Fred Hutch
Cancer Center

Building the Foundation of Discovery

An opportunity to accelerate scientific progress and expand our understanding of biology

Beyond
50

Discoveries with life-changing potential

Some of the biggest leaps in medicine happen when scientists researching fundamental questions have the freedom and resources to follow where the science leads. We have penicillin because Alexander Fleming noticed that mold in his Petri dish was killing the bacteria he was studying, and he wanted to know how.

At Fred Hutch Cancer Center, research into how viruses infect cells — conducted in our Basic Sciences Division during the 1980s and 1990s — made it possible for blood cancer patients today to receive CAR T-cell therapy. This immunotherapy, made of turbocharged versions of a patient's immune cells, is now used in cancer centers across the world to treat and cure some of the sickest patients.

Real-world progress comes from unraveling fundamental questions about how cells grow, work together, defend against pathogens and disease, and change with age. **A deeper understanding of fundamental biology is critical to knowing what goes wrong in diseases including cancer, and, most important, what we can do about it.**

Three ways we do science differently

Fred Hutch scientists are innovators who are asking and answering questions that others have not even thought of yet. They are relentlessly pushing the boundaries of what we currently know about biology and creatively challenging the ways research has been done before. To do so, they are:

- **Inventing new technologies**
- **Disrupting established paradigms**
- **Creating entirely new fields**

A Petri dish under a microscope in the Singhvi Lab.

Breakthroughs begin here

We can't predict what the next breakthrough will be. But we know from 50 years of trailblazing research that bringing together top scientists in a world-class research environment makes it more likely for the next leap to happen here.

When we push science forward, we also accelerate the timeline for new discoveries to reach those in our community who don't have time to wait.

The investments made in fundamental research now will enable the treatments and cures of tomorrow, making life beyond cancer and related diseases possible for more patients. **We invite you to join us in creating the conditions for discovery and asking and answering the questions that will electrify the next decade of life sciences research.**

Beyond 50

As we mark our 50th Anniversary in 2025, Fred Hutch is looking beyond what's possible today to a new era of discovery. With your partnership, our Campaign for Fred Hutch will transform the pace and scale of innovation so we can redefine cancer and infectious disease for generations to come.

Members of the bone marrow transplant team, including Paul Neiman, MD, PhD, first director of the Basic Sciences Division (left), and E. Donnall Thomas, MD (center).

Cultivating a culture ripe for discoveries

The Basic Sciences Division at Fred Hutch was founded in 1981 as an evolution of work already underway in immunology and cancer biology alongside **E. Donnall Thomas, MD**, as part of his Nobel Prize–winning development of bone marrow transplantation to cure leukemia and other blood diseases. **Early on, our center leadership knew that fundamental science would be essential for future advances in care.**

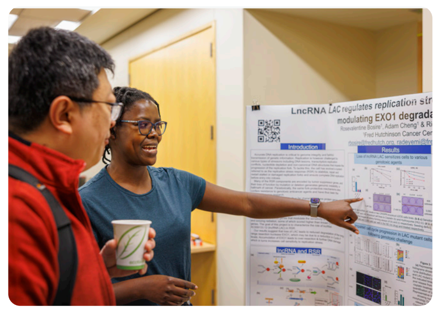
The founding researchers at that time adopted an egalitarian philosophy that still holds true today as part of a unique culture primed for scientific progress. All faculty members have an equal say in division matters, and success is measured in the quality of science — not the number of grants secured. More than 40 years on, this approach continues to foster scientific excellence and attract talented researchers.

Fred Hutch has been home to **three** Nobel prizewinners, including Dr. Thomas, former President and Director **Lee Hartwell, PhD**, who discovered key regulators of the cell cycle, and current professor **Linda Buck, PhD**, who discovered the receptors and organization of the olfactory system.

Science as a team sport

The intentional choices of the Basic Sciences Division encourage:

- **Curiosity-driven research** and the **freedom to take risks** with the support and encouragement of division leadership, who know the importance of following where the science leads
- **Collaboration** because faculty members do not compete against each other for resources
- **Mentorship**, as future successes are shaped by junior faculty members and trainees, including graduate students and postdoctoral fellows



Postdoctoral Research Fellow Rosevalentine Bosire, PhD, shares her work at a poster session.

The cycle of discovery

Fundamental science has been a core element of Fred Hutch's success from the start. It's the first step in transforming care and finding cures, followed by science that translates these discoveries into new treatments, then clinical trials. When other areas of research hit a roadblock or new information is learned from patients, the cycle repeats. Fundamental science is also a key part of our status as one of 57 National Cancer Institute–designated Comprehensive Cancer Centers in the country, and just one of two such centers in the Pacific Northwest.

The powerhouse combination of Fred Hutch philanthropy and science

Anatomy of a scientific success

More than two decades ago when she set out to extract and study the kinetochore —a molecular machine that assembles every time a cell is ready to divide — she wasn't sure it would work. She was determined to try anyway.

"Good fundamental science is inherently risky," says Sue Biggins, PhD, director of the Basic Sciences Division and Howard Hughes Medical Institute Investigator.

Sue Biggins, PhD, joined Fred Hutch in 2000 and has served as director of the Basic Sciences Division since 2019.

Her background was in genetics, not biochemistry. **Her colleague, biochemist Toshio Tsukiyama, PhD, DVM, was more than happy to help her with the techniques she needed to learn.**

She knew the process was going to be long and hard. **She had a graduate student who was committed to seeing the experiments through.**

Her proposal for federal funding was rejected because she lacked proof-of-concept data. **A foundation grant allowed her to begin testing her bold idea.**

Building on breakthroughs and donor support

Biggins Lab Postdoctoral Research Fellow **Anderson Frank, PhD**, won an early career training award from the National Institutes of Health to help move Dr. Biggins' technique from yeast cells to human cells for the next phase of kinetochore research. Along the way, he's learning how to run a lab from Dr. Biggins so he's ready to start his own lab when the time is right. This is an example of the dual power that trainees have to advance research now and in the future.

Leading by example

With these key ingredients, her team was the first to isolate the kinetochore from yeast cells so it could be studied in test tubes.

The system she developed has helped her make seminal contributions to our understanding of cell biology that she continues to build on. These findings are changing our understanding of biology and may shed new light on cancer and other diseases.

"At Fred Hutch, I always felt that I was expected to try the harder things as opposed to doing research that could be done somewhere else," says Dr. Biggins. Now, as the division director overseeing nearly 30 independent labs, she's fostering the same culture that helped her succeed. And consistent funding plays a large role in setting the stage for breakthroughs.

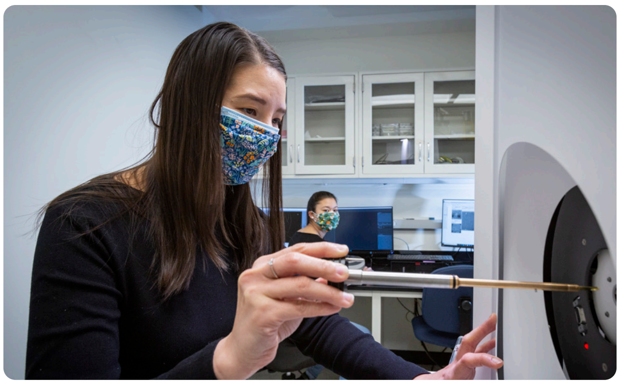
Dr. Biggins has experienced firsthand how donor support can provide the stable launchpad from which she and her colleagues achieve success.

As federal funding for science overall has slowly decreased over the last few decades and changing priorities may accelerate that trend, **Dr. Biggins sees an opportunity for supporters to make an even greater impact on the science that seeds breakthroughs.**

Investing in the tools of the scientific trade

When **Barry Stoddard, PhD**, professor, joined Fred Hutch in 1992, the standard way to visualize the structure of a protein was to immobilize it in a crystal and look at it with X-rays. It's similar to how the double helix structure of DNA was first discovered. But not every protein crystallizes well — especially those that are large, complex, or particularly flexible.

Thanks to generous gifts, Fred Hutch purchased equipment for cryogenic electron microscopy (cryo-EM), a rapidly developing technology that gives researchers unprecedented insight into the tiniest biological structures.



Melody Campbell, PhD, adjusts cryo-EM hardware in 2021.

Scan the QR code to watch a time-lapse of the construction of our cryo-EM facility.

Unlocking the mystery of proteins

Proteins, which perform the bulk of the work in our cells, give hints about what their job is through their structure. Now, researchers can freeze their protein of choice and visualize it from many angles and in different configurations through cryo-EM.

Samples are prepared at such a cold temperature that ice forms in a "vitreous" glass-like state for the clearest view of what's inside. Scientists use advanced computational methods to turn the raw data into 3D models that can show exactly how a protein interacts with other molecules.

"Cryo-EM is revolutionizing structural biology," Dr. Stoddard says. In less than a year, his team was able to solve the structure of a protein they had been working on for a decade.

New technology draws innovative researchers

To spearhead this revolution at Fred Hutch, cryo-EM expert **Melody Campbell, PhD**, assistant professor and scientific director of the Electron Microscopy Core, arrived in 2020 to support the construction of the new facility. She focuses on elbow-shaped proteins called integrins, which are involved in cell growth and communication and may have a hand in cancer and other diseases.

Dr. Campbell's work has already led to a collaboration with University of Washington Nobel Laureate David Baker, PhD. Together, they designed a new protein that binds with an integrin, using her model to know where the two needed to attach. The designed protein promotes wound healing and could be applied as a coating on titanium screws and other implants used for surgical repair.

Summer Intern Anthony Kemp helps prepare a sample.

Fred Hutch scientists are ... inventing new technologies

Steven Henikoff, PhD, professor and Howard Hughes Medical Institute Investigator, joined in 1981.

From deciphering DNA's software to detecting cancer earlier

Almost every cell in the human body has the same DNA with instructions to create every protein it will ever need. But different cells serve different functions and require different combinations of proteins. **Steven Henikoff, PhD**, and his team found a way to map chromatin, the organizational structure of DNA that allows genes to be switched on and off to make different kinds of cells.

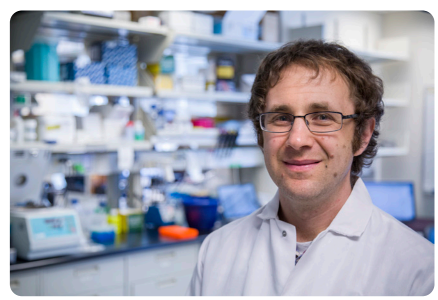
This method, called CUT&Tag (Cleavage Under Targets and Tagmentation) gives the highest resolution picture of the system that acts like software by modifying how DNA is read from cell to cell.

A slight variation of this technique, called CUTAC (Cleavage Under Targeted Accessible Chromatin) has allowed Dr. Henikoff to **mine previously inaccessible genetic information** from tumor samples preserved in paraffin blocks. Tumor samples are commonly stored this way, which makes genetic material unreadable to standard sequencing methods. Dr. Henikoff collaborated with **Eric Holland, MD, PhD**, senior vice president and director of Fred Hutch's Human Biology Division, to test existing samples.

Unexpectedly, this work revealed an overlooked mechanism driving aggressive brain and breast cancer hiding in chromatin — and a biomarker that could both aid in early detection and provide a target for future precision therapies. Fred Hutch has collections of preserved samples dating back decades, so the next step is to expand this study to include other cancer types.

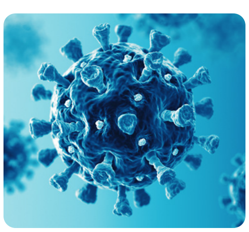
Forecasting how viruses change like the weather

Viruses like influenza and COVID-19 always seem to be one step ahead of vaccine researchers as different strains emerge. These changes are caused by random mutations that accumulate as viruses spread. Small changes to the outside of a virus can make it harder for our immune system to recognize the danger, even if a vaccine has trained it using a past relative.



Jesse Bloom, PhD, professor and Howard Hughes Medical Institute Investigator, joined in 2011.

Jesse Bloom, PhD, and his collaborators created a method to identify the most concerning mutations to the "spike" protein on the COVID-19 virus and predict which ones may pop up in the near future.

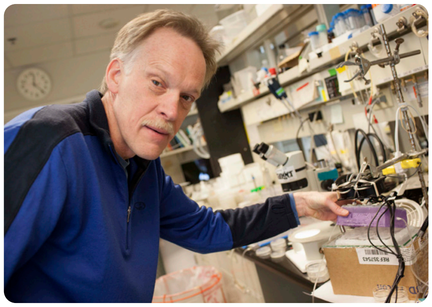


SARS-CoV-2 virus with spike proteins. Illustration by Getty Images.

This technique, called pseudovirus-based deep mutational scanning, allows Dr. Bloom to **study how infectious thousands of variations on the "spike" are** in a single experiment — and how well they evade the immune system. He uses pseudoviruses, which act like the real virus but cannot reproduce or spread, for a safer research environment.

The result could be a way to predict how the COVID-19 virus and other viruses could evolve in the future, including more infectious mutations that researchers could use to inform public health measures and vaccine development as the situation changes.

Fred Hutch scientists are ... disrupting paradigms



Mark Roth, PhD, professor, joined in 1989.

Hitting the pause button for the critically ill

Inspired by stories of people pulled out of icy water appearing dead, only to be revived later when they warmed up, **Mark Roth, PhD,** has been looking for ways to replicate this death-defying state to buy precious time during a life-threatening medical issue.

He first narrowed in on oxygen deprivation as a common thread in unlikely survival stories. He then focused on natural molecules that decrease the demand for oxygen. After investigating several of these agents, he chose iodide because it is safe to administer.

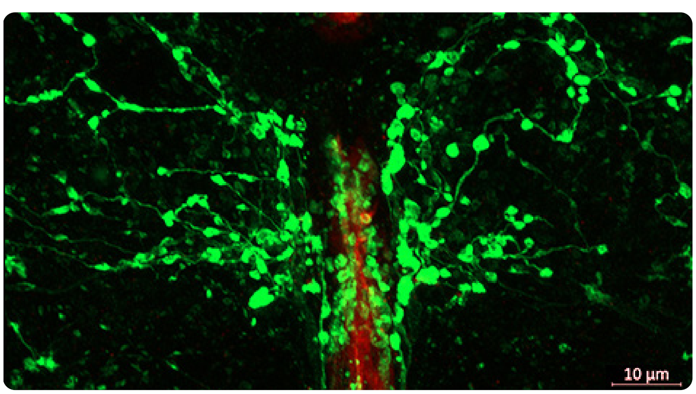
The compound not only reduces the need for oxygen but also protects tissue from damage caused by oxygen's rapid return. Dr. Roth saw an opportunity to **make a difference for heart attack patients**, who can suffer injury when blood rushes back to the oxygen-deprived areas of the heart after treatment. His goal is to reduce mortality, as well as heart failure rates, with the potential to explore expanding use of the compound to other types of trauma.

What fat cells are saying to the brain

The brain manages our metabolism by maintaining a delicate balance between how much we eat and how active we are. Cascading signals from the gut after a meal help the brain judge how full we are and how much energy we have available. But that's not the full picture.

Akhila Rajan, PhD, found that fat cells send signals to the fly brain using molecules that control many of the body's functions, including immunity, reproduction, and cognition. These signals — something flies and humans have in common — are a completely new puzzle piece in our picture of homeostasis, or how the body keeps everything running smoothly and in balance.

Akhila Rajan, PhD, associate professor, joined in 2016.



Connections between neurons that receive signals from fat cells (green) and insulin producing neurons (red) in a fruit fly brain.

The Rajan Lab is studying how problems with this signaling pathway **can lead to obesity and diabetes, reduced immune function, and even cognitive decline**. Dr. Rajan and her team are also looking for other ways fat cells might communicate with the brain and the immune system.

Her results could reveal new ways to manage obesity, which is a risk factor for 13 types of cancer including breast, colorectal, and pancreatic.

Fred Hutch scientists are ... creating new fields

Harmit Malik, PhD, professor and associate director of the Basic Sciences Division, joined in 1998 as a postdoctoral fellow in the Henikoff Lab, then as a faculty member in 2003.

Viral clues for cancer prevention and treatment

Did you know that 8% of your DNA comes from ancient viruses that infected your ancestors? **Harmit Malik, PhD**, found viral "fossils" in human genomes after theorizing that retroviruses, which insert a copy of their genetic material into ours when they infect us, may leave a trace behind in some cases. And if a retrovirus infects an egg or a sperm, the changed DNA is passed down through the generations.

This revelation helped Dr. Malik create the field of **paleovirology**, the study of extinct viruses. Using tools developed to study the evolution of genes, researchers can even predict how long ago these ancient viruses plagued humans.

With his now-retired colleague, virologist **Michael Emerman, PhD**, Dr. Malik first explored this idea with human immunodeficiency virus (HIV), tracking its evolution in primates across 33 million years. They uncovered an arms race as both the virus and primate cells evolved in response to each other. Some viral DNA was even co-opted to serve completely different, beneficial functions in primates, including humans.

It's not all looking backwards, though. Analyzing winning strategies from our remote past may help identify and refine future therapies for viruses like HIV, which is linked to an increased risk for many cancers. And other Fred Hutch researchers are building on this work to investigate viral DNA that becomes more active in certain cancers to look for precision treatment targets.

As paleovirology itself evolves, we may learn more strategies for preventing the estimated 15% of cancers caused by viruses.

A smart thermostat for the gut's immune response

Jhimmy Talbot, PhD, assistant professor, joined in 2021.

While most of the body's neurons are in the brain, a smaller network lines the gut and regulates the complex process of digestion, including activating muscles and releasing hormones at different stages. This network can also influence appetite, mood, and sleep, which is why it's often referred to as the "second brain."

Jhimmy Talbot, PhD, and his team discovered that these neurons are also in constant contact with the immune system, but not in the way that he expected.

Immune cells maintain a natural barrier between the contents of our gut and the rest of our body to keep pathogens out that might hitch a ride on our meals. But when food arrives to be digested, **neurons temporarily dial down the immune response to allow more nutrients to be absorbed**, like a thermostat calibrated with different settings for during and after meals.

Knowing how the "second brain" senses the food we eat to bring in nutrients while keeping pathogens out opens the door to a new understanding of how a dysfunctional thermostat may play a role in irritable bowel disease (IBD), colorectal cancer, and more.

Join Us

Fred Hutch's trailblazing scientists are charting new courses in the pursuit of answers to fundamental questions about human biology. Their discoveries have the potential to change how we prevent, treat, and cure cancer, infectious diseases, and more. Through the Campaign for Fred Hutch, you can ensure that our cycle of discovery accelerates to meet the urgent needs of our community and patients everywhere. A gift to any of the areas below will be a crucial injection of support for Fred Hutch science.

You may also choose to designate your gift to the director of the Basic Sciences Division to address the most urgent or time-sensitive needs of the division.

Train the next generation of basic scientists – $100,000+

Trainees — including postbaccalaureate scholars, graduate students, and postdoctoral fellows — power discoveries while getting valuable research experience. By the time they complete their training, our early-career scientists have a solid foundation upon which to build new knowledge and pursue tomorrow's advances. But the uncertain future of funding is putting a generation of promising scientists at risk just as they start their careers. Your support can throw a lifeline to trainees and ensure they have the opportunity to contribute to Fred Hutch research and continue on their path within science.

Launch a pilot project – $250,000+

Fred Hutch scientists are brimming with ideas that could lead to the next breakthrough. Now, the future of funding is uncertain, underscoring the importance of developing the exceptionally strong proof-of-concept data required to win the shrinking number of available grants. Your investment can help launch the study of an original idea that would not otherwise get off the ground.

Expand the Basic Sciences Endowment – Gifts of all sizes

Join with other donors to grow the endowment that provides flexible funding that our Basic Sciences Division can count on. This enduring source of support allows Fred Hutch scientists to take risks, pursue their boldest ideas, and maintain the highest level of scientific excellence.

Endow a chair in basic sciences research – $2 million

Fred Hutch faculty are building on 50 years of fundamental science, powering progress to transform how we care for patients. By establishing an endowed chair in basic sciences research, you will link your legacy to our future and ensure a succession of researchers have funding in perpetuity to accelerate the pace and scale of innovation.

Name a lab in the Basic Sciences Division – $500,000+

With a gift of $500,000 or more, we would welcome the opportunity to recognize your generosity by naming a lab in honor of you or someone of your choosing. This physical reminder of your commitment will inspire scientists in that lab and our community for decades to come.

Name, Title, Philanthropic Gifts
1100 Fairview Ave. N. ▪ Mail Stop LG-400 ▪ Seattle, WA 98109 ▪ 206.667.5253 ▪ email@fredhutch.org

Basic Sciences Division Faculty Members

Richard Adeyemi, DVM, PhD
Assistant Professor

Investigating how cells repair DNA damage to prevent cancer formation and find new ways to treat chemotherapy-resistant cancers

Yasuhiro Arimura, PhD
Assistant Professor

Visualizing the structure of DNA-linked molecular complexes that change during the cell cycle and malfunction in cancer and other diseases

Jihong Bai, PhD
Professor

Studying how neurons communicate and discovering ways to rewire neuronal circuits that go awry due to disease

Sue Biggins, PhD
Professor and Director, Basic Sciences Division
Howard Hughes Medical Institute Investigator*

Uncovering the machinery that ensures cells preserve the correct genetic information each time they multiply

Jesse Bloom, PhD
Professor
Howard Hughes Medical Institute Investigator*

Tracing the evolution of viruses to understand how they evade the immune system for better vaccines and prevention strategies

Linda Buck, PhD
Professor
Howard Hughes Medical Institute Investigator Emerita*
Nobel Laureate

Investigating how the immune system protects the brain from viral infection, and the long-term risks of this protection failing

Melody Campbell, PhD
Assistant Professor
Scientific Director, Electron Microscopy Core

Visualizing integrins, flexible cellular machines that let cells interact and communicate with other cells and their environment

Robert N. Eisenman, PhD
Professor

Discovering cellular pathways that can be used to slow the progression of cancer

Steven Hahn, PhD
Professor

Rewriting our understanding of how cells transcribe their genes and what happens when this process goes awry in cancer

***Howard Hughes Medical Institute Investigators**

Fred Hutch has been the proud home of 13 Howard Hughes Medical Institute Investigators, including Dr. Biggins and other 11 basic scientists, four of whom are current faculty members. This recognition from the prestigious nonprofit showcases the quality of science happening in our labs every day.

Basic Sciences Division Faculty Members

Steven Henikoff, PhD
Professor
Howard Hughes Medical Institute Investigator*

Creating powerful tools to see how genes are turned on and off, and how this is different in healthy cells compared to cancer cells

Megan Koch, PhD
Assistant Professor

Expanding our understanding of how breast milk influences an infant's immune system, microbiome, risk of allergies, and more

Christopher Lapointe, PhD
Assistant Professor

Using advanced microscopes to make movies of the protein assembly line to understand how it malfunctions in disease

Nicolas Lehrbach, PhD
Assistant Professor

Investigating how cells recycle old or damaged proteins and the role of this process in aging, cancer, rare genetic disorders, and neurodegenerative diseases

Harmit Malik, PhD
Professor and Associate Director, Basic Sciences Division
Howard Hughes Medical Institute Investigator*

Studying how genes and proteins with opposing functions drive evolutionary changes within cells and species, with implications for cancer and viral infections like HIV

Cecilia Moens, PhD
Professor
Raisbeck Endowed Chair for Basic Science

Untangling the timeline of neuron development by studying zebrafish embryos, including genes that control the process, which can also promote cancer later in life

Susan Parkhurst, PhD
Professor
Mark Groudine Chair for Outstanding Achievements in Science and Service

Uncovering the components cells use to repair injuries to their outer surfaces and how those components can be used to accelerate healing

James Priess, PhD
Professor

Understanding how the cell nucleus deteriorates with age and how this process can be slowed or prevented to extend lifespans

Akhila Rajan, PhD
Associate Professor

Learning how fat tissue communicates with the brain and how these pathways can cause obesity, diabetes, and dementia

Mark Roth, PhD
Professor

Exploring how to extend the limits of survival during trauma and other life-threatening conditions

Basic Sciences Division Faculty Members

Manu Setty, PhD
Assistant Professor

Developing computational models to map how stem cells develop and how that process can change with blood cancer

Aakanksha Singhvi, PhD
Associate Professor

Illuminating the “dark matter” of the brain, called glia cells, which affect how neurons send signals and may play a role in many diseases

Gerald Smith, PhD
Professor

Investigating how bacteria and yeast repair their DNA when it breaks, which could inform the development of new antibiotics

Sanjay Srivatsan, PhD
Assistant Professor

Creating new DNA sequencing technologies that maximize how much we can learn from each cell in order to design cells from scratch for use in a range of applications

Barry Stoddard, PhD
Assistant Professor
Director, NCI Interdisciplinary Training Program in Cancer

Figuring out the structures of molecular machines to understand what their cellular jobs are

Roland Strong, PhD
Professor

Studying key molecular structures in the immune system and engineering new versions that could form the basis of therapies or vaccines for cancer, HIV, and more

Arvind (Rasi) Subramaniam, PhD
Associate Professor

Using experimental and computational methods to understand how cells make proteins and how the process can go wrong, including in cancer

Jhimmy Talbot, PhD
Assistant Professor

Investigating how neurons and immune cells in the gut communicate and how infections and diet can affect the delicate balance

Toshio Tsukiyama, PhD, DVM
Professor
Associate Director, Basic Sciences Division

Uncovering how normal cells go in and out of dormancy, and how cancer can use this trick to resist treatment