. They also compared these to healthy cells that aren't infected at all. The researchers studied how high levels of dopamine, similar to what's found in drug users, might affect these cells. The Marcondes Lab's goal was to develop a method to identify the silently infected HIV cells and figure out how HIV can remain dormant and reactivate in both non-drug users and drug users. They used advanced technology to look at individual cells and see how HIV and dopamine interact. This study overall helps us understand more about how drugs might affect brain damage in people living with the virus.



The figure above displays a visual summary of the findings and while it is riddled with technical terms, it is simpler to understand the bigger picture. Each section shows an innate immune cell under different conditions. The upper left shows a healthy immune cell that stays in a balanced state with the help of certain genes that support normal metabolism and nutrient absorption. The bottom left shows HIV-infected cells (where the virus is present but not active), in which they stay quiet through high levels of proteins that keep the DNA tightly packed. But this comes with increased cell activity that might cause brain damage over time. The right side of the figure shows the presence of high dopamine which causes immune cells to activate pathways linked to addiction and reduce the expression of helpful genes. Ultimately, HIV-infected cells exposed to dopamine lose their ability to stay silent, leading to inflammation and reactivation of the virus.



Behind the scenes



THE LAB SPACE IS SAN DIEGO BIOMED'S EPICENTER OF TRAFFIC AND LIFE. NO ONE DAY AT THE BENCH IS THE SAME.

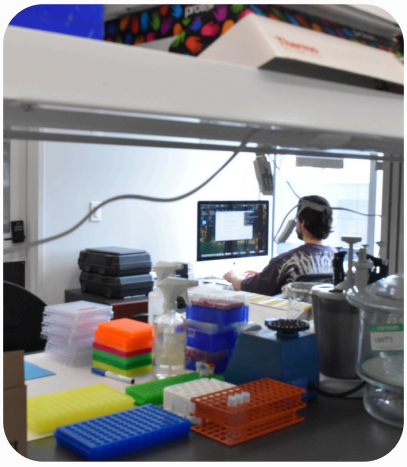
PICTURED TO THE LEFT: KAYLIN AU OF THE MARCONDES LAB

PICTURED BELOW: FRANCISCO ALMANZA OF THE DAVIES LAB

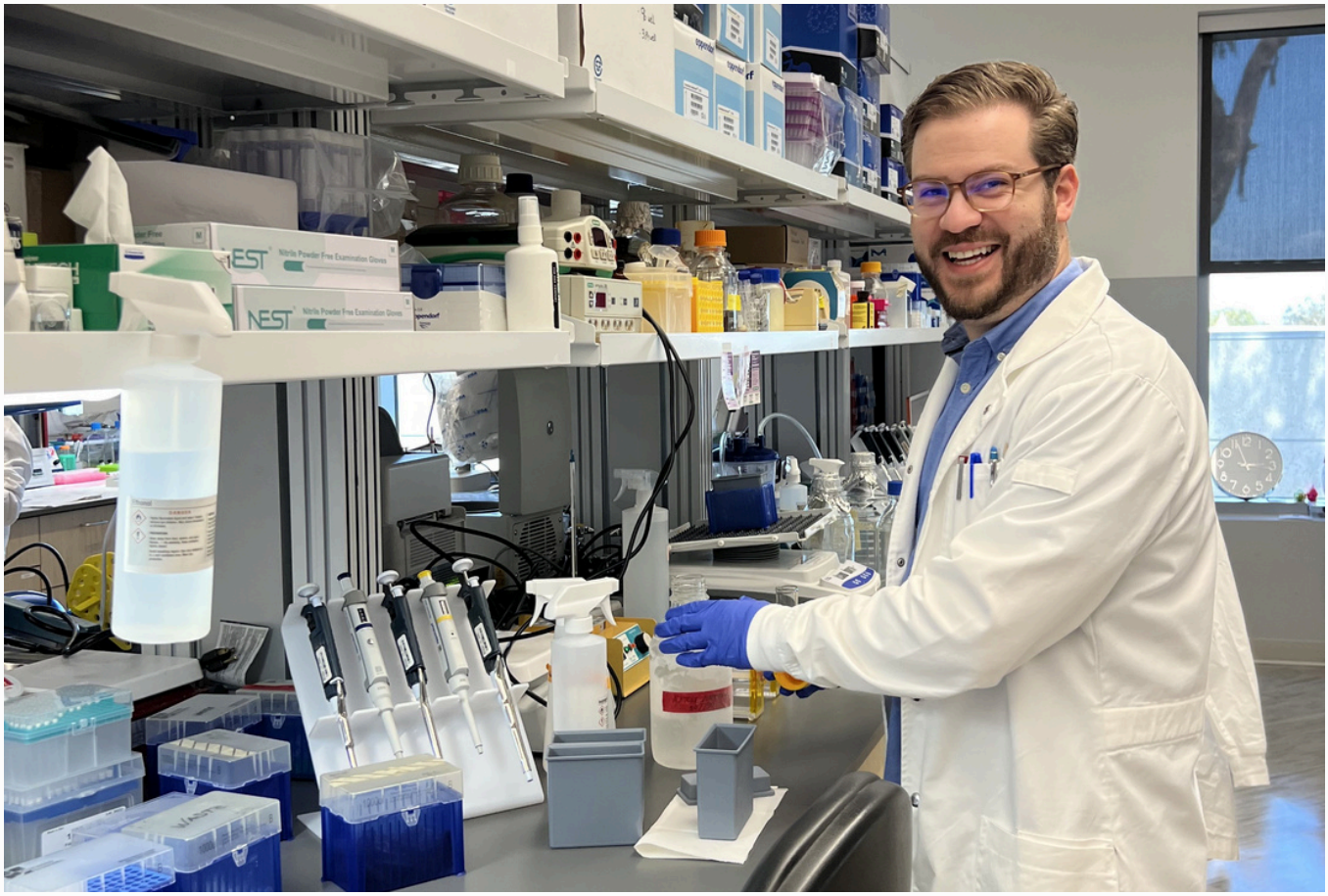
The daily lives of the technicians

Hear some words about daily work at San Diego BioMed from our Research Technicians pictured, Kaylin Au and Francisco Almanza --

Kaylin: "My time at San Diego BioMed has allowed me to engage in hands-on, detail-oriented work that contributes to meaningful outcomes. I enjoy the day-to-day work of solving problems, analyzing data, and being part of a process that advances scientific understanding or supports important applications. The structured environment, combined with the opportunity to continually learn and apply new techniques, keeps me motivated and curious every day. What makes it even more rewarding is being surrounded by knowledgeable, supportive colleagues—I'm constantly learning with and from them, which fosters both personal and professional growth in a collaborative environment."



Francisco: "A day at San Diego BioMed for me involves a blend of wet lab work and data analysis. I focus on flow cytometry experiments, staining human PBMCs and analyzing the resulting flow data. I also work on preparing libraries for single-cell RNA sequencing (scRNA-seq), so I try and balance the workload accordingly. I have learned a lot in my time here and hope to continue growing."



Celebrating National Cancer Survivors Day - June 01

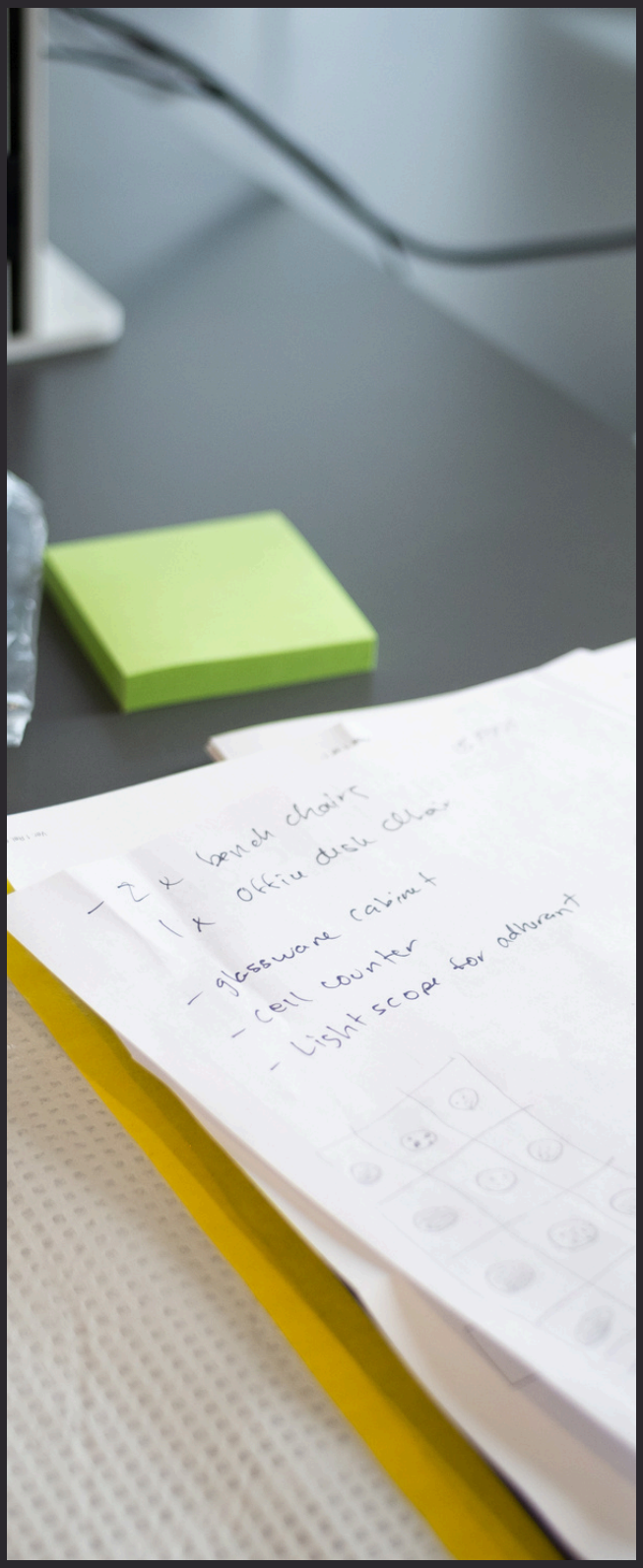
“This experience has also brought an unexpected gift: a renewed perspective on life, a deeper sense of kindness towards myself, and a profound reminder to live each day to its fullest." - Daniel Lima, MD

The San Diego BioMed team encourages the community to rally together as a moving celebration of life for those who are living with a history of cancer. More people are surviving cancer and living longer after diagnosis than ever before. However, despite this progress, a cancer diagnosis can leave a host of problems in its wake. This is a time to acknowledge the victories, both big and small, and to look forward to the future with optimism and joy. It is also a call to action for further research, more resources, and increased public awareness to improve the lives of cancer survivors.

Today we would like to support, honor, and share the journey of San Diego BioMed’s own cancer survivor -

Daniel Lima; Thyroid Cancer survivor
Statement: "In 2019, a thyroid nodule led to a cancer diagnosis – a discovery made by a colleague, as I was already an MD. The journey through tests, surgery, and treatment was significant, but as anyone who has faced cancer knows, its impact is ongoing. From daily medication and regular blood work to the permanent absence of a part of my body, it's a constant presence."

Keep up with San Diego BioMed today!



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