FRED HUTCH
CURES START HERE®

2019-2020 ANNUAL REPORT

# Basic Sciences

## Making Foundational Discoveries at Fred Hutch

**Katharine Chen**, Graduate Student in the Subramaniam Lab

**Dr. Sue Biggins**

## FROM THE DIRECTOR OF THE BASIC SCIENCES DIVISION

**REFLECTING ON THE PREVIOUS ACADEMIC YEAR I AM AMAZED AT WHAT WE'VE ACCOMPLISHED AS A DIVISION.** We have faced and continue to face numerous challenges, but I am inspired by the division's determination to adapt and continue our mission of making foundational discoveries about biology and disease. I am writing this letter from my home "remote work" office, an office that did not exist three months ago. I am sure many of you will be reading this report from a place you did not expect to be prior to the COVID-19 pandemic. While the pandemic has overturned almost every sense of normalcy, I am struck by the remarkable resilience and dedication of everyone in the Basic Sciences Division. The labs have exhibited great teamwork, ingenuity, and flexibility as we have adjusted workflows to stay productive while keeping the division safe. Some labs in the division have leveraged their expertise to encompass SARS-CoV-2 research, including those of Drs. Jesse Bloom, Roland Strong and Mark Roth. Together their work has contributed both to understanding the virus and helping in the development of treatments.

Among our successes from last year are the recruitments of three outstanding new faculty: Drs. Melody Campbell, Nic Lehrbach and Manu Setty. Together, they will bring expertise that will enhance both our research capabilities and the breadth of the science in the division. We've also continued to welcome talented new trainees and scientists to the division, and we look forward to mentoring them and helping them achieve scientific success.

In the next year, I hope we continue our tradition of tackling hard problems and achieving our goals. The Black Lives Matter movement has highlighted and accelerated our need to improve diversity, equity and inclusion. As a division we are committed to dismantling structural racism in science, diversifying our workforce and ensuring that all the members of the division have a supportive environment.

As a result of economic shortfalls and health concerns due to the pandemic, our usual scientific and social interactions will move to remote seminar series, retreats and award symposiums for the next year. While we will need to be creative to stay connected, it is more important than ever that we work together and continue to make scientific progress.

2021 is the 40th anniversary of the Basic Sciences Division. Over the years, we have maintained a unique egalitarian and supportive culture that has fostered innovation and discovery. The pandemic is an example of why basic science continues to be so important; there will always be new scientific problems to address and understanding basic biology and developing new techniques will continue to be the foundation for progress. I look forward to celebrating our 40th with you.

**Dr. Sue Biggins**
Director of the Basic Sciences Division,
Senior Vice President of Fred Hutch

# Providing the foundation for curing cancer and other diseases by engaging in fundamental science that leads to key discoveries.

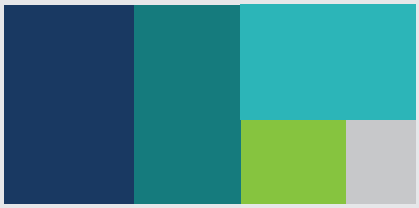
Basic research is at the foundation of all scientific discoveries, underlying the innovative cures and treatments developed at Fred Hutch. Founded in 1981, the Basic Sciences Division has continually evolved to be at the forefront of discovery, seeking to understand the fundamental underpinnings of our own biology as well as the dysregulations that cause disease. Our research has yielded numerous landmark breakthroughs and scientific advances. We believe an inclusive, collaborative, egalitarian and creative environment is the basis for scientific innovation and world-changing discoveries.

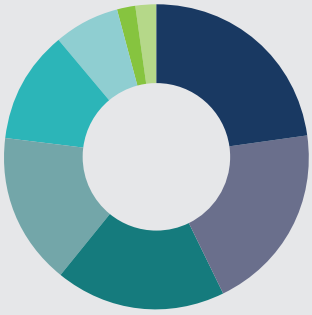
**PROFESSORS**

| | |
|---|---|
| Primary | 27 |
| Affiliate | 5 |
| Joint | 2 |
| Emeritus | 2 |

**RESEARCHERS**

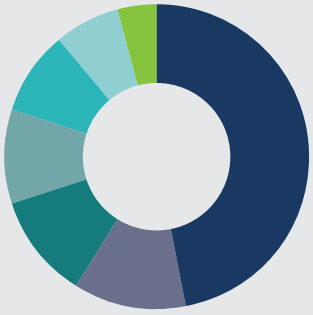
| | |
|---|---|
| Postdocs | 57 |
| Research Techs | 49 |
| Grad Students | 45 |
| Staff Scientists | 22 |
| Lab Aides | 12 |





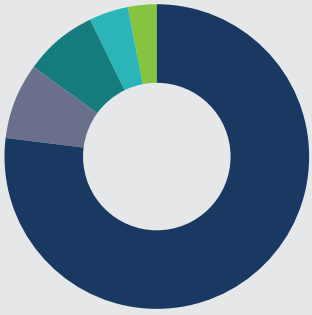
**2010-2018 POSTDOC OUTCOMES**

| | |
|---|---|
| Tenure Track Faculty | 23% |
| Industry | 20% |
| Non-Tenure Track Faculty | 18% |
| Postdoc | 16% |
| Other | 12% |
| Unknown | 7% |
| Government | 2% |
| Unemployed | 2% |



**FEDERAL FUNDING BY AGENCY**

| | |
|---|---|
| National Institute of General Medical Sciences | 47% |
| Other Federal Sources | 12% |
| National Cancer Institute | 11% |
| National Institute on Deafness and Communication Disorders | 10% |
| National Institute of Allergy and Infectious Diseases | 9% |
| Department Of Defense - Army Command | 7% |
| National Institute of Neurological Disorders and Stroke | 4% |



**SPONSORED FUNDING BY TYPE**

| | |
|---|---|
| Federally Sponsored | 77% |
| Howard Hughes Medical Institute | 8% |
| Foundation and Other Sponsored | 8% |
| Subawards | 4% |
| Industry Sponsored | 3% |

**1**
**Nobel laureate**
Dr. Linda Buck

**6**
**Faculty elected to the American Academy of Arts & Sciences**
4 current

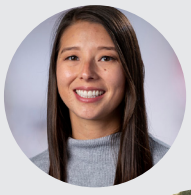
**10**
**Faculty elected to the National Academy of Sciences**
7 current

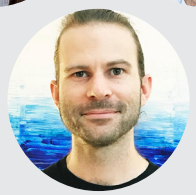
**10**
**Faculty named fellows of the American Association for the Advancement of Science**
8 current

**11**
**Howard Hughes Medical Institute investigators**
4 current

WELCOME

## We are thrilled to welcome three new professors to the Basic Sciences Division





**Dr. Melody Campbell**, top left, joins us from the University of California, San Francisco following a postdoctoral fellowship in Dr. Yifan Cheng's lab. The Campbell Lab uses structural biology techniques to understand proteins involved in cell communication and signal transduction, the dysregulation of which is associated with autoimmune and inflammatory diseases. Campbell is helping establish Fred Hutch's state-of-the-art cryo-EM suite while working to advance structural biology methodologies. Started July 2020.

**Dr. Manu Setty**, top right, joins us from Sloan Kettering, following a postdoctoral fellowship in Dr. Dana Pe'er's lab. The Setty Lab uses computational modeling and machine learning techniques to investigate the mechanisms of cell differentiation and fate, informing our understanding of the development and progression of cancer. Setty is a member of both the Basic Sciences Division and the Translational Data Science Integrated Research Center. Starts Jan. 2021.

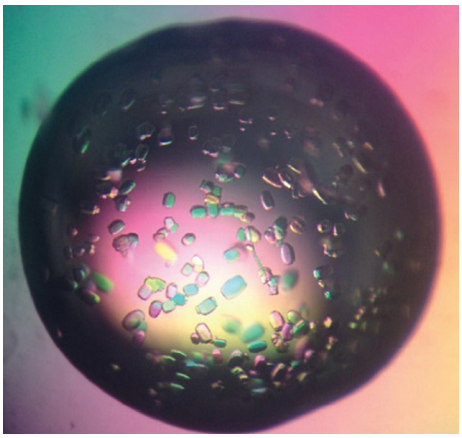
**Dr. Nicolas Lehrbach**, bottom, joins us from Harvard and the Massachusetts General Hospital, following a postdoctoral fellowship in Dr. Gary Ruvkun's lab. The Lehrbach Lab uses genetic, imaging and biochemical approaches to discover new regulators of protein synthesis, folding, trafficking and degradation while investigating how these regulators impact aging, neurodegeneration and drug responses. Starts Jan. 2021.

FOCUS ON

## Structural Biology in the Basic Sciences Division

Each cell in our body contains millions of protein and nucleic acid molecules which can have thousands of different forms and functions. Proteins are responsible for much of the work carried out by a cell, including transporting nutrients, targeting invading pathogens, and transmitting material and information to and from the cell. One of their most crucial functions is regulating cellular division and maintaining the integrity of our genes. The breakdown of these processes is the underlying cause of cancer. Our well-being depends on the proper functioning of our proteins. This is why structural biologists in the Basic Sciences Division are working to understand the structure and function of proteins and other biological molecules, improving our knowledge of human biology and helping overcome disease.

When we eat food, our body breaks down the contained protein molecules into their constituent parts, and then synthesizes the necessary building blocks for making new cells, including amino acids. Using little biological machines called ribosomes, our cells take those amino acids and construct new proteins. Our genes determine the order and length of amino acids in newly created proteins. Their interactions cause the protein chain to fold up in a series of stages, ultimately giving the protein three-dimensional structure. The shape of the protein determines how it interacts with other molecules, conferring function. Knowing the structure of a protein informs how that protein works. Mutations can change how a protein functions, but knowing its structure helps researchers understand how and why. Even swapping out a single amino acid for another can have detrimental effects on a protein's activity. Understanding protein function is essential to overcoming just about every health challenge humanity has faced, from genetic disorders to cancer and pandemics.



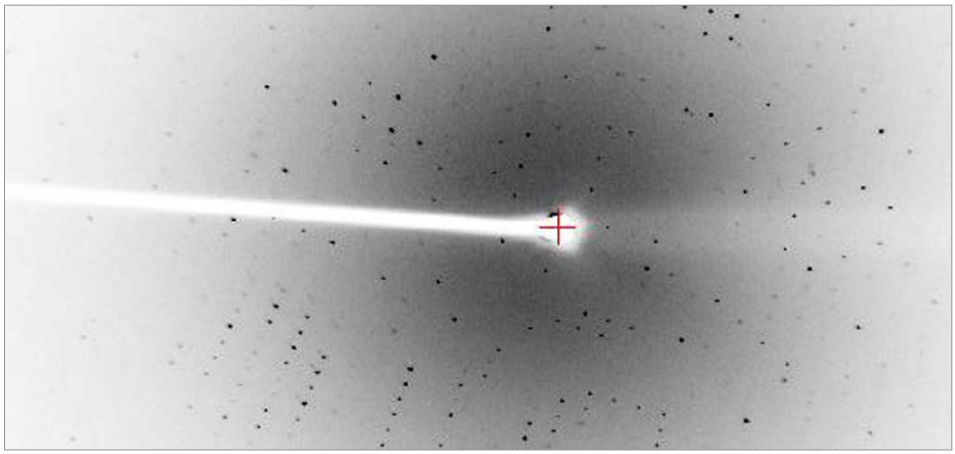
Protein crystals suspended in Fluid.
Image by Lindsey Doyle.

CONTINUED >>

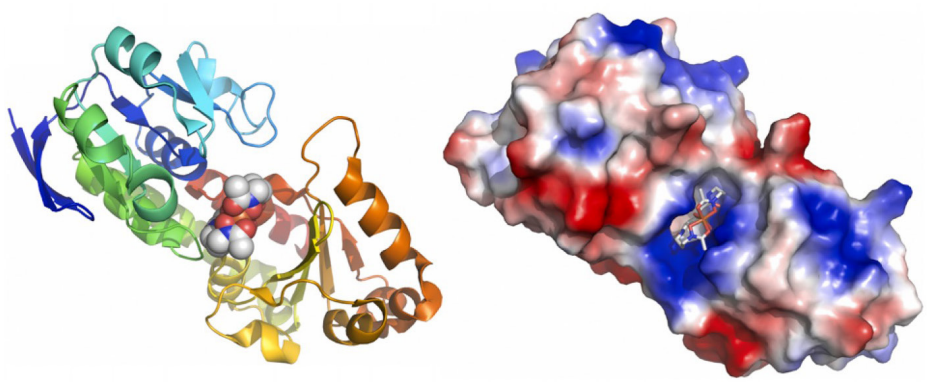
X-Ray Crystallography Suite at Fred Hutch

Determining the structure of proteins presents a major challenge though: they are extraordinarily tiny, but constructed from many thousands (or even hundreds of thousands) of atoms. Despite this, researchers have developed numerous techniques to help them discern the shape of proteins and other biological molecules, including X-ray crystallography, cryogenic electron microscopy and computational modeling.

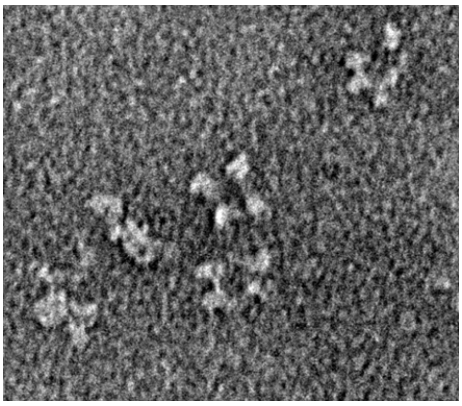
Using **X-ray crystallography,** structural biologists bombard protein samples with X-rays to measure how they are scattered by the sample. The pattern of scattering allows scientists to reconstruct the three-dimensional shape of the protein sample. Purifying and crystallizing proteins prior to analysis by this powerful technique can be technically challenging. Despite this difficulty, X-ray crystallography remains one of the most widely used techniques for structural biologists because it excels at resolving the detail of even the smallest proteins. We have recently been awarded funding to upgrade and improve our equipment for performing X-ray crytollography, enhancing our research capabilities and ensuring that we stay on the forefront of discovery.



**X-RAY CRYSTALLOGRAPHY:** Diffraction pattern of protein crystal captured by Lindsey Doyle of the Stoddard lab.



**COMPUTATIONAL MODELING:** Schematic of a bacterial substrate-binding protein developed by the Strong lab. The left image shows a ribbon diagram, describing the pattern of folding required to create the protein. The right image shows a surface diagram which gives a more accurate view of what the protein looks like. The surface model is color coded to show its electrostatic potential, which helps describe its interactions with other molecules.



**CRYOGENIC ELECTRON MICROSCOPY:** Electron microscope image of proteins captured by Betty Shen of the Stoddard lab.

**Cryogenic electron microscopy,** more commonly called "cryo-EM", also enables scientists to capture the structure of proteins by stabilizing them in a rapidly frozen water solution that can be imaged with an electron microscope. Unlike crystallography, cryo-EM does not require the preparation of crystallized protein samples and can be used with tiny amounts of protein samples and on molecules that are much larger and more complex than can otherwise be visualized. The extreme detail achieved by illuminating protein samples with electrons allows researchers to visualize them at extremely high resolution while keeping the proteins in a more natural, aqueous environment. This technique is rapidly growing in prominence and Fred Hutch is in the process of establishing a state-of-the-art cryo-EM suite.

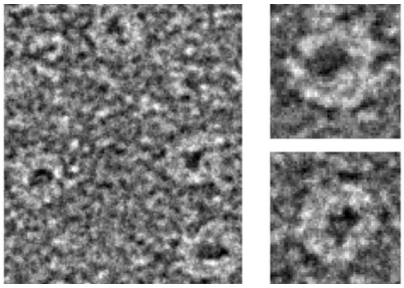
Structural biologists use **computational modeling** to uncover the rules that dictate how a chain of amino acids folds to form a protein. Given our current understanding of protein production, knowing the sequence of amino acids is not always enough to determine a protein's ultimate shape. However, using a combination of modeling and imaging techniques, the algorithms that explain protein folding are growing more accurate and sophisticated over time.

These techniques enable researchers to construct schematics of proteins that inform both how they are constructed and how they interact with other molecules.

Progress in the understanding of how cells create proteins allows scientists to engineer completely new proteins not found in nature. Protein engineering opens the possibility of creating custom proteins that can treat or cure disease such as genetic disorders or viral infection and is a prominent area of inquiry and discovery in the division.

We are home to four prominent structural biologists, all working to uncover the three-dimensional structure of proteins in order to better understand our own biology and cure disease.

## The Stoddard Lab

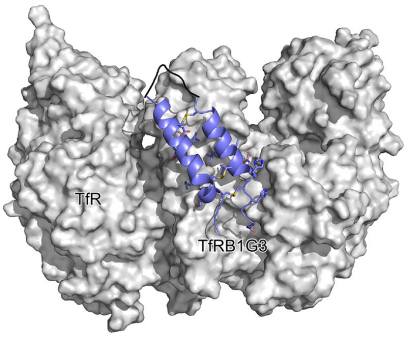


Electron microscopy image of engineered protein scaffold.

**The Stoddard Lab** seeks to engineer novel proteins with the explicit purpose of developing targeted therapeutics to treat and even cure disease. Through a better understanding of the rules that govern protein production, it could be possible to engineer proteins capable of correcting mutations that underlie genetic diseases like cystic fibrosis and treating other chronic infections.

Recently the lab has been working on a collaborative project, alongside the Bradley Lab, to engineer custom protein scaffolds that could help streamline immunotherapy production and improve the manufacturing of engineered anticancer immune cells.

## The Strong Lab

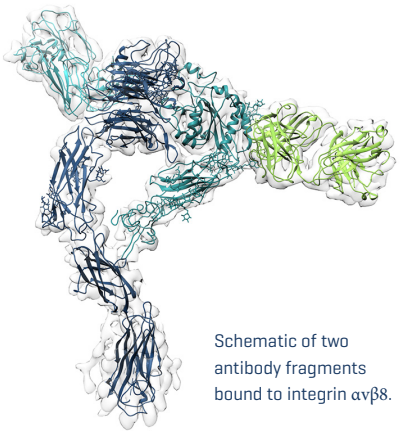



Schematic of a peptide bound to the protein transferin (TfR), a potential target for ferrying compounds into the brain.

**The Strong Lab** is focused on understanding the structure and function of the proteins in our immune system and those of pathogens. A deeper knowledge of these proteins underlies the possibility of new cancer therapies and improved vaccines. The lab led the development of Daedalus, a rapid protein-production system used in numerous preclinical trials.

Recent work from the Strong lab seeks to overcome the challenges of delivering medication to the brain by better understanding the proteins that are actively trafficked across the blood-brain barrier. This work opens the door to improved brain cancer treatments and psychopharmaceuticals.

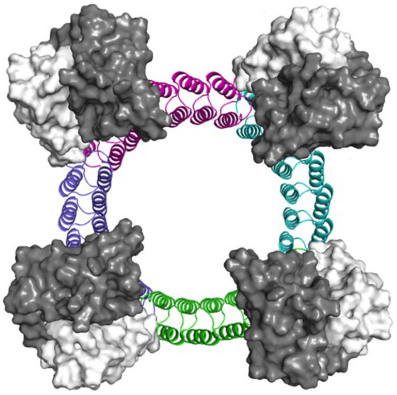
## The Campbell Lab



Schematic of two antibody fragments bound to integrin αvβ8.

**The Campbell Lab** uses structural techniques to study integrins, proteins involved in cell communication and signal transduction, the dysregulation of which is associated with autoimmune and inflammatory diseases. Additionally, her lab is working to improve methodologies for cryo-EM, specifically working to computationally offset instabilities and motion from the imaging process. These advancements will make it possible to image a greater variety of proteins at ever higher resolutions.

## The Bradley Lab



Schematic of an engineered T-cell 'superagonist.'

**The Phil Bradley Lab** develops and applies powerful computational approaches to model and examine protein structure and behavior, studying proteins involved in immunology as well as DNA and RNA recognition, and designing artificial proteins with novel folds and properties.

His lab, in conjunction with the Stoddard lab, has recently described the creation of novel protein scaffolds termed circular Tandem Repeat Proteins, or 'cTRPs', that have been turned into novel T-cell stimulatory molecules for the manufacture of therapeutic T cells.

# Trainee Highlights

## Founding A Virtual Society for Chromatin Researchers

In response to the physical distancing necessities of COVID-19, **Dr. Christine Cucinotta**, a postdoctoral fellow in the Tsukiyama Lab, and **Dr. Pravrutha Raman**, a postdoctoral fellow co-mentored by Drs. Toshio Tsukiyama and Harmit Malik, spearheaded an effort to create a virtual society for chromatin researchers called the Fragile Nucleosome. The organization has grown to more than 800 members from all over the world and offers a forum for scientists to share and discuss their research, including holding weekly seminars. Their efforts represent the ingenuity and tenacity of the trainees in the Basic Sciences Division, helping ensure that scientific inquiry progresses, even when faced with the challenges of a pandemic.

## Mollie McDonnell Named to the Husky 100

Each year the University of Washington names exceptional students to the Husky 100 for their exemplary work in the classroom, in our communities and beyond. We are ecstatic that **Mollie McDonnell**, graduate student in the Emerman Lab, was selected from more than 1,700 nominees. We are grateful for her advocacy for inclusivity at Fred Hutch, and her work as a supportive mentor for young scientists.

## Training the Next Generation Through Fred Hutch Girls Who Code

Fred Hutch Girls Who Code is a weekly after school club for high school aged girls that seeks to help them build a foundation in the fundamentals of computer science through collaborative projects and mentorship. Many trainees in the Basic Sciences Division have served as mentors over the last year including **Sarah Hilton** and **Kate HD Crawford** from the Bloom Lab, and **Emma Hoppe, Khrystyna North** and **Emma De Nee**f from the Rob Bradley Lab. In January of 2020, Sarah Hilton was selected as a Mentor of the Month for her work with the Fred Hutch chapter of Girls Who Code. We are proud to have such dedicated trainees, who take the time to help train the next generation of scientists.

## Serving as Officers of UW SACNAS

*The Society for Advancement of Chicanos/ Hispanics and Native Americans in Science, or SACNAS*, is dedicated to fostering the success of Chicanos/Hispanics and Native Americans throughout their careers in STEM fields. Graduate students **Vanessa Montoya**, from the Emerman Lab, and **Cera Hassinan**, from the Bai Lab, served as UW SACNAS president and treasurer respectively. We are thankful for their work, time, and effort that went into furthering the important mission of SACNAS.


## Trainee-led Diversity, Equity and Inclusion Discussion Group

As part of ongoing efforts at Fred Hutch and the Basic Sciences Division to improve diversity, equity and inclusion in science, trainees **Cera Hassinan** from the Bai Lab, **Dr. Christine Cucinotta** from the Tsukiyama Lab, **Dr. Pravrutha Raman** from the Tsukiyama and Malik Labs and **Dr. Anna Mammel** from the Hatch Lab have initiated the creation of a discussion group that will help us as a division continually engage with, learn about, and challenge discrimination.

LAB HIGHLIGHTS

# Gene Regulation and Genomic Integrity

The structure, organization and regulation of chromatin (the complex of DNA and structural components) is critical to ensuring that cells activate relevant genes correctly and maintain the integrity of their genome. Malfunctions in these processes can result in genetic diseases and cancer formation. Researchers in the division seek to understand the multiple complex molecular systems that govern chromatin structure as well as DNA transcription, RNA processing and translation, and other controls of gene expression.

## The Bradley Lab

**Dr. Robert Bradley**
RNA Biology and Biophysics

Promoted to Full Professor in 2020

Appointed to the McIlwain Family Endowed Chair in Data Science

JAN. 7, 2020

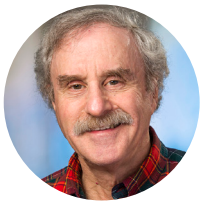
### CRISPR-based tool solves genetic mystery 80 million years in the making

**Certain DNA sequences haven't evolved since humans and mice diverged. But why?**

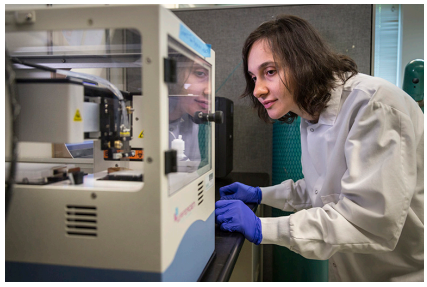
Looking at a subclass of ultraconserved DNA elements known as poison exons, the Bradley Lab found that certain poison exons were essential for cell growth while others acted to suppress the growth of lung tumor cells in mice.

**Joey Pangallo**, Graduate Student, Defended Ph.D. dissertation

## The Henikoff Lab



**Dr. Steve Henikoff**
Epigenetics



APRIL 29, 2019

### New method quickly, precisely maps epigenome in single cells

**CUT&Tag speeds process of precisely locating molecules that turn genes on or off**

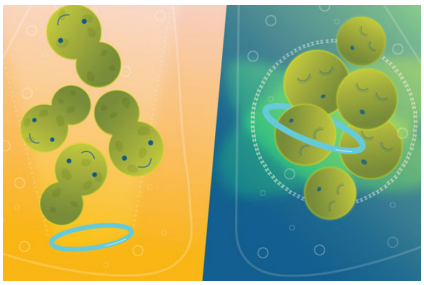
New method published by the Henikoff Lab allows investigators to map chromatin — the DNA modifications, packaging proteins and molecular factors that work together to turn genes on or off — precisely, quickly, at low cost and in single cells.

**Dr. Mike Meers**, Postdoc, Awarded National Institute of General Medical Sciences Ruth L. Kirschstein National Research Service Award Postdoctoral Fellowship (NIGMS F32)

**Dr. Jay Sarthy**, Postdoc, Received Alex's Lemonade Stand Foundation 2019 Young Investigator Award

## The Tsukiyama Lab

**Dr. Toshi Tsukiyama**
Chromatin and Quiescence



JAN. 03, 2019

### For cells, keeping quiet is a cinch

**Researchers show how dormant cells turn genes off by pulling DNA into loops**

Armed with Micro-C XL, the Tsukiyama Lab looked at the 3D structure of chromatin in dormant, quiescent yeast cells, compared to quickly dividing yeast cells. A better understanding of this quiescent state could help scientists discover ways to awaken dormant tumor cells or sensitize them to anti-cancer drugs.

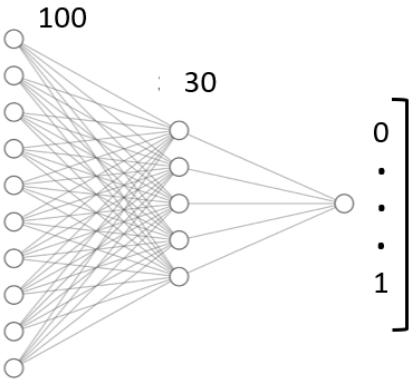
**Dr. Sarah Swygert**, Postdoc, Received National Institute of General Medical Sciences Pathway to Independence Award (NIGMS K99)

**Dr. Christine Cucinotta,** Postdoc, Received Institute of General Medical Sciences Ruth L. Kirschstein National Research Service Award Postdoctoral Fellowship (NIGMS F32)

# *Continued:* Gene Regulation and Genomic Integrity

## The Hahn Lab

**Dr. Steve Hahn**
Transcriptional Regulation




JULY 20, 2020

### ADpred: a deep learning model for accurately predicting transcription activation domains

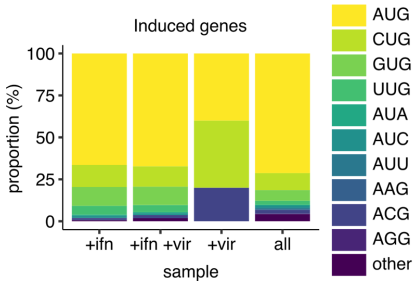
**Using machine learning to improve the understanding of gene regulation**

Interested in the molecular mechanisms of transcription, the Hahn Lab and collaborators developed artificial neural networks to help predict and identify transcription activation domains. The disruption of transcriptional activators can be an underlying cause of cancer.

## The Subramaniam Lab

**Dr. Rasi Subramaniam**
Translation and Ribosomal Function

Received National Science Foundation CAREER Award




MAR. 8, 2019

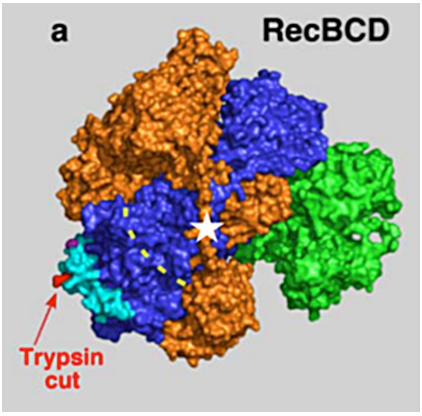
### Influenza exploits an alternate route when it comes to protein synthesis

**Mapping the sites of protein translation initiation in influenza-virus infected cells**

Filling a critical need to comprehensively identify sites of translation initiation during influenza virus infection, the Subramaniam and Bloom Labs integrated computational and experimental approaches to investigate the extent and impact of alternate translation in cells infected with influenza virus.

## The Smith Lab

**Dr. Gerry Smith**
DNA Repair and Recombination




JAN. 21, 2019

### Taking a swing at a fixed arm's length

**Heading into the future of atomic biology**

Exploring the processes of DNA repair, the Smith Lab carried out an extensive mutational analysis of RecBCD helicase-nuclease function, identifying how its activity is regulated to ensure that DNA is repaired at the proper time.

**Dr. Andrew Taylor**, Staff Scientist, Retired after 37 years

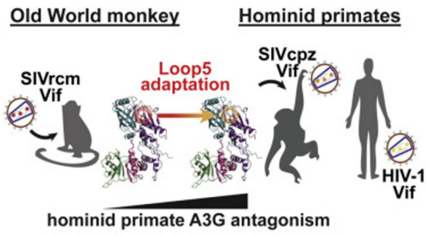
**Dr. Yihua Zhu**, Postdoc, Joined the lab

# Immunology and Evolution

Studying the evolution of viruses, bacteria and the immune system enables researchers to understand how these infectious agents evade immune response and develop resistance to existing therapies. These investigations provide a deeper understanding of human immunity while revealing novel means for protecting the body from viruses like HIV and influenza.

## The Emerman Lab

**Dr. Michael Emerman**
Virology of HIV




MARCH 16, 2020

### Tracing the structural changes that helped HIV-1 become a human pathogen

**Understanding cross-species viral transmission**

Tracing how HIV evolved to become a human pathogen, the Emerman lab, in collaboration with the Gross Lab at UCSF, structurally and functionally characterized the simian immunodeficiency virus gene Vif to reveal the adaptations that underlie the virus' jump between species.

**Mollie McDonnell**, Graduate Student, Named to the Husky100

**Vanessa Montoya**, Graduate Student, Served as UW SACNAS president

## The Malik Lab

**Dr. Harmit Malik**
Genetic Conflict

Elected AAAS fellow

Elected to National Academy of Sciences

Elected fellow of American Academy of Microbiology

Elected president of the Society for Molecular Biology and Evolution for 2021

OCT. 1, 2019

### Age-old arms race points way to new-and-improved antiviral protein

**Guided by evolution, scientists create more potent antiviral that unexpectedly continues blocking dissimilar viruses.**

Using insights from the ancient tug-of-war between viruses, the Malik and Emerman Labs addressed fundamental questions about evolution, including whether antiviral genes that adapt against certain viruses become less equipped to deal with new viral challenges.

**Dr. Courtney Schroeder**, Postdoc, Received National Institute of General Medical Sciences Pathway to Independence Award (NIGMS K99)

**Dr. Kevin Forsberg**, Postdoc, Received National Institutes of Health Director's New Innovator Award (NIH DP2)

**Dr. Tera Levin**, Postdoc, Started as Assistant Professor in the Department of Biological Sciences at the University of Pittsburgh

**Dr. Antoine Molero**, Postdoc, Started Junior group leader position at the GReD Institute in Clermont-Ferrand, France

**Rini Kasinathan** and **Michelle Hays**, Graduate Students, Defended Ph.D. Dissertation

## The Bloom Lab

**Dr. Jesse Bloom**
Viral Evolution

Brotman Baty Institute Catalytic Collaborations Award

McDougall Mentoring Award

AUG. 27, 2019

### Why does flu make some people sick, but not others?

**New study points to single mutations that allow flu to slip past immune system of some people, but not others.**

The Bloom Lab showed that a single mutation in a flu virus can sometimes give it the power to evade one person's antibody immunity, but not another's. The findings could help explain why individuals vary so much in their susceptibility to infectious diseases like influenza.

**Dr. Tyler Starr**, Postdoc, Named 2019 Damon Runyon Foundation Fellow

**Dr. Adam Dingens**, Postdoc, Recipient of 2019 Weintraub Award

**Dr. Tal Einav**, Postdoc, Named Damon Runyon Quantitative Biology Fellow

**Kate Crawford**, Graduate Research Assistant, Awarded National Institute of Allergy and Infectious Diseases Ruth L. Kirschstein National Research Service Award Predoctoral Fellowship. (F30 NIAID)

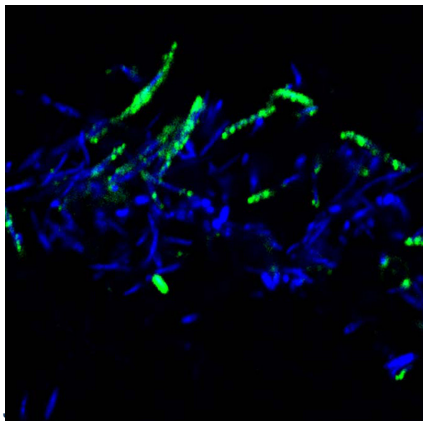
**Dr. Alistair Russell**, Postdoc, Started as Assistant Professor in the Division of Biological Sciences at UC San Diego

## *Continued:* **Immunology and Evolution**

### The Koch Lab

**Dr. Meghan Koch**
Immunology and Microbiota

2019 Rita Allen Foundation Scholar
2020 Pew Scholar in the Biomedical Sciences



#### Studying how maternal immune factors shape infant health

**Understanding the biology of how health is set up early in life**

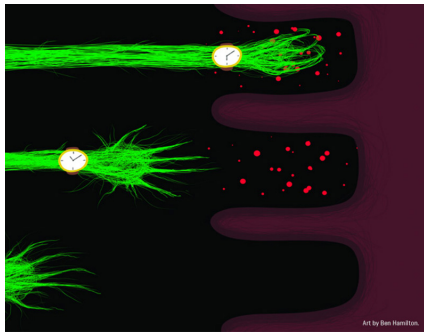
Interested in how signals from mom shape infant development, immunity and metabolism, the Koch Lab worked to understand how maternal immune proteins in breast milk interact with a mouse pup's developing immune system and gut microbiota to shape growth and long-term health.

## Neuroscience

Disruptions in the proliferation, migration and signaling of cells in the brain can lead to disease and mental illness. Researchers in the division study the mechanisms behind these complex systems to better understand nervous system function and the underlying causes of neurological disorders, including brain cancers.

### The Moens Lab

**Dr. Cecilia Moens**
Neurodevelopment




APRIL 16, 2020

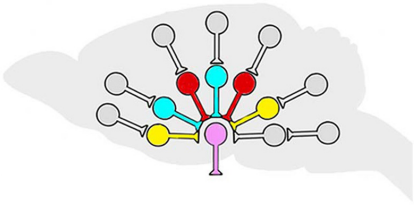
#### Helping the developing brain chart its course

**New study shows vitamin A derivative orchestrates timing as 'brain map' forms**

Discovering that timing is key in shaping the topographic map that represents the muscles of the throat, the Moens Lab reveals the molecular cue that controls vagus nerve development.

### The Buck Lab

**Dr. Linda Buck**
Sensory Systems and Stress



MARCH 10, 2020

#### A new guidebook to the brain

**'Connect-seq' technique overlays key signaling information from individual neurons on brain road maps.**

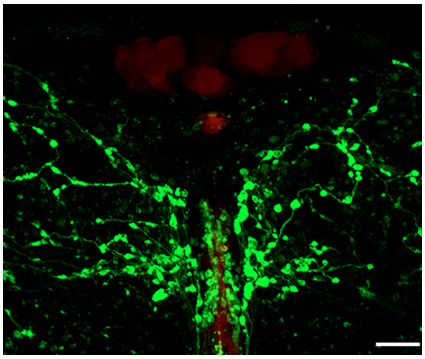
Seeking to discern the complex connectivity of the brain, the Buck Lab developed a new technique dubbed Connect-seq, making it possible to map neural connections while gathering information about the key signals sent by individual neurons within a circuit.

# *Continued:* **Neuroscience**

The structure, organization and regulation of chromatin (the complex of DNA and structural components) is critical to ensuring that cells activate relevant genes correctly and maintain the integrity of their genome. Malfunctions in these processes can result in genetic diseases and cancer formation. Researchers in the division seek to understand the multiple complex molecular systems that govern chromatin structure as well as DNA transcription, RNA processing and translation and other controls of gene expression.

## The Rajan Lab

**Dr. Akhila Rajan**
Neurobiology of Obesity



JAN. 20, 2020

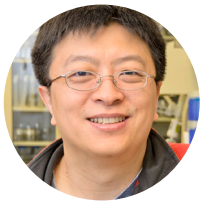
### Ways to improve body image in Drosophila

**How hormones regulate fat-sensing neuronal circuits**

Interested in the molecular mechanisms underlying signaling between fat cells and the brain, the Rajan lab showed how hormone signaling regulates the number of synaptic contacts made by fat-sensing neurons involved in energy homeostasis.

**Terry Hafer**, Graduate Student, Awarded Cell and Molecular Biology Training Grant

## The Bai Lab



**Dr. Jihong Bai**
Neurotransmission and Neuromodulation

DEC. 16, 2019

### Worms taste bitterness

**Electrical synapses modulate sensory response**

Seeking to understand how neural circuits enable animals to sense and interpret their surroundings, the Bai lab investigated the underlying mechanisms that regulate bitter taste sensation in the worm, Caenorhabditis elegans. They identified specific gap junction proteins that form neuron-neuron connections, where ions and small signaling molecules can pass directly from one nerve cell to the next, allowing signaling modulation to coordinate the action of multiple neurons and neural circuits.

**Lisa Voelker**, Graduate Student, Defended Ph.D. Dissertation

**Manuel Rosero**, Graduate Student, Awarded Cell and Molecular Biology Training Grant

**Monet Jimenez**, Graduate Student, Awarded National Institute of Neurological Disorders and Stroke Ruth L. Kirschstein National Research Service Award Individual Predoctoral Fellowship to Promote Diversity in Health-Related Research (NINDS F31)

**Cera Hassinan**, Graduate Student, Joined the lab with support from National Institute of Neurological Disorders Diversity Supplement

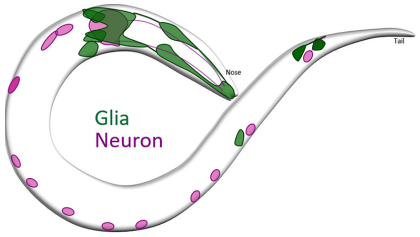
**Aaradhya Pant**, Undergraduate Researcher, Received Mary Gates Research Scholarship

## The Singhvi Lab

**Dr. Aakanksha Singhvi**
Glia-Neuron Interactions

Received Junior Investigator Grant from the Glenn Foundation for Medical Research and the American Federation for Aging Research

Awarded Fred Hutch Pilot Grant




### The molecular mechanisms of glia-neuron interactions

**Understanding glia, critical but understudied players in brain function**

Working to uncover how glia and neurons interact with each other, the Singhvi Lab studied multiple aspects of glial function including glial pruning, a process that helps regulate how neurons connect with each other. Disruptions in glial cell activity can contribute to brain cancer, multiple sclerosis, autism and neurodegenerative disorders such as Alzheimer's and Parkinson's disease.

**Dr. Maria Purice**, Postdoc, Awarded Washington Research Foundation Postdoctoral Fellowship

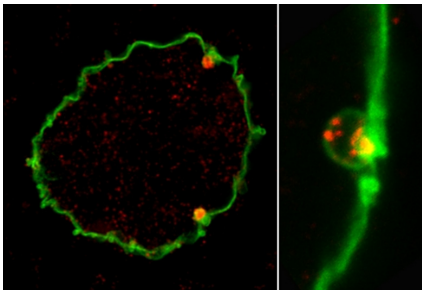
**German Rojas**, Graduate Student, Awarded Howard Hughes Medical Institute Gilliam Fellowship for Advanced Study

# Cell Proliferation and Fate

Normal cellular processes as well as environmental stressors can disrupt the genetic and structural integrity of a cell. Researchers in the division are investigating the processes by which cells recover from these stressors. Additionally, they seek to understand cellular division, metabolism and fate by answering fundamental questions about normal and abnormal cell function, development and how dysregulation of these processes contribute to disease, including cancer.

## The Parkhurst Lab

**Dr. Susan Parkhurst**
Wound Healing and Nuclear Architecture



MARCH 16, 2020

### [(Wash)ing the nuclear envelope]

**Discovering the mechanisms of how large complexes can cross the nuclear envelope**

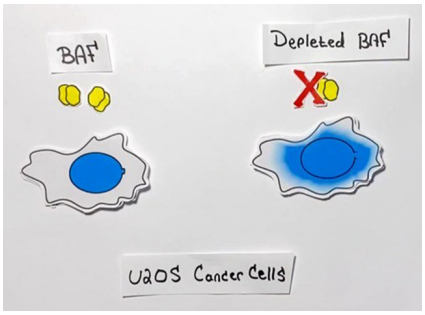
Working to understand the processes by which large molecules can cross the nucleus of a cell, the Parkhurst Lab identified the protein Wash, its regulatory complex, and actin related proteins as drivers of nuclear envelope budding. The findings that may hold insights into the nuclear egress mechanism used by herpesviruses.

**Clara Prentiss**, Research Tech II, Accepted to Graduate School at The University of California, San Diego

## The Hatch Lab

**Dr. Emily Hatch**
Micronuclei and Nuclear Envelope Repair

Received Brotman Baty Institute Catalytic Collaborations Award




MARCH 16, 2020

### [A (BAF)ling story of nuclear envelope repair]

**How cells repair their nuclear envelope when ruptured**

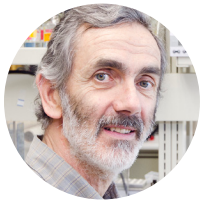
Exploring the molecular mechanisms underlying nuclear envelope rupture and repair, the Hatch Lab investigated the role of BAF (barrier to autointegration factor) in maintaining the integrity of the nuclear envelope between cellular division.

**Lucian di Peso**, Graduate Student, Awarded Chromosome Metabolism and Cancer Training Grant

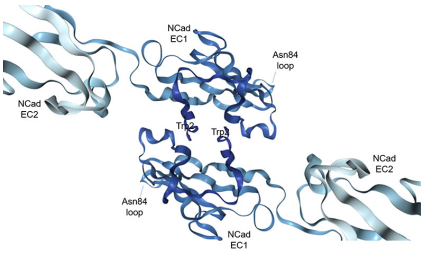
**Dr. Anna Mammel, Postdoc**, Awarded Chromosome Metabolism and Cancer Training Grant

**Molly Zych**, Graduate Student, Awarded Cell and Molecular Biology Training Grant

## The Cooper Lab



**Dr. Jon Cooper**
Cell Signaling and Migration




JAN. 20, 2020

### [An unconventional partnership encourages neuron migration]

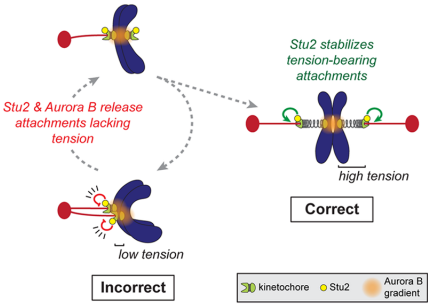
**Understanding how neurons migrate from their birthplace**

Studying the signaling pathways that direct neuron migration, the Cooper lab examined the mechanisms underlying neuron-migration control by the neuronal cadherin protein.

# *Continued:* **Cell Proliferation and Fate**

## The Biggins Lab

**Dr. Sue Biggins**
Cell Division and Chromosome Segregation




NOV. 18, 2019

### Chromosomes are safer with Stu2

**Discovering a kinetochore tension-sensing mechanism**

Investigating the processes of cell division, the Biggins lab identified mutations that cause abnormal chromosome segregation. The tight regulation of cell division is essential to minimize inaccurate partitioning of genetic material which can lead to genomic instability, a common hallmark of cancer.

**Dr. Andrew Popchock**, Postdoc, Received National Institutes of Health Ruth L. Kirschstein National Research Service Award Postdoctoral Fellowship (NIH F32)

**Dr. Amanda Roca**, Postdoc, Received American Cancer Society Postdoctoral Fellowship

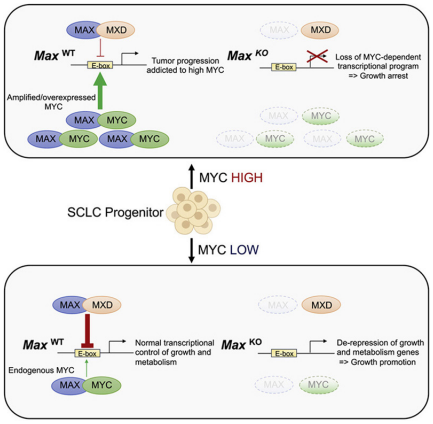
**Abe Gutierrez**, Graduate Student, Defended Ph.D. dissertation

## The Eisenman Lab

**Dr. Robert Eisenman**
Transcriptional Control of Proliferation and Neoplasia

Received Brotman Baty Institute Catalytic Collaborations Award

Awarded Joint Research Project Grant from The National Cancer Institute




JUNE 1, 2020

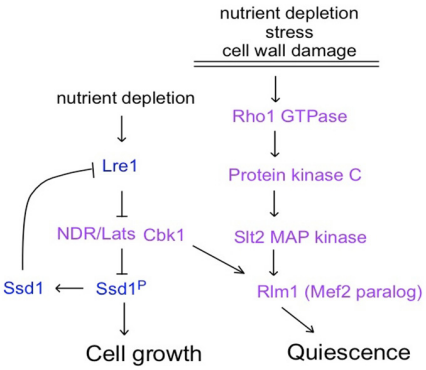
### In cancer, the context 'makes' the mutation

**Whether a mutated gene suppresses or promotes small-cell lung cancer depends on other mutations**

Attempting to discern the role that gene expression plays in cancer, the Eisenman, Sullivan and MacPherson Labs collaborated to reveal why the gene Max, which partners with a known tumor driver, is defective in certain small-cell lung tumors.

## The Breeden Lab

**Dr. Linda Breeden**
Cell Stress and Quiescence




JULY 15, 2019

### Rousing the sleeping beauty

**Understanding how the cell cycle is stably but reversibly arrested in quiescence**

Using a combination of genetics, genomics and biochemistry, the Breeden Lab showed signaling cascades that promote quiescence and that defects in these signals lead to cell death. The ability for cells to transition in and out of quiescence is key for the proper regulation of cell division.

# *Continued:* Cell Proliferation and Fate

## The Roth Lab

**Dr. Mark Roth**
Metabolic Flexibility and Suspended Animation

NOV. 19, 2019

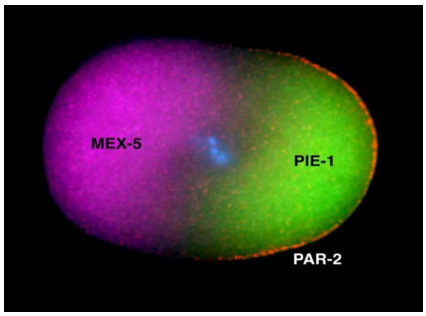
### Phase 2 Trial for Treatment of Reperfusion Injury Following a STEMI Heart Attack

**Possibly promising, novel first-generation therapy**

Spinning off from the research of the Roth Lab, Faraday Pharmaceuticals concluded a phase 2 trial of FDY-5301, demonstrating that "the treatment was well tolerated, with encouraging signals of efficacy in reducing cardiac damage."

## The Priess Lab

**Dr. Jim Priess**
Developmental Systems




### From a single cell to an organism

**The mechanisms of making a worm**

Studying embryogenesis; the process by which a fertilized egg becomes a multicellular organism, the Priess Lab made discoveries on morphogenesis, gastrulation, germ line specification, and cell fate.



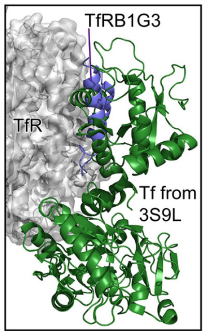
# Biophysics and Quantitative Biology

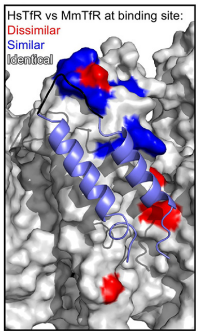
The molecular structure of proteins determines their functionality within cells and organisms. Researchers in the division are working to discover the structure of existing molecules and to synthesize new ones that might prevent or treat disease. Investigators also examine the symbiotic relationships among cell communities and how these affect human health.

## The Strong Lab

**Dr. Roland Strong**
Translational Biophysics and Vaccine Design

Awarded Fred Hutch Evergreen Fund Beyond Pilot




APRIL 15, 2020

### Cystine-Dense Peptide Promotes Blood–Brain Barrier Penetration

**New insights into protein trafficking across the blood-brain barrier**

Collaboration between the Strong and Olson Labs determined the structure of TfRB1G3, a cystine-dense peptide, that binds to the transferrin receptor, helping open the door to improved brain cancer treatments and psychopharmaceuticals.

# *Continued:* **Biophysics and Quantitative Biology**

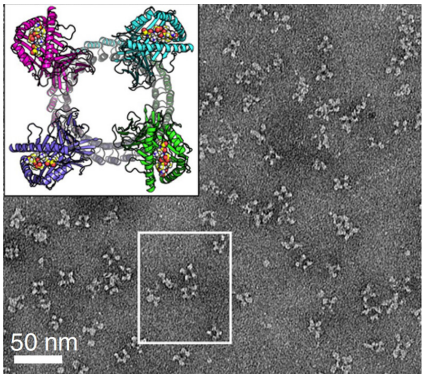
## The Stoddard Lab

**Dr. Barry Stoddard**
Protein Structure and Design

Amazon Web Services Cloud Grant

Among most collaborative scientists in gene editing according to an analysis by Nature

S10 Instrument Grant




MARCH 24, 2020

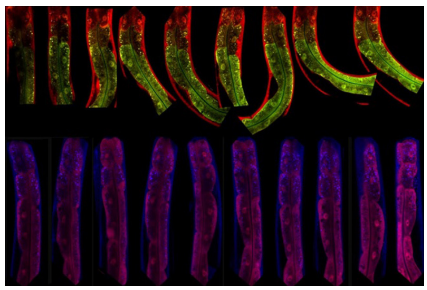
### Self-assembling, donut-shaped nanoparticles form novel platform for development of new biomolecules

**Scientist-designed protein scaffolds offer several advantages over molecular backbone currently used in research and clinical applications.**

Collaboration between the Stoddard Lab, the Phil Bradley lab and Dr. Colin Correnti created self-assembling protein nanoparticles designed from scratch. The nanoparticles could enhance clinical and research applications by simplifying biomolecule production or by enabling scientists to engineer entirely new biomolecules.

## The Brent Lab

**Dr. Roger Brent**
Systems Biology



JAN. 17, 2020

### Like snowflakes, no two cells are alike

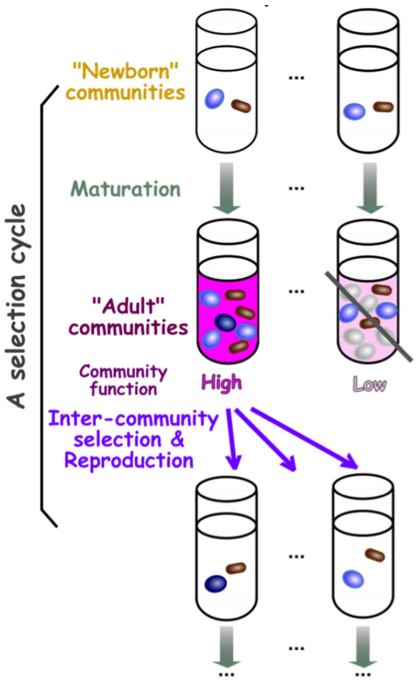
**Study shows that differences in cells' ability to turn genes into proteins change how mutations manifest; offers insights into disease risk.**

The Brent Lab and the University of Washington's Mendenhall Lab studied variation in a cell's capacity to turn genes into proteins. The findings could help explain why only certain mutated cells turn cancerous, or why only certain members of a family carrying the same disease-causing mutation get that disease.

## The Shou Lab

**Dr. Wenying Shou**
Competition and Mutualism

Secured Full Professorship at University College London, starting in January 2021



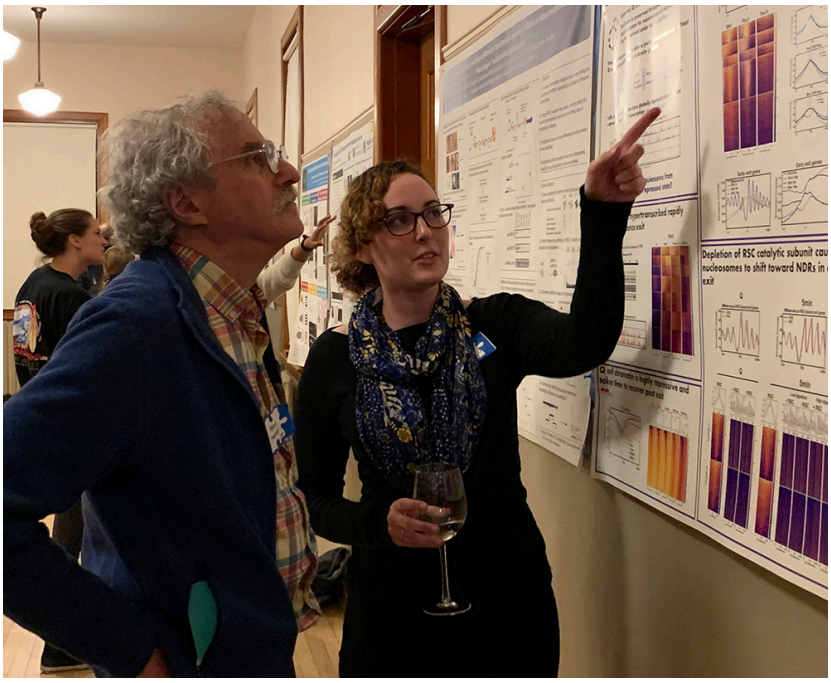

AUG. 19, 2019

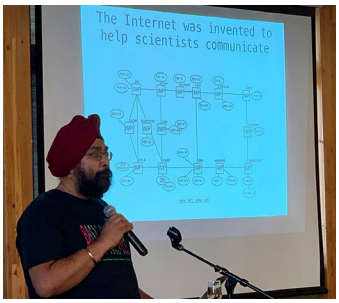
### The quest for the perfect community

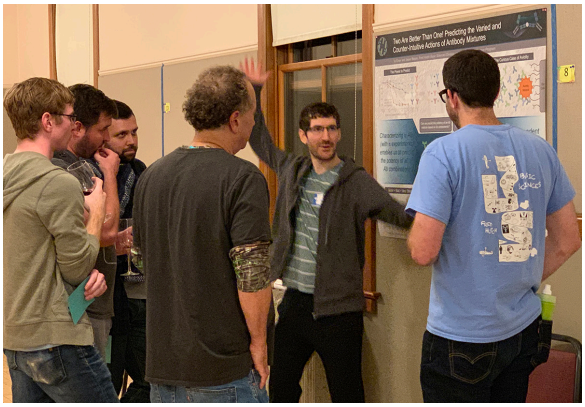
**Strategies for artificial community selection**

The Shou Lab worked to understand microbial evolution and fitness through artificial selection experiments, helping decipher complex species interactions and inform processes for shaping microbial communities.

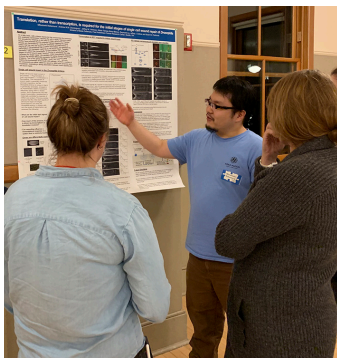
## EVENT HIGHLIGHTS



## EVENT HIGHLIGHTS



## DIVISION LEADERSHIP

**Sue Biggins**, Ph.D.
Director of Basic Sciences
Senior Vice President of Fred Hutch

**Toshio Tsukiyama**, Ph.D., D.V.M.
Associate Director of Basic Sciences

**Harmit Malik**, Ph.D.
Associate Director of Basic Sciences

**Susan Silbernagel**, M.P.A.
Senior Operations Director

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