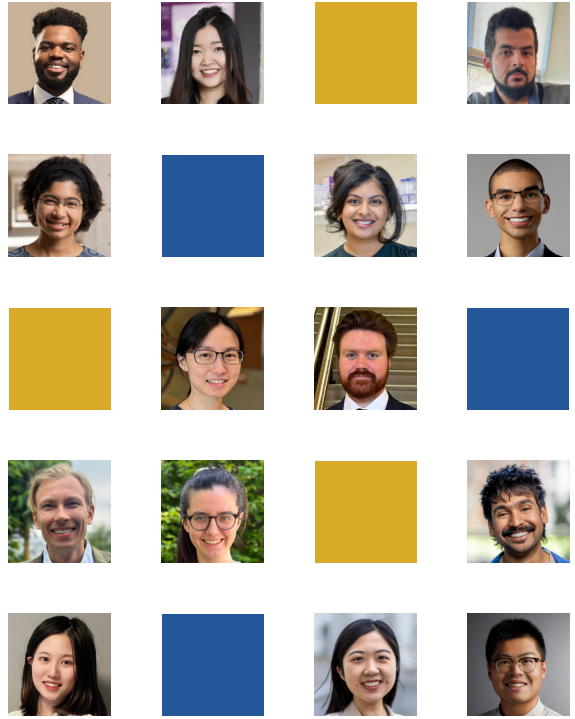


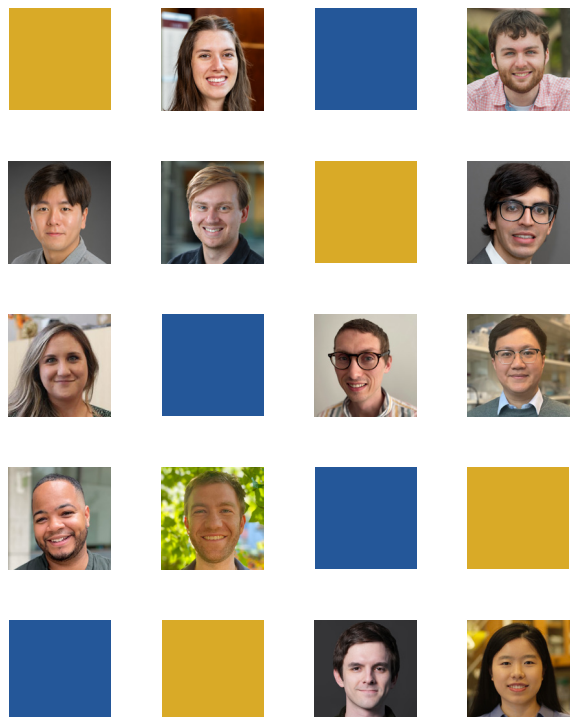
# JANE COFFIN CHILDS

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# 2024

# JANE COFFIN CHILDS FELLOWS





# STEPHEN ABINI-AGBOMSON, Ph.D.

LABORATORY OF DR. IBRAHIM CISSÉ

DEPARTMENT OF BIOLOGICAL PHYSICS

MAX PLANCK INSTITUTE OF IMMUNOBIOLOGY AND EPIGENETICS

## JANE COFFIN CHILDS FELLOW

Epigenetic modifications are changes that affect how our genes are turned on or off, without changing the underlying DNA sequence. These changes can be influenced by factors like our environment, diet, and lifestyle. The epigenetic modifications of DNA and chromatin-associated proteins play a crucial role in regulating cell-type specific gene expression. Methylation of DNA, for example, is associated with turning genes off via transcriptional repression. In most cells, DNA methylation occurs in the context of “CG” dinucleotides. Neurons, however, are also methylated at “CA” sequences.

Dr. Stephen Abini-Agbomson predicts that the oligomerization, or the process of small molecules joining together to form a larger structure, of DNA methyltransferases (DNMT) is important for their appropriate genomic localization and activity. He will use cutting edge single-molecule approaches to investigate the role of DNMT oligomerization in gene expression during neuronal development in [Dr. Ibrahim Cissé's lab](#) at the Max Planck Institute of Immunobiology and Epigenetics. Mis-regulation of DNA methylation is frequently observed in neurodevelopmental disorders and many types of cancer. Dr. Abini-Agbomson's findings may produce new mechanistic insights to inform future therapeutic targeting of these diseases.

Abini-Agbomson honed his expertise in epigenetics and chromatin biology as a graduate student in [Dr. Karim-Jean Armache's lab](#) at the New York University Grossman School of Medicine. There, he demonstrated that the histones encoded by [giant viruses can form nucleosomes](#). This was quite surprising as previously it was thought that only eukaryotes have nucleosomes. Additionally, Abini-Agbomson showed that the lysine methyltransferase SUV420H1 impacts chromatin dynamics through [both enzymatic and non-enzymatic mechanisms](#). With this research background, Abini-Agbomson is poised to make breakthrough discoveries on the impact of epigenetic protein oligomerization in neurodevelopment.

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# GREEN AHN, Ph.D.

LABORATORY OF DR. DAVID BAKER  
INVESTIGATOR, HHMI  
DEPARTMENT OF BIOCHEMISTRY  
UNIVERSITY OF WASHINGTON & INSTITUTE FOR PROTEIN DESIGN

## JANE COFFIN CHILDS-HHMI FELLOW

Cell surface proteins can drive diametrically opposed phenotypic outcomes when bound by ligands, distinct molecules that attach to other specific molecules. Therefore, efforts to rewire membrane protein signaling, introducing a specific function could improve and change how we develop treatments.

Dr. Green Ahn will engineer novel membrane protein effectors in [Dr. David Baker's lab](#) at the University of Washington. Using artificial intelligence protein design tools, Dr. Ahn will design a library of de novo extracellular effectors against particular ectodomains of cell surface proteins and investigate how those effectors impact downstream function. Ahn's studies will provide fundamental insight into membrane protein signaling and set the stage for future therapeutic targeting of these pathways.

Ahn's expertise in targeting membrane proteins stems from her graduate studies in [Dr. Carolyn Bertozzi's lab](#) at Stanford University. There Ahn developed the [first cell-type-specific degrader for a membrane protein](#). Ahn built on that study to discover [cellular factors that are required for targeted membrane protein degradation](#). She also helped develop the [first de novo designed proteins that trigger membrane protein degradation](#) in collaboration with Dr. David Baker's lab. With this experience Dr. Ahn is poised to make future discoveries with implications for our fundamental knowledge of protein membrane biology as well as future therapeutic strategies.

FELLOW



# IBRAHEEM ALSHAREEDAH, Ph.D.

LABORATORY OF DR. TAEKJIP HA  
INVESTIGATOR, HHMI  
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BOSTON CHILDREN'S HOSPITAL  
HARVARD MEDICAL SCHOOL

## JANE COFFIN CHILDS-HHMI FELLOW

Homologous recombination (HR) is an important pathway for error-free DNA strand break repair. Proper repair of DNA breaks is crucial for preventing cancer, as indicated by the number of frequent genetic mutations in this pathway that lead to breast, ovarian, and other types of cancer. Therefore, a better mechanistic understanding of DNA break repair may open up new avenues for therapeutic targeting of cancer.

Dr. Ibraheem Alshareedah is taking a novel approach to investigate DNA break repair in [Dr. Taekjip Ha's lab](#) at Harvard Medical School. It is known that BRCA2 loads RAD51 onto single stranded DNA (ssDNA), yet HR still occurs in BRCA2-mutant cancers, suggesting that there is redundancy in this pathway. Dr. Alshareedah hypothesizes that RAD52 nanoclusters in cells recruit RAD51 and load it onto ssDNA, even in the absence of functional BRCA2. To investigate this hypothesis, Alshareedah will examine if RAD51, ssDNA, and other DNA-break repair proteins are recruited to RAD52 nanoclusters in cells. He will then determine which RAD52 protein features are required for cluster formation. By understanding the partial redundancies in the DNA repair pathway, Alshareedah's research may reveal novel targets for treating BRCA2-mutant cancers.

Alshareedah's expertise in protein and nucleic acid clusters stems from his Ph.D. research in [Dr. Priya Banerjee's lab](#) at the University at Buffalo. There, Alshareedah focused on the formation and material properties of protein-nucleic acid biomolecular condensates. He developed an in-condensate passive micro rheology assay and showed that condensates behave as an [elastic solid on short time scales, but like a viscous liquid on long time scales](#). Alshareedah also used this method to [probe the aging process of condensates](#), which is thought to be related to protein aggregation in neurodegenerative diseases. Now in his postdoctoral research, Alshareedah will investigate the functional importance of RAD52 condensates in BRCA2-mutant cancers.

FELLOW



# MEENAKSHI ASOKAN, Ph.D.

LABORATORY OF DR. ANNEGRET FALKNER  
PRINCETON NEUROSCIENCE INSTITUTE  
PRINCETON UNIVERSITY

## JANE COFFIN CHILDS FELLOW

Social interactions and behaviors are mediated by a hormone-sensitive brain network. For example, female mice are sexually receptive only during a certain phase of their estrous cycle around ovulation. Yet, it is still unclear how hormones modulate this network's circuit architecture and dynamics to dictate changes in behavior.

Dr. Meenakshi Asokan will examine this missing link in [Dr. Annegret Falkner's lab](#) at Princeton University. Dr. Asokan hypothesizes that sex hormones reorganize neural dynamics and functional coupling in crucial hubs for top-down control of sociability to drive flexible female social choice. Asokan will use a behavioral assay and computational tools to quantify the hormone-dependent changes in social motivation and preference. She will then pinpoint the location of these differences in the brain, address how these neural ensembles alter the coding of social interactions and manipulate these regions to verify their causal role in hormone-dependent changes in social behaviors. These studies will provide fundamental insight into how sex hormones rewire information processing to impact social behaviors. This information will be invaluable in situations where steep changes in hormone levels are linked to depressive symptoms such as during post-partum, perimenopausal, and pre-menstrual stages in women.

Asokan built her expertise in understanding how neural circuits influence perception and behaviors in [Dr. Daniel Polley's lab](#) at Harvard University. During her graduate studies, Asokan focused on neural substrates that underlie changes in perception following noise-induced hearing loss. She localized this change to [layer 5 cortico-collicular axons that innervate the amygdala and striatum](#), which explains the exacerbated sound-triggered anxiety and aversiveness in hearing loss patients. Additionally, through multi-regional extracellular recordings and optical measurements, Asokan discovered [cooperative plasticity in inputs to amygdala as mice learn to reappraise neutral stimuli as possible threats](#). Asokan will now use her expertise in linking brain regions to changes in social behavior to investigate how sex hormones influence these processes during her postdoctoral research.

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# DIVYA BEZWADA, Ph.D.

LABORATORY OF DR. BENJAMIN F. CRAVATT  
DEPARTMENT OF CHEMISTRY  
SCRIPPS RESEARCH INSTITUTE

## JANE COFFIN CHILDS-MERCK FELLOW

Allostery is a fundamental biochemical process in which one site on a protein influences the function of a different site on the same protein, even if they are far apart. Given this relationship, allosteric sites are versatile drug targets as they can activate, inhibit, or even provide a new function to the protein depending on the specific ligand. Yet, therapeutic cooption of allosteric sites remains limited, in part, due to the prevalence of invisible, cryptic allosteric sites that only appear upon ligand binding.

Dr. Divya Bezwada aims to transform our understanding of cryptic allosteric sites in [Dr. Benjamin Cravatt's lab](#) at The Scripps Research Institute. There Dr. Bezwada will use a chemoproteomic approach to investigate the prevalence of cryptic allosteric sites across protein paralogs. Bezwada's research will provide first principles regarding the evolution of cryptic allosteric sites and develop novel chemical tools with broad relevance for biological understanding and therapeutic applications.

Bezwada provided novel insight into cancer metabolism during her doctoral research in [Dr. Ralph DeBerardinis' lab](#) at UT Southwestern Medical Center. There she found that clear cell renal cell carcinomas (ccRCC) have defects in the electron transport chain which suppresses oxidative phosphorylation. This result is consistent with decades of research into cancer metabolism. Unexpectedly, Bezwada found that [ccRCC metastases upregulate oxidative phosphorylation and that this change is functionally important for metastasis](#). Bezwada's discovery has crucial and paradigm-shifting implications for cancer patient treatment. Now, Bezwada will leverage chemical biology techniques to make her next important insights into human biology and disease during her postdoctoral research.

FELLOW



# JULIAN BRAXTON, Ph.D.

LABORATORY OF DR. ZHEN CHEN

DIVISION OF BIOLOGY AND BIOLOGICAL ENGINEERING

CALIFORNIA INSTITUTE OF TECHNOLOGY

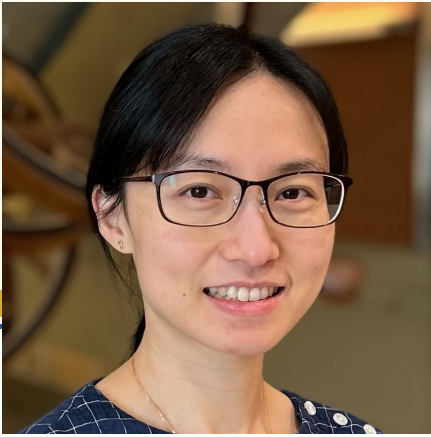
## JANE COFFIN CHILDS FELLOW

Traditionally, structural biology efforts have been limited to studying purified samples in isolation. While we have learned a great deal via these efforts, such approaches unfortunately strip away much of the biological context from the sample of interest.

Dr. Julian Braxton will overcome these limitations by using cryo-electron tomography (cryo-ET) to examine proteostasis, or the process by which cells maintain the proper balance, folding, and function of proteins, within sperm cells in [Dr. Zhen Chen's lab](#) at the California Institute of Technology. Proteostasis plays important yet understudied roles in cellular development processes, as the proteome must be reprogrammed to enable new functions. Braxton will apply cellular cryo-ET to analyze such developmental process in mammalian sperm, where highly specialized functional compartments are assembled. This research will provide foundational understanding into the posttranslational regulation of sperm maturation and expand the frontier of cryo-ET development and analysis.

Braxton's expertise in proteostasis stems from his graduate studies in [Dr. Daniel Southworth's lab](#) at the University of California, San Francisco. There, Braxton used the related structural technique cryo-EM to reveal the intricate details of how the autophagy-related adapter UBXD1 regulates the hexameric AAA+ chaperone p97. His findings revealed that [UBXD1 separates two adjacent p97 protomers to open the p97 ring, allowing for a new mode of substrate entry and/or exit into the p97 central pore](#). In a related project, Braxton revealed a [novel asymmetric state of the mitochondrial chaperone Hsp60 that enables client refolding](#). In his postdoctoral work, Braxton will expand his structural biology toolkit to include cryo-ET and use this technique to provide unprecedented insight into the role of nuclear proteasomes in spermatogenesis.

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# YI FU, Ph.D.

LABORATORY OF DR. JAY SHENDURE  
INVESTIGATOR, HHMI  
DEPARTMENT OF GENOME SCIENCES  
UNIVERSITY OF WASHINGTON

## JANE COFFIN CHILDS-HHMI FELLOW

Mitochondria are cellular organelles that house their own DNA. There are hundreds to thousands of copies of the mitochondrial genome (mtDNA) in each cell. Often, mtDNA copies are not the same, rather a fraction of them carries mutations. Moreover, the composition of mtDNA varies drastically across cells and cell types. Mitochondrial diseases manifest when the pathogenic mutations reach a high percentage in a substantial fraction of cells. However, it is still unclear how mtDNA mutations expand and how cell-to-cell variation of mtDNA composition is formed.

Dr. Yi Fu will address these questions in [Dr. Jay Shendure's lab](#) at the University of Washington. Dr. Fu will develop a method to accurately genotype mtDNA at single-cell resolution and employ this method to monitor mtDNA mutations during differentiation. Fu will also combine this approach with CRISPR perturbation to identify factors that impact the mitochondrial mutation burden in various cell types. These experiments will uncover cell type-specific regulation of mitochondrial genome maintenance. Furthermore, Fu's research may provide insight into novel therapeutic approaches for mtDNA-associated diseases.

Fu's expertise in mtDNA stems from her graduate studies in [Dr. Agnel Sfeir's lab](#) at New York University and Memorial Sloan Kettering Cancer Center. There Fu discovered that [double-strand breaks in mtDNA activate the integrated stress response](#), highlighting the cellular program to cope with defective mitochondrial genome. Fu also investigated mtDNA deletions and their impact on cellular metabolism. Now, Fu will leverage genomics and single-cell technologies to elucidate the dynamic regulation of mtDNA during her postdoctoral research.

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# JARVIS HILL, Ph.D.

LABORATORY OF DR. SETH B. HERZON  
DEPARTMENT OF CHEMISTRY  
YALE UNIVERSITY

## JANE COFFIN CHILDS-MERCK FELLOW

Glioblastoma is one of the deadliest forms of brain cancer. All glioblastomas contain fast-growing and aggressive tumor cells. The current standard of care, temozolomide (TMZ), extends patient's lives by a median of 7 months, however this chemotherapy only works for a subset of patients and many of those patients rapidly acquire resistance to this treatment. Additional, more efficacious treatments are direly needed for glioblastoma patients.

Dr. Jarvis Hill's postdoctoral research in [Dr. Seth Herzon's lab](#) at Yale University aims to enable the next generation of glioblastoma therapies. The Herzon lab recently identified a novel small-molecule, KL-50, that is [effective against glioblastomas lacking the O6-methylguanine-DNA-methyltransferase \(MGMT\)](#). However, this small molecule does not work on MGMT positive glioblastomas. In this research Dr. Hill will develop tumor-specific MGMT inhibitors that can be combined with KL-50 to treat patients with MGMT positive glioblastoma.

Part of Dr. Hill's interest in brain tumors grew out of his Ph.D. research in [Dr. David Crich's lab](#) at the University of Georgia. As an organic chemist, Hill devised a novel synthesis for trisubstituted hydroxylamines. Recognizing that these are underrepresented functional groups in medicinal chemistry, Hill next evaluated the drug-like properties of molecules where he replaced hydrocarbons, ethers, or amines with a trisubstituted hydroxylamine. In contrast with long-standing expectations, Hill found that these substitutions were stable and generally well tolerated. Then, Hill used the trisubstituted hydroxylamine motif as a key structural unit to develop an [epidermal growth factor receptor \(EGFR\) inhibitor with excellent brain penetration](#), which may be useful for treating brain metastases driven by aberrant EGFR. Now Dr. Hill will turn his dual focus on synthetic medicinal chemistry and neuro-oncology towards finding glioblastoma therapeutics during his postdoctoral research.

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# TOM HINDMARSH STEN, Ph.D.

LABORATORY OF DR. LIQUN LUO  
INVESTIGATOR, HHMI  
DEPARTMENT OF BIOLOGY  
STANFORD UNIVERSITY

## JANE COFFIN CHILDS-HHMI FELLOW

Neural circuits have been honed by evolution to enable animals to instinctively survive and reproduce in the world that surrounds them. Mammals, however, also have a distinct ability to weigh primal instinct against experience, allowing us to learn how to appropriately respond based on our unique knowledge of the dynamic world around us. However, how the mammalian brain balances the innate robustness of neural circuits with the flexibility afforded by learning remains unclear.

Dr. Tom Hindmarsh Sten aims to answer these questions as a JCC-HHMI Fellow in [Dr. Liqun Luo's lab](#) at Stanford University. To investigate how instinctive behaviors can be modified by learning, Dr. Hindmarsh Sten will leverage natural variation in the ability of mice to suppress their innate fears and learn how to hunt live prey. He will delineate an anatomical blueprint of neural circuits that mediate evasion and predation, and pinpoint the plastic nodes impacted by learning. These studies will reveal how neural circuits, which have been refined by eons of evolution, are modulated to meet immediate and novel demands in the present.

As a Ph.D. candidate in [Dr. Vanessa Ruta's lab](#) at Rockefeller University, Hindmarsh Sten investigated neural circuits mediating reproduction in fruit flies. He pioneered a novel virtual reality based behavioral preparation which revealed that [sexual arousal in male flies reconfigures how they see and respond to female flies](#). Additionally, Hindmarsh Sten examined how male flies coordinate aggression amongst rivals with courtship towards females in competitive environments where more than one male fly is vying for each female's attention. This study revealed [neural populations that allow males to rapidly switch between aggression and courtship](#). With this background, Hindmarsh Sten is primed to investigate how learning modulates innate instinct in mammals.

FELLOW



# CAROLINE HOLMES, Ph.D.

LABORATORY OF DR. MICHAEL DESAI  
DEPARTMENT OF ORGANISMIC AND EVOLUTIONARY BIOLOGY  
HARVARD UNIVERSITY

## JANE COFFIN CHILDS FELLOW

Inferring the genetic basis of quantitative traits is foundational to understanding the biological mechanisms that underlie complex phenotypes such as behavior, homeostasis, and disease. Mapping genotype to phenotype has been transformational for understanding and treating diseases controlled by a single gene, or monogenic. However, understanding complex, highly polygenic phenotypes with currently available approaches can take decades of research from fields of researchers to make progress, if the problem is even solvable with current methodologies.

Dr. Caroline Holmes will transform the process of unraveling polygenic phenotypes in [Dr. Michael Desai's lab](#) at Harvard University. Dr. Holmes will develop new computational approaches and use high-throughput experiments to learn the structure of interactions between genes involved in a particular phenotype. Holmes then will test her predictions of interactions with mutational perturbations. Ultimately, Holmes will develop methods to improve the generalizability of genotype to phenotype maps and test their accuracy on a distinct microbe that was not used to train the system. If successful, Holmes' methods would rapidly catalyze the process of understanding and rationally perturbing polygenic phenotypes.

Holmes' longstanding interest in both biology and physics dates back to her studies and research as an undergraduate student at Emory University. Her graduate studies emphasized the physics side as Holmes mainly used theoretical approaches in the labs of Dr. Bialek and Dr. Palmer at Princeton University. However, many of Holmes' research applications were still biological in nature. For example, Holmes [demonstrated that non-24 hour circadian periods can compensate for systematic error that arises as a result of seasonality](#). Holmes will now develop quantitative experimental systems during her postdoctoral research and combine this with her expertise in theoretical approaches to make inroads into complex polygenic phenotypes.

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# AMER AZIM HOSSAIN, Ph.D.

LABORATORY OF DR. JOHN MACIEJOWSKI  
MOLECULAR BIOLOGY PROGRAM  
MEMORIAL SLOAN KETTERING CANCER CENTER

## JANE COFFIN CHILDS FELLOW

Extrachromosomal DNAs (ecDNAs) are circular DNA elements that amplify oncogenes and mediate chemotherapy resistance. Despite their importance in cancer, currently no therapies directly target these aberrant molecular structures.

Dr. Amer Hossain will investigate innate immune system recognition of ecDNAs to limit their oncogenic potential in [Dr. John Maciejowski's lab](#) at Memorial Sloan Kettering Cancer Center. Dr. Hossain's research will provide a fundamental understanding of the recognition and processing of ecDNAs by the immune system. Furthermore, his studies may provide insight into defects in this process that lead to cancer, and into therapeutic strategies to reinforce immune clearance of ecDNAs.

Hossain studied bacteria-phage conflicts as a graduate student in [Dr. Luciano Marraffini's lab](#) at The Rockefeller University. Specifically, [he developed a novel functional assay to screen for antiphage defense elements, and discovered a DNA glycosylase that inhibits phage replication](#). At first glance, this might seem like a distant subject from cancer biology. Yet, Hossain notes in many ways the immune-ecDNA conflict mirrors the host-pathogen conflict in that they both involve recognition and degradation of DNA substrates. Therefore, Hossain will apply his expertise to cancer biology during his postdoctoral research.

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# YANYAN HU, Ph.D.

LABORATORY OF DR. WILLIAM KAELIN, JR.  
INVESTIGATOR, HHMI  
DEPARTMENT OF MEDICAL ONCOLOGY  
DANA-FARBER CANCER INSTITUTE & HARVARD MEDICAL SCHOOL

## JANE COFFIN CHILDS-HHMI FELLOW

Dr. Yanyan Hu's research focuses on discovering new biomarkers to help diagnose, monitor, and treat cancer. In particular, Dr. Hu hypothesizes that studying the tumor cell surface proteome will reveal an abundance of potential therapeutic and diagnostic targets against cancer.

In [Dr. William Kaelin, Jr.'s lab](#) at Dana-Farber Cancer Institute, Hu has devised a proximity labeling method that enables the direct quantification of proteins on the surface of cancer cells. Hu will now use this method to examine two types of cancer: clear cell renal cell carcinoma, and tumors with homologous recombination defects. In addition to revealing novel and fundamental information on cancer cell surface proteomes, Hu's research has direct implications for future diagnostic and therapeutic approaches.

Hu's Ph.D. research in [Dr. Sheng Ding's lab](#) at Tsinghua University focused on totipotent stem cell biology. Totipotent stem cells are capable of producing every kind of differentiated cell in both embryonic and extraembryonic tissues. Previously, they had only been generated through IVF or SCNT using germline cells. Hu discovered [a cocktail of three small molecules that converted mouse pluripotent stem cells into totipotent stem cells](#). Now Hu will apply her expertise of stem cell biology to explore similar mechanisms – such as cellular plasticity, self-renewal, and differentiation – to cancer biology during her postdoctoral research.

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# SHIJIA LIU, Ph.D.

LABORATORY OF DR. BERNARDO SABATINI  
INVESTIGATOR, HHMI  
DEPARTMENT OF NEUROBIOLOGY  
HARVARD MEDICAL SCHOOL

## JANE COFFIN CHILDS-HHMI FELLOW

Sometimes less is more. Our ability to stop an action is an important aspect of executive control, and the lack of this ability is linked to neuropsychiatric disorders like Obsessive-Compulsive Disorder and Attention-Deficit/Hyperactivity Disorder. Yet, it remains unclear how we make and execute stop decisions.

Dr. Shijia Liu will investigate the neural mechanisms and pathways underlying voluntary stop decisions in [Dr. Bernardo Sabatini's lab](#) at Harvard Medical School. Dr. Liu will focus her studies on how mice voluntarily stop licking in response to the absence of water, as a specific instantiation of the broader question. Liu has designed a “licking-for-water” task that will enable her to dissect this process temporally and in different contexts. She will identify the modes of action and neural pathways that mediate stop decisions using optogenetics, large-scale neural recording, and real-time decoding approaches. Liu's research will improve our understanding of voluntary stop decisions, related neuropsychiatric disorders, and computational mechanisms for context-dependent behavioral switching.

Liu's expertise in neuroscience stems from her Ph.D. research in [Dr. Sung Han's lab](#) at the Salk Institute for Biological Studies. Her graduate studies focused on the neural connection between perceived pain and breathing, and how opioid drugs impact this connection. Liu identified [two subpopulations of lateral parabrachial nucleus \(PBL\) neurons that express the m-opioid receptor and project to pain and breathing centers](#). By manipulating activity at the cellular and molecular levels, Liu discovered [how to decouple morphine administration and respiratory depression](#), which would prevent opioid overdose deaths. With this expertise in involuntary physiological-behavioral connections, Liu will now focus on voluntary decisions and their impact on behavior during her postdoctoral research.

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# TIANYANG MAO, Ph.D.

LABORATORY OF DR. DARRELL J. IRVINE  
INVESTIGATOR, HHMI  
KOCH INSTITUTE FOR INTEGRATIVE CANCER RESEARCH  
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

## JANE COFFIN CHILDS FELLOW

Proper functioning of our immune systems depends on the precise timing of an orchestra of molecular events. One such important event is the release of cytokines, which are signaling molecules, into the extracellular space to mediate intercellular communication. For cytokines to exert appropriate immunomodulatory roles, their bioavailability must be strictly yet dynamically regulated in space and time. However, the mechanisms by which the immune system interprets the timing of cytokine release remain poorly understood.

Dr. Tianyang Mao will investigate the temporal encoding of cytokine signaling in anti-tumor immunity in [Dr. Darrell Irvine's lab](#) at the Massachusetts Institute of Technology. Dr. Mao will use a novel controlled drug release technology which enables programmable control over the duration of cytokine exposure in vivo. This unique approach will allow Mao to make novel insights into how cytokine temporal dynamics shape cancer immunosurveillance. Better understanding of the immunological impact of cytokine release kinetics will guide the development of temporally reprogrammed cytokine therapeutics for cancer treatment.

Mao's expertise in immunology emerged as a graduate student in [Dr. Akiko Iwasaki's lab](#) at Yale University. There Mao developed [an intramuscular prime-intranasal boost vaccine strategy for SARS-CoV-2 termed "prime and spike,"](#) which leverages preexisting immunity generated by primary mRNA-LNP vaccines to elicit mucosal immunity within the respiratory tract using unadjuvanted intranasal spike boosters. In addition, he developed several antiviral strategies that trigger type I interferon-based immune protection against SARS-CoV-2, including [a short stem-loop RNA agonist for the innate immune receptor RIG-I](#) and [an aminoglycoside antibiotic with unexpected antiviral properties](#). Collectively, these strategies hold great promise to not only prevent disease, but also viral transmission. Now, Mao will build on this experience, using novel bioengineering techniques in the Irvine Lab, to make new inroads into the importance of timing in immune responses to cytokines.

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# MARIJA NADJSOMBATI, Ph.D.

LABORATORY OF DR. ALANA WELM  
DEPARTMENT OF ONCOLOGICAL SCIENCES  
UNIVERSITY OF UTAH & HUNTSMAN CANCER INSTITUTE

## JANE COFFIN CHILDS FELLOW

Metastasis, which includes the dissemination of tumor cells from a primary site and subsequent colonization of faraway sites, is the primary cause of cancer deaths. This process requires a failure of our immune system to recognize and destroy metastasizing cancer cells. As such, targeting cancer during the metastasis step will help create therapies for patients with many different types of cancers (breast, prostate, colon, etc.).

Dr. Marija Nadsombati will investigate the immune response during metastasis in [Dr. Alana Welm's lab](#) at the University of Utah. Dr. Nadsombati will use mouse models of breast cancer which faithfully recapitulate metastatic propensity. Nadsombati will develop new cancer models and investigate their transcriptional regulatory networks to decipher the role of T cell regulation in metastasis. These studies will provide novel insights on both T cell regulation and on targeted therapies for cancer immunology.

Nadsombati built her expertise in immunology as a graduate student in [Dr. Jakob von Moltke's lab](#) at the University of Washington. There she studied a specialized type of epithelial cells, called tuft cells, which initiate immune responses in the small intestine. Nadsombati discovered that [succinate triggers the downstream signaling in tuft cells that initiates a type 2 immune response](#). Additionally, by comparing different mice strains, and performing genetic crosses, Nadsombati showed that [Pou2af2 isoform expression is a key regulatory mechanism that determines tuft cell frequency](#). With this strong immunological background, Nadsombati is poised to make new breakthrough discoveries on the immune regulation of metastasis.

FELLOW





# VICTOR NATURALE, Ph.D.

LABORATORY OF DR. AMY SHYER AND DR. ALAN RODRIGUES  
LABORATORY OF MORPHOGENESIS  
THE ROCKEFELLER UNIVERSITY

## JANE COFFIN CHILDS FELLOW

Organismal development is an elegant progression from a single cell to billions or trillions of different cells that form our tissues and organs. While much is known about development at the molecular level, important questions remain about how subcellular molecular inputs integrate with “supracellular” physical behaviors of large cell collectives to shape our tissues. Little is known about how subcellular and supracellular dynamics relate among the mesenchymal cell types that give rise to all connective tissues including skin.

Dr. Victor Naturale will make inroads into these questions using a [novel vertebrate skin cell](#) platform developed in [Dr. Amy Shyer's](#) and Dr. Alan Rodrigues' lab at The Rockefeller University. Dr. Naturale expects that understanding how biological organization translates across length scales will provide novel insight into diverse areas including cancer microenvironments and mesenchymal birth defects that lack a single genetic cause.

Naturale developed his interest in developmental biology as a graduate student in [Dr. Jessica Feldman's lab](#) at Stanford University. Working largely at the molecular to cellular scale, Naturale discovered that in *C. elegans* the polarity [scaffold PAR-3 and the transmembrane protein HMR-1/E-cadherin collaboratively build polarity networks at epithelial cell-cell contacts](#). He demonstrated that HMR-1 also communicates cell polarity at the tissue level. Importantly, Naturale additionally identified a novel symmetry breaking cue arising at the supracellular scale due to emergent cell-cell contact patterns. This research, and the beautiful images within, were highlighted on the [journal cover](#). In his postdoctoral research, Naturale will translate his experience identifying supracellular cues to a novel model system with relevance to cancer and developmental diseases.

FELLOW



# JUNG-UN PARK, Ph.D.

LABORATORY OF DR. DAVID SAVAGE  
INVESTIGATOR, HHMI  
DEPARTMENT OF MOLECULAR & CELL BIOLOGY  
UNIVERSITY OF CALIFORNIA, BERKELEY

## JANE COFFIN CHILDS-HHMI FELLOW

CRISPR-Cas systems have revolutionized genetic engineering and led to novel genetic medicines. As powerful as these systems are, they have some disadvantages such as their large size and a lack of orientation bias which limits their therapeutic usage. CRISPR-associated transposons (CASTs) are mobile genetic elements that use CRISPR-Cas systems for RNA-guided transposition. CASTs may represent the next generation of genome editors due to their enhanced features relative to CRISPR-Cas. Yet, CASTs still require further optimization to realize this potential.

Dr. Jung-Un Park will engineer novel forms of CASTs to optimize properties for genome editing in [Dr. David Savage's lab](#) at the University of California, Berkeley. Using structural biology, biochemistry, and protein engineering approaches, Dr. Park will enhance the activity of individual CAST proteins, as well as tune the functional association between different CAST proteins. Ultimately, Park's research will provide vast insight into genome editing and may result in the next generation of gene editing technologies.

Park's interest in CAST biology stems from his graduate work in [Dr. Elizabeth Kellogg's lab](#), while at Cornell University. There, he solved structures for CAST that informed on both [RNA-guided](#) and [RNA-independent transposition](#). Park will leverage his extensive knowledge of CAST structural details to optimize this system for genome editing during his postdoctoral work.

FELLOW



# NOAH PETTIT, Ph.D.

LABORATORY OF DR. RACHEL WILSON  
INVESTIGATOR, HHMI  
DEPARTMENT OF NEUROBIOLOGY  
HARVARD MEDICAL SCHOOL

## JANE COFFIN CHILDS-HHMI FELLOW

In adaptive behavior, we take in information from the world around us and use that information to execute certain actions to interact with the surrounding environment. For example, successful navigation requires us to remember the spatial position of a goal and transform that information into actions that will move us towards that goal. Mechanistically, it is still unclear how neural circuits perform these computations.

Dr. Noah Pettit will approach this question using fruit fly interaction with wind direction in [Dr. Rachel Wilson's lab](#) at Harvard Medical School. Dr. Pettit hypothesizes that specific cell types form a circuit that encodes wind direction, maintains it in memory, and transforms this information to influence body movement. Pettit will use multisensory virtual reality, two-photon imaging, and genetic silencing approaches to investigate this circuit at the cellular and molecular levels. These studies will provide a detailed description of how environmental perception is sensed, stored, and translated into action, thereby providing a general framework for understanding these computations in different systems and organisms.

Pettit generated expertise in the underlying neurobiology of spatial learning in [Dr. Christopher Harvey's lab](#) at Harvard Medical School. During his graduate studies he examined the role of Fos, a transcription factor implicated in memory, and spatial learning. Pettit discovered that [Fos-induced neurons are more likely to be place cells](#) – cells that are activated when an animal experiences a certain place in its environment. Additionally, Pettit found that the [place code degrades when mice voluntarily disengage from a spatial task](#) – suggesting that the internal state exerts a strong influence on place cell activity. With this experience, Pettit will now transition to fruit flies and understanding how these animals transform and respond to external cues.

FELLOW



# DANIEL RICHARD, Ph.D.

LABORATORY OF DR. ANNE BRUNET  
DEPARTMENT OF GENETICS  
STANFORD UNIVERSITY

## JANE COFFIN CHILDS FELLOW

Aging is associated with decreased cognitive ability and enhanced risk of developing neurodegenerative diseases such as Parkinson's and Alzheimer's. The declining function of neural stem cells (NSCs) is partially responsible for these trends in the aging brain. While much is known about the genetics of late-stage neurodegenerative diseases, relatively little is known about changes that lead to the decline in NSC function.

Dr. Daniel Richard will investigate the accumulation of somatic mutations in NSCs in [Dr. Anne Brunet's lab](#) at Stanford University. He will examine how these mutations change NSC gene expression and neuron production. Additionally, Dr. Richard will look for routes to genetically manipulate somatic mutations to improve NSC function. Richard's studies will provide much needed insight into fundamental NSC biology during aging and may reveal novel therapeutic strategies for neurodegenerative diseases and cognitive decline.

Richard's interest in the link between genetic changes and aging arose from his graduate studies in [Dr. Terence Capellini's lab](#) at Harvard University. There, Richard focused on the genetic regulation of knee development. By comparing functional regulatory regions in human and mouse fetal limbs, [Richard discovered mutations that are associated with increased risk for osteoarthritis later in life](#). Now Richard will switch his focus on aging-related biological changes to NSCs and neurodegenerative diseases during his postdoctoral research.

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# EMILY RUNDLET, Ph.D.

LABORATORY OF DR. JASON McLELLAN  
DEPARTMENT OF MOLECULAR BIOSCIENCES  
UNIVERSITY OF TEXAS

## JANE COFFIN CHILDS FELLOW

The international outbreak of mpox (monkeypox) in 2022 incited global health concerns and underscored the need for an innovative vaccine. However, little is known about potential vaccine targets within the causative orthopoxvirus, mpox virus.

Dr. Emily Rundlet will explore the structure and function of potential mpox vaccine targets in [Dr. Jason McLellan's lab](#) at the University of Texas at Austin. Dr. Rundlet will structurally characterize antigen complexes using cryo-EM and X-ray crystallography, which will enable her to probe their function in the viral lifecycle and design vaccine candidates. In sum, Dr. Rundlet's work is expected to provide valuable insights into mpox biology and pave the way for future mpox vaccines.

Dr. Rundlet developed her expertise in structural biology in [Dr. Scott Blanchard's lab](#) at Weill Cornell Medicine. During her graduate studies, Dr. Rundlet used cryo-EM and single-molecule FRET assays to make important discoveries about protein translation. With these methods, Dr. Rundlet [elucidated how the ribosome initiates movement of tRNAs during protein synthesis](#) and demonstrated that [mRNA decoding by ribosomes is kinetically and structurally different in humans and bacteria](#). Now Dr. Rundlet is using her expertise to uncover the structural secrets of orthopoxviruses to guide vaccine design and prevent future outbreaks.

FELLOW



# TREY SCOTT, Ph.D.

LABORATORY OF DR. NAOMI PIERCE

DEPARTMENT OF ORGANISMIC AND EVOLUTIONARY BIOLOGY

HARVARD UNIVERSITY

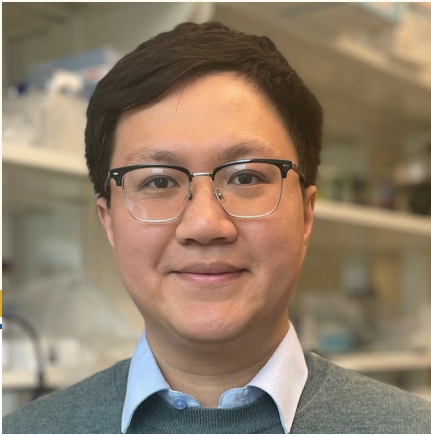
## JANE COFFIN CHILDS FELLOW

Social interactions between distinct species are important at ecological scales yet are mediated at the molecular level by the transfer of biomolecules such as small chemicals and proteins between organisms. Symbiosis is an example of a relationship among species where both species benefit from a social behavior or interaction.

Dr. Trey Scott will examine the symbiotic relationship between butterfly larvae in the Lycaenidae family and ants in [Dr. Naomi Pierce's lab](#) at Harvard University. Lycaenid caterpillars secrete nutritious and psychoactive substances that are ingested by ants. Ants, in return, protect their renewable food source, the caterpillar, during its vulnerable developmental stage. Dr. Scott will determine the molecular, cellular, and evolutionary bases for this example of symbiosis. Scott's research will provide novel insight into social interactions, broadly speaking, including their evolution.

Scott examined social interactions as a graduate student in [Dr. Joan Strassmann's](#) and [Dr. David Queller's labs](#) at Washington University. Although the above example of symbiosis between ants and Lycaenid butterflies is relatively straightforward, most examples of social interactions contain context-dependent elements of both cooperation and conflict. Using *Dictyostelium discoideum* amoebae and *Paraburkholderia* bacteria as a model for social interactions, Scott discovered that the [bacteria may benefit or be harmed by the amoebae depending on current environmental conditions – in this case, rainfall](#). Scott proposed that this flexibility helps the amoebae host survive in harsh soils with variable prey. Furthermore, Scott showed how [long-term social interactions influence evolutionary adaptation](#). With this extensive background in social interactions, Scott is poised to make breakthroughs investigating the evolution of symbiosis between butterflies and ants during his postdoctoral research.

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# BING SHUI, Ph.D.

LABORATORY OF DR. TYLER JACKS  
KOCH INSTITUTE FOR INTEGRATIVE CANCER RESEARCH  
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

## JANE COFFIN CHILDS FELLOW

Tissue regeneration, in a normal developmental context, and cancer are both forms of cellular proliferation. However, tissue regeneration is regulated and responsive to the surrounding environment, whereas cancer sheds these restraints. Understanding the commonalities and the differences between tissue regeneration and cancer may provide insight into novel avenues for cancer therapeutics.

Dr. Bing Shui will investigate the role of tissue damage in facilitating the early pre-neoplastic to neoplastic transition in colorectal cancer in [Dr. Tyler Jacks' lab](#) at the Massachusetts Institute of Technology. Dr. Shui will examine how tissue damage cooperates with oncogenic mutations to initiate cancer. He will also compare damaged mutant and wildtype cells to identify vulnerabilities that can be leveraged to selectively destroy precancerous cells. Ultimately, a better understanding of the role of tissue damage in this early precancerous transition may reveal novel prophylactic cancer treatments.

Shui's interest in the relationship between tissue regeneration and cancer burgeoned in [Dr. Kevin Haigis' lab](#) at Harvard University. During his Ph.D. studies, he examined the role of microRNAs (miRNAs) in colon regeneration and colon cancer. First, Shui demonstrated that [miRNAs are required for tissue regeneration and miRNA suppression exacerbated colon damage due to failed regeneration](#). Next, he examined the role of miRNAs in colon cancer and discovered a novel form of [posttranslational regulation mediated by oncogenic K-Ras that governs global miRNA function](#). Now Shui will use his expertise in tissue damage and regeneration to identify vulnerabilities in colorectal cancer during his postdoctoral research.

FELLOW



# DONTÉ (ALEX) STEVENS, Ph.D.

LABORATORY OF DR. KEREN LASKER

DEPARTMENT OF INTEGRATIVE STRUCTURAL  
AND COMPUTATIONAL BIOLOGY

THE SCRIPPS RESEARCH INSTITUTE

## JANE COFFIN CHILDS FELLOW

Tauopathies are diseases such as Alzheimer's that are characterized by the aggregation of tau protein. Unfortunately, no disease-modifying therapies currently exist for tauopathies, and the impact of these diseases will increase as the global population trends towards an aging demographic.

Dr. Alex Stevens will investigate a novel mode for treating tauopathies in [Dr. Keren Lasker's lab](#) at the Scripps Research Institute. Autophagy-based degradation methods are making progress, yet a hallmark of tauopathies is that these solid tau aggregates resist degradation. To circumvent this issue, Dr. Stevens will engineer biomolecular condensates to clear tau aggregates. Stevens' research will set the foundation for next generation tauopathy therapies and provide a general framework using biomolecular condensates to modulate pathological events.

Stevens investigated how viruses hijack cellular transport mechanisms during his Ph.D. research in [Dr. Samara Reck-Peterson's lab](#) at the University of California, San Diego. By exploring the conflicts between viruses and the host intracellular transport machinery, Stevens [discovered a previously unknown transport mechanism that potentiates the innate immune response](#). His research provides insight into how cells mount a defense against infecting viruses and highlights the important role of cellular transport in this process. Now, Stevens will attempt to rationally hijack autophagy to enable degradation of aggregated tau.

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# JONATHAN TULLIS, Ph.D.

LABORATORY OF DR. MICHAEL COHEN

DEPARTMENT OF CHEMICAL PHYSIOLOGY AND BIOCHEMISTRY

OREGON HEALTH AND SCIENCE UNIVERSITY

## JANE COFFIN CHILDS FELLOW

Poly ADP-ribose polymerase 1 (PARP1) is a protein involved in the DNA damage response and an important drug target against many cancers. There are a number of PARP1 inhibitors, but current drugs targeting PARP1 can have limited therapeutic potential due to cancer cells frequently acquiring resistance to these drugs.

Dr. Jonathan Tullis aims to understand the mechanistic details of a class of PARP1 inhibitors in [Dr. Michael Cohen's lab](#) at Oregon Health and Science University. PARP1 inhibitors are thought to function by inhibiting the enzymatic activity of this protein. However, "type I" inhibitors exhibit an additional feature – they lock PARP1 onto sites of DNA damage. Dr. Tullis will use mechanistic studies to tease apart the relative importance of these two features – enzymatic inhibition vs locking PARP1 onto DNA – for therapeutic efficacy. These detailed studies promise to reveal novel information about PARP1 biology and may pave the path for more effective PARP1 drugs in the future.

Tullis' passion for mechanistic studies dissecting protein function stem from his graduate research in [Dr. Ulli Bayer's lab](#) at the University of Colorado. His Ph.D. focused on a protein kinase, CaMKII, that is crucial for long-term potentiation, a fundamental process in learning and memory. It was thought that CaMKII's kinase activity was required for long-term potentiation. Using careful biochemical and chemical biological approaches, Tullis convincingly demonstrated that [it is actually a structural role of CaMKII that is required for inducing long-term potentiation and its enzymatic activity was only required to enable that role](#). Next, Tullis will leverage his expertise in mechanistic studies to tease apart the important functions of PARP1 inhibitors during his postdoctoral research so that more efficacious targets against cancer cells can be developed.

FELLOW



# IVAN ZHELUDEV, Ph.D.

LABORATORY OF DR. MELANIE OTT  
INSTITUTE OF VIROLOGY  
GLADSTONE INSTITUTE

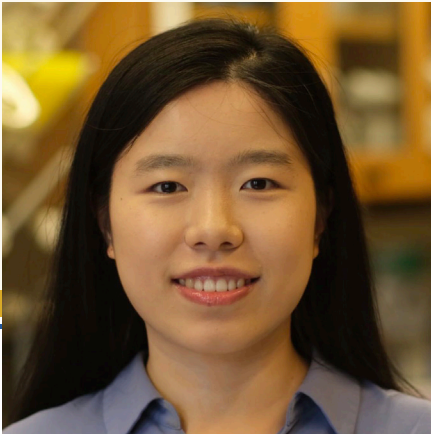
## JANE COFFIN CHILDS FELLOW

The first century of molecular biology discoveries was enabled by the study of Nature's original molecular biologists: viruses. Viruses and their simpler cousins, sub-viral RNAs are extremely well adapted to manipulate their host cell. By studying how these agents alter their host, scientists have been able to both understand the mechanisms of diseases as well as derive tools to fight them. Yet there is still much we don't know about viruses, but even less-so about sub-viral RNAs. Obelisk RNAs are a recently discovered class of widespread sub-viral RNAs with small, structured genomes that seem to bear no resemblance to any known biological entity. The study of Obelisk biology then might reveal molecular mechanisms that have yet to be seen.

Dr. Ivan Zheludev will characterize a novel class of sub-viral RNAs, termed Obelisk RNAs, in [Dr. Melanie Ott's lab](#) at the Gladstone Institute of Virology using a model Obelisk-host system based on a human oral bacterium. Using this system, Zheludev will probe how Obelisk RNA replicates and spreads between cells, the function of the Obelisk-encoded protein Oblin-1, and how Obelisk RNA impacts the host bacterium within complex microbial communities such as the human oral microbiome. Zheludev's studies will provide foundational knowledge for understanding Obelisk RNAs and provide a general framework for investigating sub-viral RNAs.

Zheludev's interest in sub-viral RNAs stems from his Ph.D. research in [Dr. Andrew Fire's lab](#) at Stanford University. There, Zheludev created a bioinformatic discovery tool and used it to [discover a new class of sub-viral RNAs that he named "Obelisk" RNAs](#). He demonstrated that Obelisk RNAs are widespread, with examples found on every continent, and that they are diverse, having identified roughly 30,000 distinct Obelisks. Further, they are also found in the microbiomes of between five to fifty percent of assayed human donors. Now in his postdoctoral research, Zheludev will investigate Obelisk molecular biology and their host interactions.

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# ZHUONING ZOU, Ph.D.

LABORATORY OF DR. CHUAN HE  
INVESTIGATOR, HHMI  
DEPARTMENT OF CHEMISTRY  
THE UNIVERSITY OF CHICAGO

## JANE COFFIN CHILDS-HHMI FELLOW

Translation is a key step in gene regulation that dynamically responds to cell stress, signaling, and metabolic alterations. While there are techniques that allow for investigating transcription with single-cell resolution, similar tools for examining translation are lacking.

Dr. Zhuoning Zou will develop a method for analyzing translation in single cells from complex samples in [Dr. Chuan He's lab](#) at the University of Chicago. Dr. Zou's method will use in situ reverse transcription to develop a spatially resolved single-cell translome profiling method. This method will enable measuring differences in translation between distinct types of cells in a heterogeneous mixture. For example, Zou will apply her method to patient biopsies and surgical colon cancer samples. In such samples this method will distinguish translation between different individual cancer cells as well other types of cells in the tumor microenvironment. This research will uncover the translation landscape in real human tissues, provide novel insights into translation regulation in the tumor microenvironment, and may reveal potential biomarkers for cancer prognosis and targets for future therapies.

Zou developed sensitive methods for monitoring translation and applied them to rare and heterogenous samples in [Dr. Wei Xie's lab](#) at Tsinghua University. During her graduate studies she helped pilot a method that [investigates translation of a single mouse oocyte](#). Zou then applied that method to human oocytes and early embryos to reveal [novel and dynamic translational regulation in early embryogenesis](#). Now Zou will apply her expertise to examine translational regulation in cancer cells and other cells in the surrounding tumor microenvironment during her postdoctoral research.

FELLOW