NIH NATIONAL CANCER INSTITUTE

iCURE

Intramural Continuing Umbrella of Research Experiences (iCURE) – 2024 Possible Projects

This document includes tables listing NCI PIs who have expressed interest in hosting an iCURE scholar. Possible projects or information on their research groups are described in the table but do not represent an inclusive description of all research activities.

If you are interested in working with PIs from the

- **Center for Cancer Research**
- **Center for Global Health (CGH)**
- **Division for Cancer Control and Population Sciences**
- **Division for Cancer Epidemiology and Genetics**

Possible Projects in the Center for Cancer Research (CCR)

Investigator	Scholar Level	Currently Available Research Areas and Projects	Location (In Maryland)
Jairaj Acharya, MBBS, PhD	All	Our laboratory studies Sphingolipid/Phospholipid Metabolic Signaling using in vivo model organisms Drosophila and mice. Projects in the laboratory include evaluating effects of mutations in de novo sphingolipid biosynthetic pathway during hematopoiesis, lymphocyte differentiation and function, in natural killer cells, and in tumor susceptibility. At the cellular levels we examine gene regulation, metabolic and lipidomic changes and establish if the observed changes contribute to phenotypic changes observed in the mutants. https://ccr.cancer.gov/staff-directory/jairaj-k-acharya	CCR Frederick
Mirit Aladjem, PhD	All	The DNA Replication Group at the NCI's Developmental Therapeutics Branch investigates cellular signaling pathways that monitor and direct DNA synthesis. Since many regulatory networks affecting chromosome duplication are deregulated in cancer, such studies can help portray critical aspects of cancer biology and elucidate the cellular responses to chemotherapeutic drugs. Specifically, our studies use a combination of biochemistry, cell biology and bioinformatics to reveal regulatory pathways that coordinate chromosome duplication with gene expression, chromatin condensation and cellular stress responses to preserve genomic stability. https://ccr.cancer.gov/Developmental-Therapeutics-Branch/mirit-i-aladjem	CCR Bethesda
Leslie Aldrich, PhD	Post-Baccalaureate, Postdoctoral Candidate	Our primary research focus is the discovery and development of small-molecule modulators of challenging biological targets and pathways. A major area of interest is the autophagy pathway, which is important for metabolism and cellular homeostasis. Recent efforts to target autophagy in cancer have focused on late-stage inhibition with compounds that disrupt lysosome function, which is not specific for autophagy, or early-stage kinase inhibition, which has led to molecules that lack specificity due to the multiple roles of the kinases involved in the autophagy pathway. For example, the lipid kinase VPS34 is present in two multi-protein complexes, and inhibition of VPS34 enzymatic activity inhibits both autophagy and vesicle trafficking due to inhibition of both complexes. An alternative approach to potentially provide selective autophagy inhibitors is to target key protein-protein interactions that are required for the initiation of autophagy. We recently identified a small-molecule inhibitor of the Beclin1-ATG14L protein-protein interaction, which is required for the formation, proper localization, and function of VPS34 Complex I, that does not affect the Beclin1-UVRAG protein-protein interaction found in VPS34	CCR Frederick

		Complex II, and thus does not cause vesicle trafficking defects like treatment with VPS34 inhibitors. Additionally, our group has developed a high-throughput screen to identify small-molecule inhibitors of the ATG5-ATG16L1 protein-protein interaction, which is involved in LC3 lipidation and autophagosome formation. Current work in our lab combines several interdisciplinary approaches, including medicinal chemistry to improve the properties/potency of initial hits, chemical biology to study binding modes of the small molecules with target proteins and the impact of protein-protein interaction inhibition on the autophagy pathway and other cellular pathways, and cell biology to evaluate the efficacy of autophagy inhibition as a therapeutic strategy in cancer. https://ccr.cancer.gov/staff-directory/leslie-n-aldrich	
Christine Alewine, MD, PhD	Post-Baccalaureate	The current position is laboratory-based on the Bethesda campus focused on a new cancer health disparities project that aims to: 1) characterize the tumorigenicity of genetic variants of unknown significance found in tumor specimens from African-American patients with pancreatic cancer and, 2) explore the efficacy of targeted therapeutics in this setting. The project will potentially involve the use of pancreatic cancer cell lines and organoids, site-directed mutagenesis and other molecular biology techniques, recombinant protein production, biochemical analyses of enzymatic activity, viral transduction of pancreatic cancer cells, and murine survival surgery to implant tumors in the pancreas. https://ccr.cancer.gov/staff-directory/christine-campo-alewine	CCR Bethesda

Michael Aregger, PhD	All	Our group's research focuses on how cancer cells rewire gene expression and metabolism to adapt to changing environmental conditions. We apply CRISPR-based genome engineering tools and functional genomics approaches to reveal genetic interactions and cancer dependencies, and to identify regulators of metabolic plasticity in cancer cells. Our lab focuses on developing innovative genetic screening approaches and we have access to state-of-the art facilities including next-generation sequencing, single-cell analysis platforms, mass spectrometry, live cell imaging, microscopy, flow cytometry, natural products and synthetic compound libraries, and animal facilities. Several projects are currently available including: 1) Applying high-throughput strategies to identify context-dependent fitness genes across changing environmental conditions 2) Mapping genetic interactions between metabolic genes 3) Identification of synergistic targets with metabolic inhibitors Recent related publications: 1) Application of CHyMErA Cas9-Cas12a combinatorial genome-editing platform for genetic interaction mapping and gene fragment deletion screening. Nature Protocols, 2021. 2) Genetic interaction mapping and exon-resolution functional genomics with a hybrid Cas9-Cas12a platform. Nature Biotechnology, 2020. 3) Systematic mapping of genetic interactions for de novo fatty acid synthesis identifies C12orf49 as a regulator of lipid metabolism. Nature Metabolism, 2020. https://ccr.cancer.gov/staff-directory/michael-aregger	CCR Frederick
A. Rouf Banday, PhD	All	The Banday Laboratory explores the mechanisms underlying genetic alterations in bladder cancer to identify therapeutically actionable pathways. The ongoing projects include studying the role of non-coding genomic alterations and mRNA splicing alterations induced by APOBEC3 enzymes, transcriptional regulation of APOBEC3 enzymes, and the role of innate immunity in bladder cancer and therapeutic resistance. The candidate will have an opportunity to take on a research project on any of these specific research areas. The research projects will involve using a combination of molecular biology, cell biology, genome editing, tumor genomics/transcriptomics/epigenomics, mouse genetics, and computational tools to address pressing questions in cancer biology.	CCR Bethesda

		Our laboratory is committed to representing an exciting and highly diverse group of scientists from various backgrounds and biological training. Candidates should be self-motivated, driven, and thorough, able to multitask, think independently, and work in a highly creative and interactive environment. Together with our collaborators at CCR NCI, we expect to take basic science discoveries to the bedside and contribute to integrating precision medicine into clinical practice. https://ccr.cancer.gov/staff-directory/a-rouf-banday#research	
Munira Basrai, PhD	All	We use multi-organismal (yeast, mouse, and human cells) and multi-disciplinary (genetic, cell biology, biochemical) approaches to study faithful chromosome segregation, a fundamental process of every living cell. Chromosomal instability (CIN) is a major cause of aneuploidy and is observed in nearly all cancers. Hence, identification and characterization of genes involved in preventing CIN are critical for advancement of cancer biology. Our research focuses on centromeric (CEN) DNA and associated proteins which are key determinants to prevent CIN. CEN histone H3 variant CENP-A in humans (Cse4 in budding yeast, Cid in flies) is essential for chromosomal stability. We study the assembly and regulation of CEN chromatin, define mechanisms that prevent CENP-A mislocalization to non-centromeric regions and examine the causes and consequences of CENP-A mislocalization. We provided the first evidence showing that mislocalization of CENP-A contributes to CIN in budding yeast, human cells and xenograft mouse model. These studies are significant because CENP-A is overexpressed in several cancers and this correlates with poor prognosis. Our results provide insights into how defects in kinetochore function contribute to aneuploidy in human and how errors in these pathways contribute to CIN, a hallmark for cancer. The conceptual innovation for our research is reliant on a group of extremely talented trainees at all levels (postbac, postdoc and staff scientists), an impressive network of multi-talented and diverse collaborative investigators whose skills and interests span techniques at the cutting edges and the NIH intramural resources. We are optimistic that our research will help translate basic science research to the clinic and aid in the diagnosis, prognosis, and treatment of cancers with elevated levels of CENP-A. Novel and rapid advances in cancer research are likely to originate from approaches that exploit aneuploidy-related proteins such as CENP-A. https://ccr.cancer.gov/staff-directory/munira-a-basrai	CCR Bethesda

Pedro Batista, PhD	Post-Baccalaureate, Postdoctoral Candidate	The primary objective of our lab is to investigate how RNA post-transcriptional modifications, known as the epitranscriptome, react to alterations in the cellular metabolic conditions. To achieve this, we employ genome engineering techniques and utilize cell lines obtained from patients' tumors as model systems. Our aim is to unravel how disruptions in RNA biogenesis and function facilitate the initiation and proliferation of cancer. To dissect how changes in the tumor microenvironment affect gene expression through modifications in the epitranscriptome, we leverage these cell models and employ molecular biology and next-generation sequencing methods. We have a specific focus on comprehending how the epitranscriptome contributes to cancer cells' ability to evade treatment. Ultimately, this research will lead to the identification of novel targets for cancer therapy. Both metabolic pathways and the regulation of gene expression through RNA methylation can be manipulated to sensitize cancer cells, enhancing the effectiveness of treatment. https://ccr.cancer.gov/staff-directory/pedro-j-batista	CCR Bethesda
Avinash Bhandoola, MB, PhD	All	Immune cells have to reside and function in distinct environments. We recently discovered that transcription factor Tox2 is required by one type of immune cell termed ILC3, but only when they reside in the gut. Mice deficient in Tox2 therefore lack ILC3 specifically in the gut, and they lack functions bestowed by ILC3 which include recovery from intestinal bacterial infections. Our studies suggest Tox2 is required to metabolically program ILC3 for residence and function in hypoxic environments, such as at sites of infection. ILC3 also infiltrates some tumors, which also constitute hypoxic environments, and our initial results indicate Tox2 is also required for ILC3 to appear in tumors. The project is therefore to first repeat and assess whether Tox2-deficient mice lack ILC3 in tumors, whether Tox2 is playing a similar or distinct role in tumor environments as it does in gut ILC3, and whether and how colonization of tumors by ILC3 contributes to effective anti-tumor immunity. https://irp.nih.gov/pi/avinash-bhandoola	CCR Bethesda
Remy Bosselut, MD, PhD	Post-Baccalaureate, Graduate Student	My laboratory studies T cell differentiation, especially the intrathymic differentiation of conventional CD4+ and CD8+ T cells, which form the vast majority of T cells in the body. CD4+ T cell defects, inherited or acquired, result in potentially fatal immunodeficiency, reflecting the central role of CD4+ T cells in controlling multiple aspects of immune responses and of immune homeostasis. Recent research in the laboratory has investigated CD4+ T cell differentiation (in the thymus) and their function after thymic egress. Potential projects focus on two questions. The first regards a transcription factor, Thpok, necessary for CD4+ T cell differentiation in the thymus. Combining genetic, biochemical and transcriptomic (single cell RNA and ATAC sequencing) approaches, we are exploring how Thpok expression is controlled in T cells and their intrathymic precursors, and how it	CCR Bethesda

		controls CD4+ T cell responses to virus or parasite infection. The second question addresses mechanisms that allow the thymus to delete, or functionally inactivate, T cell precursors that are self-reactive and therefore at risks of causing auto-immune disease. In addition to approaches mentioned above, we started major efforts in the past few years to implement in situ transcriptomics, and the corresponding computational analyses. https://ccr.cancer.gov/staff-directory/remy-bosselut	
Myriem Boufraqech, PhD	All	Identification of novel genetic vulnerabilities in anaplastic thyroid cancer cells to overcome resistance to BRAFV600E inhibition using CRISPR-based screens: Anaplastic thyroid cancer (ATC) is one of the deadliest human cancers, with a median overall survival of 6 months. The most common metastatic sites in ATC are the lungs, bones, and the brain. ATC cells are particularly resistant to most common therapeutic strategies. BRAF mutation is the most frequent alteration in thyroid cancer, with a prevalence of 35-40% in ATC cases. Most of the current targeted therapies using BRAFV600E inhibitors failed to produce meaningful outcomes, and the combination approach in which BRAF inhibitors were coupled with another agent targeting the same pathway, have shown limited efficacy and high toxicity in patients with metastatic thyroid cancer. Therefore, there is an urgent need to identify new determinants of resistance to BRAF inhibitors in order to unfold new therapeutic options for ATC treatment. Recent studies demonstrated that BRAFV600E -driven advanced and metastatic thyroid cancer cells are not sensitive to monotherapies with BRAF inhibitors due to acquired resistance mediated by genetic alterations and/or activation of oncogenic signaling pathways. Therefore, overcoming the acquired resistance to BRAFV600E inhibitors is critical to improving patient outcome. The goal of our study is to identify new determinants of resistance to targeted therapy and more specifically to BRAF inhibitors in advanced and metastatic thyroid cancer using CRISPR-screens. https://ccr.cancer.gov/staff-directory/myriem-boufraqech	CCR Bethesda
Lisa Boxer, PhD	All	The Boxer lab studies chromatin and epigenetics in brain development and how mutations in chromatin regulators lead to neurodevelopmental disorders and cancer. Current projects in the lab focus on the specific types of DNA methylation found in neurons and the proteins associated with these modifications. In most differentiated cell types, DNA methylation is found primarily in the CG sequence, but during postnatal brain development, neurons accumulate high levels of CA methylation and CG hydroxymethylation. Mutations in the known writers, readers, and erasers of these modifications are implicated in neurodevelopmental disorders and cancer, but the function of these modifications in neurons is not understood.	CCR Bethesda

		One project in our lab uses molecular and genomic approaches to understand the function of these specific types of DNA methylation in neurons. We are investigating why these modifications accumulate specifically in neurons, what proteins associate with these modifications, how these modifications regulate transcription and genome integrity, and how disruption of these modifications leads to neurodevelopmental disorders and cancer. Another project focuses on a specific methyl-DNA-binding protein, MeCP2. Loss-of-function mutations in MeCP2 cause the neurodevelopmental disorder Rett syndrome, and MeCP2 is overexpressed in multiple cancers. To investigate the function of MeCP2, we developed an approach to rapidly degrade the MeCP2 protein in the mouse brain. We are using this system to distinguish the primary and secondary consequences of acute loss of MeCP2. These experiments will lend insight into the primary function of MeCP2, and this approach can be broadly applied to other chromatin regulators implicated in neurodevelopmental disorders and cancer. https://ccr.cancer.gov/staff-directory/lisa-d-boxer	
Chongyi Chen, PhD	Post-Baccalaureate, Postdoctoral Candidate	Our lab studies DNA topology in the context of chromatin organization and gene expression in human cells, utilizing our strength of developing novel genomic technologies and single-cell assays. We seek to understand how the topological tension of the double helix interact with other chromatin features, contribute to the chromatin environment for gene regulation, as well as the involvement, regulation, and function of DNA supercoiling dynamics and topoisomerase activities upon various biological processes. The long-term goal is to apply the new knowledge in chromatin biology and the new methodologies in single-cell omics to cancer biology and medicine. Specifically, we would like to understand the role of DNA supercoiling and its regulation by topoisomerase in fundamental processes including DNA replication and mitotic chromosome condensation, and in chromatin state change processes including development and differentiation. We are also interested in studying the consequence of topoisomerase inhibition in multiple aspects upon cancer chemotherapy. https://ccr.cancer.gov/staff-directory/chongyi-chen	CCR Bethesda

Peter Choyke, MD, F.A.C.R.	All	The mission of our lab is to develop the next generation of radiopharmaceuticals (RP) for the diagnosis and therapy of cancer. Two "theranostic" agents have been approved by the FDA in recent years sparking excitement in the field of RP. We are developing new RP agents targeting cancer cells as well as cells in the tumor microenvironment. The work involves identifying good targets, developing the best targeting agents, which are typically small molecules such as peptides, nanobodies or diabodies, and then performing both in vitro and in vivo testing of these agents in mouse models of cancer. If the agent proves to be a good diagnostic agent its potential as a therapeutic agent is then tested using therapeutic radioisotopes. Very successful candidates are patented and corporate partners are sought to develop the agents for human use. The Molecular Imaging Branch has the potential to translate promising agents in Phase I/II clinical trials. Radiopharmaceutical development is an exciting new field with many job opportunities in industry and academics. A background in chemistry and animal testing is preferred and willingness to safely work with radioactivity is a requirement. https://ccr.cancer.gov/molecular-imaging-branch	CCR Bethesda
Alex Compton, PhD	All	Projects in the Compton lab (Antiviral Immunity and Resistance Section) focus on the innate immune response to virus infections. We study the processes by which individual cells defend themselves against virus infection, and in doing so, we learn new things about how viruses enter our cells. Our work examines host-virus interactions on multiple scales, from atoms to whole animals. Specifically, we are known characterizing the antiviral functions performed by interferon-induced transmembrane proteins that inhibit the cellular entry of a broad number of pathogenic viruses, including HIV-1, Influenza A virus, Zika virus, and SARS-CoV-2. iCURE scholars would be able to participate in multiple ongoing projects in the lab as well as lead their own independent project. https://ccr.cancer.gov/staff-directory/alex-compton	CCR Frederick
Ira Daar, PhD	Post-Baccalaureate	Wnt signaling is critical for embryonic development, but when this signaling pathway is misregulated it can lead to birth defects and cancer. The student will be taught to use the Xenopus (Frog) system and the project will involve completing the functional and molecular characterization of the cellular and developmental effects mediated by the main Wnt scaffold Dishevelled (Dvl) and Wnt pathway proteins. Wnt scaffold and receptor mutants will be expressed in developing embryos to determine structural motifs that are important for Wnt receptor-induced developmental effects. Wnt pathway molecules will be co-expressed with proteins found to be associated with Dvl. The ability of these proteins to physically interact and modulate Dvl-induced developmental effects will also be assessed. https://ccr.cancer.gov/staff-directory/ira-o-daar	CCR Frederick

Chengkai Dai, PhD	All	The candidates will participate in projects that elucidate proteomic instability of cancer and tumor-associated amyloidogenesis, new phenomena in cancer biology, and investigate the multifaceted pro-oncogenic roles of heat shock factor 1 (HSF1). HSF1, the master transcriptional regulator of the heat-shock or proteotoxic stress, response, plays a critical role in preserving proteomic stability and countering toxic amyloids. Contrasting with its dispensability for primary cells, cancerous cells become dependent on HSF1, a phenomenon referred to as “non-oncogene addiction”. Excitingly, the first-in-class HSF1 inhibitor is currently under clinical trials for advanced solid tumors in humans. Specifically, two projects are available: 1) how does HSF1 directly neutralize highly toxic amyloid oligomers (AOs)? This project will delineate the exact HSF1 sequences that directly block the attack on the essential mitochondrial chaperone HSP60 by highly toxic AOs. These AO-neutralizing HSF1 sequences may have therapeutic implications in neurodegenerative disorders, including Alzheimer’s disease. 2) what are novel cancer-associated amyloids? The project will utilize proteomics approaches to identify and characterize novel cancer-associated amyloids. Elucidation of this question will be crucial to our understanding of the novel phenomenon of “tumor-suppressive amyloidogenesis”. https://ccr.cancer.gov/Mouse-Cancer-Genetics-Program/chengkai-dai	CCR Frederick
Erin Davies, PhD	Postdoctoral Candidate	My team seeks to recruit an NCI iCURE Postdoctoral Fellow to determine when and how adult pluripotent stem cells (aPSCs) arise during embryogenesis in the regenerative planarian Schmidtea polychroa (Spol). Spol, an emerging developmental model species, relies on aPSCs to sustain lifelong tissue homeostasis and new tissue formation during regeneration. The fellow will investigate the mechanisms regulating the transition from embryonic to adult pluripotency using transcriptomics and functional assays. Trajectory analysis of single cell RNA-Sequencing developmental time course data from staged S. polychroa embryos will inform testable hypotheses about the transcriptional program establishing aPSCs. Using biomarkers and candidate genes identified from the scRNA-Seq analysis, the fellow will perform lineage tracing studies, RNAi knock-down experiments, and develop reagents for prospective isolation of putative aPSCs for cell transplantation assays. Finally, the fellow will undertake comparative studies between invertebrate aPSCs and mammalian embryonic stem cells to uncover transcriptional regulatory programs governing stem cell potency regulation across evolution. https://ccr.cancer.gov/staff-directory/erin-l-davies	CCR Frederick

William Figg, Pharm.D.	Postdoctoral Candidate	Our laboratory research is focused on (1) understanding the (epi)genetics and molecular mechanisms that drive prostate cancer (PCa) progression; and (2) elucidating (epi)genetic mechanisms responsible for cancer drug resistance to develop novel treatment strategies for patients with advanced prostate cancer who have progressed on standard regimens. Chromatin and epigenetic alterations in cancer have now emerged as major contributors to prostate cancer disease initiation/progression and are responsible for a wide range of transcriptional changes that link DNA mutations to tumor phenotype. The current project will investigate the contribution of chromatin- and epigenetics-related processes to prostate carcinogenesis and progression to treatment resistance. We explore the role of epigenetic regulation, chromatin biology and transcription factors in lineage commitment and plasticity in the normal prostate and PCa cells, including changes in chromatin accessibility, histone and DNA modifications through processes such as methylation, chromatin remodeling, modification of transcription factors and histone post-translational modifications. The project will provide opportunities to acquire expertise in advanced technologies in chromatin and epigenetic assays/analysis via the integration of multiple high-throughput sequencing data including chromatin conformation capture (Hi-C) to understand 3D chromatin structure and topologically associated domains, chromatin immunoprecipitation (ChIP-seq) to study histone markers, assay for transposase-accessible chromatin (ATAC-seq) to show chromatin accessibility patterns, and DNA methylation sequencing. We have embarked upon a new approach to identify novel drug targets and identify potential epigenetic cancer therapeutics for advanced, treatment-resistant prostate cancer. https://ccr.cancer.gov/staff-directory/william-douglas-figg	CCR Bethesda
Eric Freed, PhD	All	The overall goal of our lab is to elucidate basic mechanisms of retroviral replication at the molecular level, with an emphasis on the late stages of the HIV-1 replication cycle. Specifically, much of our current effort is aimed at understanding HIV-1 assembly, envelope glycoprotein (Env) incorporation and function, virus budding, and maturation. We have a special interest in the complex relationship between viral proteins and cellular factors and pathways. We believe that characterizing fundamental aspects of the HIV-1 replication cycle will suggest novel targets for the development of antiretroviral therapies; with the exception of the protease (PR) inhibitors (PIs), there are no approved drugs that target the late stages of the replication cycle. In this regard, we continue to play an important role in the development of HIV-1 maturation inhibitors (MIs). https://ccr.cancer.gov/staff-directory/eric-o-freed	CCR Frederick

Takeo Fujii, MD, MPH	Post-Baccalaureate, Postdoctoral Candidate	Our lab is studying how the unique immune cell populations in the context of thromboembolic events (e.g. stroke and deep venous thrombosis [DVT]) affects breast cancer tumor growth and metastasis. My vision is improving survival outcomes of patients with aggressive types of breast cancer such as triple negative breast cancer (TNBC), inflammatory breast cancer (IBC), and brain metastasis by bringing new clinical trials through mechanistic understanding of the role of thrombosis in TNBC growth and metastasis. It is known that patients with cancer have a high risk of developing stroke or DVT and cancer patients with stroke or DVT has worse prognosis than those without. However, it is not fully understood whether and how thromboembolic events facilitate breast cancer growth and metastasis. More importantly, there is no difference in the cancer treatment after diagnosis of stroke or DVT. Therefore, developing novel therapeutic strategies for patients with breast cancer who develop stroke or DVT by elucidating the role of thromboembolic events in breast cancer is an unmet clinical need. We have developed an animal model demonstrating that small strokes promote breast cancer brain metastasis. By using this animal model, we are conducting experiments to comprehensively understand the immune cell profile in the brain and transcriptomic changes of breast cancer brain metastasis. Particularly, our research focuses on myeloid cells such as neutrophils, neutrophil extra cellular traps (NETs), and microglia/macrophages/monocytes. Our lab analyzes samples collected from patients and experimental animals by utilizing techniques such as flow cytometry, tissue clearing, multiplex immunofluorescence and immunohistochemistry, and bulk- and single-cell RNA sequencing. https://ccr.cancer.gov/staff-directory/takeo-fujii	CCR Bethesda
Thomas Gonatopoulos-Pournatzis, PhD	All	Alternative pre-mRNA splicing, a dynamic process allowing a single gene to generate diverse mRNA and protein products, stands as a cornerstone in shaping the intricate landscape of the human transcriptome. This process significantly amplifies the coding potential encoded within the genome, weaving a complex network of alternative exons and introns. This intricate tapestry of genetic information is finely orchestrated across diverse cell and tissue types, responding to environmental cues and contributing to the vast array of transcriptomic and proteomic diversity. In this context, it is noteworthy that more than 10% of pathogenic mutations influence the activation of alternative splice sites, and the perturbation of alternative splicing has been implicated in the etiology of complex diseases, notably cancer. Despite these critical implications, a substantial portion of human alternative exons remains insufficiently characterized, both functionally and in terms of upstream regulatory mechanisms. Our research group is at the forefront of advancing knowledge in this field, employing state-of-the-art functional genomics	CCR Frederick

		and precise molecular analyses. Our focus revolves around addressing two pivotal questions: Identification of Functionally Relevant Alternative Exons: We aim to elucidate which alternative exons within the human genome are functionally relevant and contribute to phenotypes associated with diseases. Our research delves into unraveling the mechanistic intricacies underlying their operation. Understanding Regulatory Mechanisms of RNA Processing: We investigate how diverse cell types and environmental signals intricately regulate RNA processing decisions, molding the plasticity of the transcriptome. https://ccr.cancer.gov/staff-directory/thomas-gonatopoulos-pournatzis	
Tim Greten, PhD	Post-Baccalaureate, Postdoctoral Candidate	The Greten lab is studying the immune system and how it can be used to treat patients with gastrointestinal cancer. We conduct basic research in cancer immunology of the liver, perform pre-clinical studies to evaluate novel treatment approaches and conduct clinical trials in patients with different types of GI cancer. The lab conducts complex animal studies and uses techniques such as flow cytometry, immunohistochemistry, cell culture, gene expression studies including single-cell RNA sequencing as well as whole exome sequencing, microbiome studies and metabolism studies. We use samples derived from patients treated on clinical trials to better understand how and why treatments work or are not as effective as we want them to be. Currently there are a number of open projects for post-Bacs, graduate students and post-docs. Topics include microbiome studies in mice and patient derived samples, metabolism studies in mice with cancer undergoing immunotherapy and novel immune based approaches to treat cholangiocarcinoma. https://ccr.cancer.gov/staff-directory/tim-f-greten	CCR Bethesda
Shuo Gu, PhD	All	We study MicroRNAs (miRNAs), a fascinating class of small noncoding RNAs that serve as master gene regulators, playing pivotal roles in both mammalian development and human diseases. Our program's primary objective is to investigate how miRNAs themselves are regulated, and to apply gained insights into developing effective treatments for cancer. Employing a multidisciplinary approach encompassing genetic studies in living cells and animals, coupled with biochemical techniques and next-generation sequencing (NGS) methods, our laboratory focuses on elucidating mechanisms of miRNA biogenesis and the roles which miRNAs play in tumorigenesis. Ongoing projects include 1) Investigating how 3' uridylation regulates miRNA abundance and function; 2) Characterizing recurring mutations in miRNA biogenesis pathway components; 3) Developing RNA-based therapeutics for cancer treatment. We invite passionate individuals to join our team, where basic	CCR Frederick

		research converges with a commitment to making a real impact in the fight against cancer. https://ccr.cancer.gov/staff-directory/shuo-gu	
Sridhar Hannenhalli, PhD	Graduate Student, Postdoctoral Candidate	Our lab is interested in understanding the gene regulatory mechanisms underlying cancer and therapy response. Three broad themes guiding the projects are (1) tumor microenvironmental heterogeneity (2) developmental and homeostatic origins of cancer (3) Functionally characterizing non-coding somatic mutations (4) context-specific functions of genes and cells. Our lab is purely computational but we collaborate with numerous experimental labs. Analytical thinking and strong coding skills (R, Python) are prerequisites to work in our lab. Few key recent papers from the lab include: 1. Li et al. De novo human brain enhancers created by single-nucleotide mutations, Sc Advances 2023 2. Singh et al. Broad misappropriation of developmental splicing profile by cancer in multiple organs, Nat Comm 2022 3. Gopalan et al. A Transcriptionally Distinct Subpopulation of Healthy Acinar Cells Exhibit Features of Pancreatic Progenitors and PDAC, Can Res 2021 4. Magen et al. Beyond synthetic lethality: charting the landscape of pairwise gene expression states associated with survival in cancer. Cell Reports 2019 https://ccr.cancer.gov/staff-directory/sridhar-hannenhalli	CCR Bethesda
Christine Heske, MD	Post-Baccalaureate, Postdoctoral Candidate	The Translational Sarcoma Biology Section of the Pediatric Oncology Branch is seeking collaborative, inquisitive, and committed applicants to join our team and be part of bench-to-bedside efforts to improve outcomes for patients. The focus of our lab is to elucidate and target the mechanisms behind therapeutic resistance in pediatric-type sarcomas, especially as related to tumor metabolism and DNA damage repair. Our group conducts translational studies in sarcoma biology, which range from basic to clinical research. Our goal is to identify exploitable vulnerabilities specific to sarcoma cells, effectively target them in our disease models, and bring the most promising novel agents into early phase clinical trials for our patients. As a mentor, I am dedicated to fostering a collaborative research environment that values respect, communication, and diversity of ideas. For more information on our lab and work, see: https://ccr.cancer.gov/staff-directory/christine-m-heske	CCR Bethesda

Mitchell Ho, PhD	Post-Baccalaureate, Graduate Student	Our lab studies cell surface glypicans as new cancer therapeutic targets, with a focus on the generation of antibody engineering-based immunotherapies. Our area of research ranges from the investigation of molecular and cellular mechanisms by which glypicans such as GPC1, GPC2, and GPC3 regulate Wnt and Yap signaling to the design of antibody and T cell-based therapeutics. We established mammalian cell display technology and built shark and camel single-domain antibody phage libraries as new high-throughput protein engineering tools to advance drug discovery. The immune therapeutics, including CAR-T cells, created in our laboratory, are being tested at clinical stages for treating liver cancers, pediatric cancers, mesothelioma, and other cancers. We are committed to inclusivity and diversity in laboratory research. https://ccr.cancer.gov/staff-directory/mitchell-ho	CCR Bethesda
Chuong Hoang, MD, FACS	Postdoctoral Candidate	The precise molecular steps leading to Diffuse Pleural Mesothelioma (DPM) remain obscure and, in part, underlie why this recalcitrant surface tumor is difficult to diagnose and treat. Our goal is to construct next-generation model(s) of MPM that can provide insights on tumor initiation, promotion and progression. We developed a novel method to generate new mesothelial cells, those which give rise to DPM, directly from patient tissue biopsy of pleural membranes. Utilizing 3D bioprinting techniques, we incorporate these genetically defined mesothelial cells into building artificial human pleural membranes arranged in a multi-well, high-throughput pipeline. This ex-vivo equivalent of human pleura represents a novel and robust experimentation platform to conduct cell-based, real-time analyses into the origin and mechanism(s) of DPM. Another major project in our lab is directly translational in scope, being focused on developing novel locoregional therapeutics against DPM. We leverage access to newly designed nanoparticle constructs in preclinical testing to assess feasibility and efficacy of novel anti-cancer agents like, but not limited to, microRNA. Our delivery platform is amenable to carrying diverse types of nucleic acids as therapeutic cargos - so we are exploring siRNA, ultra-short noncoding RNA and/or DNA, mRNA, etc. We are also evaluating novel non-nucleic acid cargos that represent new classes of therapeutics for DPM. This therapy-related umbrella project incorporates diverse fields from chemistry, biomaterials, bioinformatics, immunology, and molecular biology to execute state-of-the-art proof-of-concept studies earmarked for high-impact journals. https://ccr.cancer.gov/staff-directory/chuong-dinh-hoang	CCR Bethesda

Jing Huang, PhD	All	The main focus of our laboratory centers on unraveling the molecular mechanisms responsible for gene expression dysregulation in cancer. We are currently studying the role of the RUNX family proteins, specifically in osteosarcoma and breast cancer. The RUNX family, composed of RUNX1, 2, and 3, share a common cofactor, CBFB, forming transcriptional complexes pivotal to physiological processes. Disruption of these complexes is a hallmark of cancer progression, with examples such as RUNX2 amplification in osteosarcoma (OS) and CBFB/RUNX1 mutations in breast cancer (BC). Our ongoing research bifurcates into two projects: Project 1, focusing on the RUNX2 transcriptional network in OS, and Project 2, exploring the roles of CBFB and RUNX1 in BC. Prospective candidates can choose either project based on their interests. Project 1 aims to address OS, a particularly devastating cancer affecting the younger population, with no FDA-approved targeted therapy available. We have identified pro-survival factors in OS cells linked to RUNX2. Through an integrative approach, we seek to unravel the functions of these epigenetic regulators in OS cells. Our ultimate goal is to identify critical factors for OS cell survival and, through mechanistic insights, design innovative strategies for targeted therapy. Project 2 centers on BC. Whole-genome sequencing studies identified frequent mutations in BC, with CBFB and RUNX1 collectively representing 10-15% of these mutations. Recently, our lab uncovered a surprising dual role of CBFB in BC, regulating not only transcription but also cytosolic and mitochondrial translation. These findings lay the groundwork for a highly effective combination strategy, combining a PIK3CA inhibitor (BYL719) and an autophagy inhibitor (Hydroxychloroquine). Ongoing research aims to unveil additional functions of CBFB in BC cells, with the overarching objective of designing novel therapeutic strategies. https://ccr.cancer.gov/staff-directory/jing-huang	CCR Bethesda

Kazusa Ishii, MD, MPH	Post-Baccalaureate, Postdoctoral Candidate	Our group discover, develop, and clinically translate T cell receptor-transduced T (TCR-T) cell therapies for the treatment of leukemia, lymphoma, and other incurable cancers. The projects open for the prospective trainees include: 1. Dissect the mechanism of how co-receptors modulate the effector functions of TCR-T cells, and apply the findings for the purpose of improving the therapeutic potency of TCR-T cells 2. Elucidate leukemia intrinsic mechanism of resistance to CAR-T cells vs. TCR-T cells 3. Study synergistic effects of CAR-T cells plus TCR-T cells 4. TCR discovery and pre-clinical development of TCRs for the treatment of a). chordoma, b). myeloid malignancies, c). metastatic cancers https://ccr.cancer.gov/staff-directory/kazusa-ishii	CCR Bethesda
Sadhana Jackson, MD	Graduate Student, Postdoctoral Candidate	Our laboratory combines CNS pharmacokinetic evaluations and cell biological approaches to understand the interplay between the blood-brain barrier (BBB) permeability and brain tumor cell proliferation. We use a combination of cell biology, molecular biology, imaging, pharmacokinetics and animal tumor models. It is expected that as a member of this lab, one will have an opportunity to be exposed to all these areas. We value a vibrant and collaborative environment where lab members share ideas, reagents and expertise and desire to work on fundamental problems focused on targeted agents that affect the highly restricted BBB and malignant brain tumor cells. Our work uses an integrated bench-to-bedside approach that aims to 1) study the efficacy of targeted tumor and BBB directed therapy, 2) define the mechanisms that drive differences in neuropharmacokinetics of agents to the CNS, and 3) evaluate exquisite parameters via neuro-imaging of CNS permeability amongst malignant brain tumors. Our overall goal is to enhance our understanding of the heterogeneity of blood-brain barrier permeability among tumor cells and develop mechanism-based therapeutic interventions to treat affected brain tumor patients at the NIH Clinical Center. https://ccr.cancer.gov/staff-directory/sadhana-jackson	CCR Bethesda

Peng Jiang, PhD	Postdoctoral Candidate	Project Title: Data-driven discovery of new cancer immunotherapies from secreted protein repertoires Background: Intercellular signaling through secreted proteins, such as cytokines, is a primary mode of immunosuppression in solid tumors. Engineering anti-tumor secretomes or neutralizing antibodies against pro-tumor secretomes may provide effective immunotherapies. The human genome contains 1903 genes coding secreted proteins, while most do not have any documented functions in cancer. Preliminary data: We have recently developed a computational framework CIDE (Cancer Immunology Data Encyclopedia). CIDE integrates 59 tumor genomics datasets from 28 clinical studies of cancer immunotherapies. The median gene risk scores can reliably predict secreted proteins' known pro-tumor versus anti-tumor functions annotated double-blindly based on literature (p-value = 1.6e-4). Based on immunotherapy endpoints in multiple malignancies, CIDE prioritized 60 and 18 secreted proteins as top anti-tumor and pro-tumor modulators, respectively. Most of them have little or no literature about functions in cancer. Aims: This proposal aims to identify novel secreted proteins modulating anti-tumor immunity and design new treatments based on validated regulators. For 78 secreted proteins prioritized from immunotherapy clinical studies, we will validate their impacts on tumor growth and anti-PD1 treatment using mouse models (Aim 1). Then, for validated secreted proteins with anti-tumor or pro-tumor functions, we will test their potential as cancer immunotherapies using armed CAR and TCR T cells, Fc-fusions (Aim 2), and neutralizing antibodies, nanobodies (Aim 3). https://ccr.cancer.gov/staff-directory/peng-jiang	CCR Bethesda

Peter Johnson, PhD	Post-Baccalaureate, Postdoctoral Candidate	Our lab is focusing on novel mechanisms that control oncogenic signaling in cancer cells. The underlying process involves subcellular localization of oncogenic kinases that are downstream effectors of RAS signaling (e.g., ERK, CK2 and others), as well as mRNAs encoding protein substrates of these kinases. We have found that 3' untranslated regions (3' UTRs) of mRNAs encoding tumor suppressor proteins (C/EBPbeta, p53) localize these transcripts to a peripheral region of the cell that lacks their activating kinases (ERK, CK2). Thus, these proteins do not acquire the necessary activating modifications and therefore lack anti-oncogenic activity in cancer cells. This subcellular compartmentalization system also involves oncogenic kinases such as ERK and CK2, which are present on perinuclear signaling endosomes tethered to the perinuclear ER. We are also investigating the role of non-coding UTR sequences on transcripts encoding oncogenic substrates of the same kinases (e.g., c-Myc), which may direct these mRNAs to, rather than away from, perinuclear signaling endosomes in tumor cells. Several projects are available in RNA biology (the role of 5' and 3' UTRs in regulating phosphorylation of the encoded proteins) and oncogenic signaling (mechanisms regulating the subcellular compartmentalization of kinases and other components of the RAS signaling pathway, including RAS itself). These projects offer opportunities in cutting edge research on a previously unknown signal transduction mechanism that plays a key role in neoplastic transformation and cancer. From a clinical perspective, our research has identified potential drug targets that we are exploiting to develop novel anti-cancer therapeutics. Research projects are also available in this area. https://ccr.cancer.gov/staff-directory/peter-f-johnson	CCR Frederick
Anupama Khare, PhD	All	Our lab is interested in dissecting the mechanistic basis of complex microbial behaviors, with the ultimate goal of defining novel targets for designing antimicrobial treatments. We are specifically interested in identifying the molecules and genetic pathways that underlie interactions between different bacterial species in a polymicrobial community, and how these affect fitness and community dynamics. Our lab also studies the evolution of antibiotic resistance. https://ccr.cancer.gov/staff-directory/anupama-khare	CCR Bethesda

Mardo Koivomagi, PhD	Post-Baccalaureate, Postdoctoral Candidate	The overarching goal of our research is to determine the biochemical mechanisms cyclin-dependent kinase use to control cell division. Specifically, much of our current effort is aimed at understanding how the first steps in cell division are controlled and to use the gained knowledge for finding novel therapeutics against cancer. New projects in the laboratory build upon our previous work. Basis for the first project is the discovery of a novel mechanism by which cyclin-dependent kinases drive G1-S transition. This highly unexpected finding linked cell cycle for the first time directly to transcriptional activation of G1/S genes and contrasts with the prevailing model that RNA Polymerase II phosphorylation is merely a basal step in transcriptional activation. In our future research we want to understand more thoroughly how cell cycle cyclin-Cdk complexes are recruited to specific promoters, how they regulate gene expression and study if there are other promoter-specific kinases capable of regulating RNA Polymerase II.The second project builds upon our previous work identifying a novel helix-based docking mechanism for cyclin D, a key driver of cell cycle entry whose major target is the retinoblastoma protein Rb. This finding allows us to search for other substrates potentially using the same docking mechanism to understand the fundamental molecular mechanisms controlled by these kinase complexes. In addition, we are trying to find novel therapeutics that target this novel type of interaction between cyclin D and Rb. To get more insight about the ongoing and starting research in our lab, please visit: https://ccr.cancer.gov/staff-directory/mardo-koivomagi	CCR Bethesda
Laurie Krug, PhD	Graduate Student, Postdoctoral Candidate	The Krug laboratory is seeking highly motivated individuals to join our team to investigate how the oncogenic viruses Epstein-Barr virus and Kaposi sarcoma herpesvirus alter host defenses and the microenvironment to promote life-long infection and cancer. Our projects integrate molecular virology in cell culture, animal pathogenesis studies, and monitoring of the host immune response to infection in mice and in clinical samples. A deeper understanding of the virus interplay with the host is key to the identification of novel, effective interventions to treat and prevent cancers driven by these oncogenic viruses, an urgent need especially for patients infected with HIV. https://ccr.cancer.gov/HIV-and-AIDS-Malignancy-Branch/laurie-t-krug	CCR Bethesda
Mioara Larion, PhD	Postdoctoral Candidate	Dr. Larion's lab is specifically focused on identifying metabolic vulnerabilities in IDH1-mutated gliomas for clinical application, as well as developing technologies that enable these discoveries. Her lab has shown that lipid pathways are important for IDH1-mutant glioma growth and that targeting specific enzymes from either fatty acid synthesis or sphingolipid pathway leads to specific cellular death in these cells. She is also interested in developing biomarkers to help image disease progression and monitor patients' response to treatment. A postdoctoral fellow is needed to	CCR Bethesda

		continue the work on lipid metabolism by combining confocal microscopy with lipidomics in cells and tissue. https://ccr.cancer.gov/staff-directory/mioara-larion	
Vanja Lazarevic, PhD	Post-Baccalaureate	The adaptive immune system must strike a balance between the potentiation of T cell effector functions to achieve protective immunity without compromising tissue integrity. While each CD4+ T helper (TH) subset is specialized in coordinating the immune responses against a particular class of pathogens, dysregulated activities of helper CD4+ T cells inevitably result in immunopathology, allergy, and autoimmunity. This dichotomous nature of TH cell responses is best exemplified by the IL-17A-producing subset of CD4+ TH cells. Protective TH17 cells are prominent at barrier tissues, where they are involved in maintaining host-commensals homeostasis, antimicrobial immunity, tissue remodeling and repair. However, increasingly appreciated is the role of TH17 cells in driving the pathogenesis of chronic inflammatory and autoimmune diseases. The observation that TH17 cells can exert opposing immunological functions – protective versus pathogenic – led us to hypothesize that distinct transcriptional regulators and their associated gene regulatory networks operate in these two subtypes of TH17 cells. While significant progress has been made in identifying environmental cues that modulate the development and maintenance of pathogenic TH17 cells, key transcriptional regulators that control pathogenic TH17 cell differentiation program remain largely unknown. In this project, we aim to identify and functionally characterize transcription factors and their gene regulatory networks that control the differentiation of pathogenic TH17 cells in the context of neuroinflammation. Our approach is focused on transcription factors that promote functional plasticity of TH17 cells and/or transcription factors whose expression is controlled in a tissue-specific or context-dependent manner. https://ccr.cancer.gov/staff-directory/vanja-lazarevic	CCR Bethesda
Andres Lebensohn, PhD	All	We are interested in how a small number of cell signaling pathways can orchestrate the thousands of cellular events that give rise to complex organisms during development and maintain tissues in adults. We focus on the WNT pathway, which controls embryonic patterning and morphogenesis, promotes tissue regeneration, and can be a potent cancer driver. We use functional genomics to discover new regulatory mechanisms, and probe their molecular underpinnings through biochemistry and cell biology. We use organoids and mouse models to understand how this new regulation enables the WNT pathway to generate distinct physiological outcomes.	CCR Bethesda

		Projects: The ubiquitin ligase HUWE1 controls WNT signaling by regulating β-catenin sub-cellular localization: The transcriptional co-activator β-catenin is the main WNT signal transducer. In response to WNT stimulation, β-catenin accumulates in the cytoplasm and enters the nucleus, where it regulates WNT target gene expression. We found that the ubiquitin ligase HUWE1 controls WNT signaling by regulating β-catenin sub-cellular localization. This project aims to identify the substrates of HUWE1 relevant for WNT signaling and to dissect the biochemical mechanism whereby HUWE1 regulates β-catenin localization. Regulation of WNT signaling by distinct R-spondin receptors: R-spondins are secreted stem cell growth factors that modulate sensitivity to WNT ligands by regulating the abundance of WNT receptors at the cell surface. R-spondins regulate two transmembrane ubiquitin ligases, ZNRF3 and RNF43 (Z/R), which in turn target WNT receptors for internalization/degradation. We found that R-spondins can use two different cell-surface co-receptors, LGRs or heparan sulfate proteoglycans (HSPGs), to regulate Z/R. This project aims to dissect the mechanisms by which R-spondins regulate Z/R, and to determine which physiological processes are regulated by LGR- or HSPG-dependent R-spondin signaling during embryonic development and tissue homeostasis. https://ccr.cancer.gov/staff-directory/andres-m-lebensohn	
Ji Luo, PhD	Post-Baccalaureate	Projects for iCURE Scholars will center around the biology of the KRAS oncogene in the context of lung cancer. We are using tumor spheroid and tissue organoid models, as well as mouse models of KRAS mutant cancer, to understand the mechanism of oncogene and non-oncogene addiction in KRAS mutant tumor cells. We are using CRISPR gene editing approaches to understand how cooperating mutations in KRAS mutant tumors modify the tumor's addiction to KRAS. We aim to understand how cell adhesion, cell metabolism and oncogenic stress response provide critical support for KRAS addiction, and how these processes can be exploited for new therapeutic strategies for treating KRAS mutant tumors. https://ccr.cancer.gov/staff-directory/ji-luo	CCR Bethesda
Lichun Ma, PhD	Postdoctoral Candidate	Tumor heterogeneity is a key factor for therapeutic failures and lethal outcomes of solid malignancies. However, what determines the observed different degrees of cellular diversity among tumors is not known. Using cutting-edge technology in single-cell and spatial omics assays, we seek to develop novel systems biology approaches to understand tumor heterogeneity in the context of tumor initiation and evolution. https://ccr.cancer.gov/staff-directory/lichun-ma	CCR Bethesda

Yuichi Machida, PhD	All	The research in the Machida lab explores the molecular mechanisms responsible for the repair of damaged DNA within cells, with a specific focus on their implications for genomic stability and tumorigenesis. We are particularly interested in proteolytic enzymes that play a crucial role in repairing DNA-protein crosslinks (DPCs), a form of bulky DNA damage blocking DNA replication and transcription. DPCs are prevalent DNA damage that require constant repair. Using a mouse model, our laboratory has successfully demonstrated that the insufficiency of SPRTN, a critical metalloprotease involved in DPC repair, leads to genomic instability premature aging, and the early onset of liver cancer. This mirrors the phenotypes observed in Ruijs-Aalfs Syndrome, which is caused by mutations in the SPRTN gene. Furthermore, the Machida lab investigates the impact of inhibiting DPC repair mechanisms on chemotherapies. We aim to sensitize tumors to DPC-inducing drugs by developing inhibitors for DPC repair enzymes. In summary, our research not only contribute to a deeper understanding of fundamental DNA repair processes but also provide new insights into innovative therapeutic approaches for combating cancer. https://ccr.cancer.gov/staff-directory/yuichi-machida	CCR Bethesda
Hiroshi Matsuo, PhD	All	My laboratory uses structural and chemical biology approaches to study the APOBEC3 proteins (A3s), including their mechanisms of substrate specificity, distinctive features between the A3 family members, and their functional interactions with HIV proteins. Our long-term goal is to exploit their therapeutic potential as natural anti-viral factors and as potential targets for chemotherapy. Despite their role in immunity, the mutagenic activity of A3s is a double-edged sword. APOBEC3A (A3A) and APOBEC3B (A3B) have been described as major endogenous drivers of mutations in various types of human cancers, including breast, bladder, head and neck, cervical, and lung cancer. Therefore, stopping A3A and A3B activity has the potential to impede cancer progression and/or contribute to chemotherapy by restricting the genomic diversity within tumor cells. Our A3:ssDNA co-crystal structures and prior biochemical characterization indicated that A3s bind longer oligonucleotides and extensive interactions are needed for activity and therefore inhibition (Kouno et al., Nat. Commun. 2017; Maiti et al., Nat. Commun. 2018). In addition, we recently solved a co-crystal structure of the active A3G catalytic domain bound to a DNA oligomer containing a 2'-deoxy zebularine (dZ-ssDNA). This structure revealed a transition state of the deamination reaction (Maiti et al., Nat. Commun. 2022) and provided structural information that has guided our design of transition state analogue inhibitors. Guided by the structure, we have designed and	CCR Frederick

		generated dZ-ssDNA inhibitors which inhibit A3A's catalytic activity with Ki value less than 50 nM in tubes. https://ccr.cancer.gov/staff-directory/hiroshi-matsuo	
Troy McEachron, PhD	Graduate Student, Postdoctoral Candidate	Our laboratory performs cutting edge and rigorous translational research to characterize and functionally investigate the osteosarcoma microenvironment to (1) identify and validate novel therapeutic approaches for subsequent clinical translation and (2) reveal the mechanisms by which tumor cells influence the phenotype and function of both immune and non-immune cells. My laboratory has generated in-depth molecular profiling datasets from metastatic osteosarcoma patient specimens, including spatial transcriptional profiling, imaging mass cytometry, single nuclei RNA sequencing, and proteomics data. The data from this profiling effort has identified several potentially actionable cellular and molecular targets associated with lymphocyte exclusion, a significant barrier to successful immune checkpoint blockade and adoptive cell therapy. Our profiling efforts have also identified several genes of interest whose expression is specifically localized to the tumor core and not the surrounding microenvironment. The function of these genes have not yet been examined in osteosarcoma. Additionally, our data suggests that a functionally distinct population of endothelial cells is localized within the tumor. It is known that endothelial cells are dynamic cells that can influence immune responses in various diseases. However, the immunoregulatory function of endothelial cells in osteosarcoma largely unknown. Available projects: 1- Targeting immunosuppressive pathways in pulmonary metastatic disease to increase the efficacy of adoptively transferred lymphocytes using metastatic osteosarcoma mouse models. 2- Determine the functional significance and therapeutic candidacy of these osteosarcoma-specific genes in patient derived cell lines and metastatic osteosarcoma mouse models. 3- Investigate phenotypic and functional evolution of tumor endothelial cells in mouse models of spontaneously metastasizing osteosarcoma and patient specimens https://ccr.cancer.gov/staff-directory/troy-a-mceachron	CCR Bethesda

Jordan Meier, PhD	All	Our group develops new approaches to understand how metabolite-derived modifications influence epigenetic signaling in cancer. Current research in the group is focused on 1) the development of chemoproteomic and targeted protein degradation technologies for studying epigenetic protein-protein interactions, 2) harnessing RNA modifications for therapeutic benefit, and 3) applying covalent ligand screening approaches to identify new signaling functions of oncometabolites. Projects in the lab are highly integrated and interdisciplinary in nature, combining chemistry, biochemistry, proteomics, and next-generation sequencing. Our lab has a great history of introducing trainees from diverse research backgrounds to the world of chemical biology, and applicants with training in synthetic chemistry, biochemistry, and molecular/cell biology are encouraged to apply. For more information see our group's website and recent publications on Pubmed. https://irp.nih.gov/pi/jordan-meier	CCR Frederick
Tom Misteli, PhD	Post-Baccalaureate, Postdoctoral Candidate	The Misteli lab explores one of the most fundamental properties of the genome, which is its physical organization in the cell. We ask: How are genomes organized in 3D space and in time? What are the molecular mechanisms that determine 3D genome organization? And how does the organization of the genome and the cell nucleus contribute to its function in health and disease? We use a combination of high-end imaging tools combined with functional genomic screens and biochemical and molecular methods. Examples of the type of work we do can be found in Shachar et al., Cell, 2015; Kubben et al., Cell, 2016; Finn et al., Cell, 2019; Puttaraju et al., Nature Medicine, 2021; Schibler et al. eLIFE, 2023; Vidak et al., Cell Reports, 2023. Available projects are: Identification of disease mechanisms in the premature aging disorder Hutchinson-Gilford Progeria Syndrome (post-doc project) One of the most dramatic examples of the importance of nuclear architecture is the premature aging disorder Hutchinson Gilford Progeria Syndrome (HGPS) which is caused by a mutation in the major nuclear architectural protein lamin A. We are working on various aspects of the disease mechanisms and on therapeutic approaches. Effect of oncogenes on nuclear morphology and chromatin (post-bac/post-doc project) Aberrant nuclear size and shape are prominent features of cancer cells and are used for pathological evaluation of tissues. Yet, the molecular mechanisms that	CCR Bethesda

		determine nuclear size and shape are only poorly understood. We will explore how oncogenes alter nuclear morphology. Centromere organization in cancer (post-bac project) Centromeres are universal elements of human chromosomes and are essential to maintain genome stability. We have recently found that the localization of centromeres in the nucleus differs significantly in various human cell types. We will now map the localization of centromeres in normal and cancer tissues to understand how centromere distribution relates to genome fu. https://irp.nih.gov/pi/tom-misteli	
Stavroula Mili, PhD	All	We are broadly interested in RNA biology, ranging from understanding basic mechanisms to therapeutic applications. Our research program focuses on the roles of localized mRNAs in mammalian physiology and tumor progression. Our goal is to explore the mechanisms leading to compartmentalized mRNA distributions in the cytoplasm, and to understand how localized mRNA translation influences the function of the encoded proteins and modulates physiological responses. We use multidisciplinary approaches with an emphasis on microscopy-based methods, including single-molecule RNA and translation imaging in fixed and live cells, bioengineering methods as well as 3D and in vivo models. Our research program is funded by the NIH Intramural program and is supported by state-of-the-art imaging, genomic and proteomic facilities. The group offers a diverse and inclusive environment of scientists and trainees at various career stages ranging from post-bac fellows to staff scientists. All trainees are involved in independent research projects and supported to lead the planning, design, and interpretation of experiments in a highly interactive environment with plenty of opportunities for formal and informal discussions. PhD and post-doctoral fellows are encouraged to apply for competitive fellowships and travel awards; to extend their expertise by participating in workshops; and to promote presentation skills and establish a scientific network through attendance at national and international conferences. All trainees have authored high-impact publications (appearing in journals such as Molecular Cell, EMBO Journal, PNAS and others) and their work has been highlighted through selection for oral presentations or poster awards in internationally attended conferences. https://ccr.cancer.gov/staff-directory/stavroula-mili	CCR Bethesda
Beverly Mock, PhD	All	Our lab is interested in pharmacologically modulating targets for intervention in multiple myeloma by studying the responses of preclinical cell line and animal models to various single agent and combination drug treatments. Our studies utilize data from a high throughput drug screen that we performed at NCATS to identify	CCR Bethesda

		new drug combinations that target oncogenes for suppression (eg., MYC, mTOR) and tumor suppressors (eg., p16, MNDA) for re-expression. We have more than 30 myeloma cell lines for use and several animal models, some of which develop bone lesions. The iCURE Scholar would be involved in assessing viability and target biomarker responses of drug treatments in cell lines selected for drug resistance to standard of care options. We are also involved in drug discovery projects to identify and validate small molecules binding to ADRM1 ((hRpn13), a component of the proteasome or mEAK-7, a protein that forms a complex with mTOR. In both projects, target engagement and eventually PK/PD studies will be performed to confirm that small molecules are directly affecting their targets –ADRM1 and MEAK7, and also inhibiting cell proliferation or inducing apoptosis. Both molecules have been implicated in various cancers including lung and myeloma. We would evaluate promising candidates in longer term efficacy studies in mouse models. Project 1 is a collaboration with Kylie Walters (CSB) and Deb Citrin (ROB), and project 2 is in collaboration with John (Jay) Schneekloth (CBL). Project 2 will also involve screening for compounds at NCATs with Craig Thomas (LYMB adjunct PI). We have cell lines available to us that have deleted these targets to allow for assessment of off-target defects, and to identify compounds which may be synthetically lethal in combination. Other projects in the lab include an analysis of several mutations occuring in the HEAT domains of mTOR to determine if they are activating or inactivating with respect to mTOR signaling. https://ccr.cancer.gov/laboratory-of-cancer-biology-and-genetics; https://ccr.cancer.gov/staff-directory/beverly-mock	
Diana C.F. Monteiro, PhD	Graduate Student, Postdoctoral Candidate	The Monteiro Lab is interested in the determination of structure and dynamics of oncogenic proteins. The lab is highly interdisciplinary, using biochemistry, protein crystallography and synthetic organic chemistry to address these complex questions. The project proposed here will focus specifically in the establishment of protocols and procedures for the generation of protein crystals suitable for room temperature diffraction as well as the collection of multi-temperature X-ray diffraction data for the determination of intrinsic protein dynamics. These protocols will be developed first with model systems already under study in the lab and deployed to further oncogenic proteins either from oncogenic fusion proteins or those derived from collaborative projects with other CCR members. We're looking for an enthusiastic scientist wanting to work in the field of protein crystallography. Strong communication skills are vital as the project requires communication with biology partners as well as scientists at national accelerators (synchrotrons). A background in medicinal chemistry or biochemistry is required. https://ccr.cancer.gov/staff-directory/diana-cf-monteiro	CCR Frederick

Leonard Neckers, PhD	Post-Baccalaureate, Postdoctoral Candidate	Understanding how metabolic dysregulation of cancer cells impacts the Hsp90 chaperone network to support chaperone addiction. Our group studies how molecular chaperones facilitate oncogenic transformation, cancer progression, and therapeutic resistance of urologic cancers. The dysregulated cell division common to all cancer cells places a substantial burden on their protein environment. This commonly results in increased dependence of cancer cells on molecular chaperones (termed chaperone addiction) for stabilization of their stressed proteome. In parallel, a cancer cell's metabolic program undergoes significant alteration to support their energy and anabolic needs. Our work in the past 10 years has focused on how molecular chaperones impact cancer metabolism. This recently culminated in our publication showing inhibition of mitochondrial Hsp70 could re-sensitize advanced castration resistant prostate cancer to androgen deprivation drugs (the primary therapy for prostate cancer). Although we have learned a lot about how molecular chaperones facilitate oncogenic programs, we know surprisingly little about how altered metabolic activity impacts molecular chaperone activities. Understanding how the Hsp90 chaperone system is influenced by the cancer cell's metabolic program will help us contextualize cancer dependence on molecular chaperones and better predict the metabolic conditions that support the chaperone addiction of cancer cells. https://ccr.cancer.gov/staff-directory/leonard-m-neckers	CCR Bethesda
Anandani Nellan, MD, MPH	Post-Baccalaureate	-Evaluate novel targets in pediatric CNS tumors utilizing antibody and chimeric antigen receptor T cell based therapies -Develop immunocompetent mouse models to evaluate immunotherapy modalities against pediatric CNS tumors -Characterize the CNS tumor microenvironment utilizing multiplex histology staining protocols to elucidate mechanisms of immunotherapy resistance -Test combination strategies to prime the CNS tumor microenvironment prior to immunotherapy delivery https://ccr.cancer.gov/staff-directory/anandani-nellan	CCR Bethesda
Joe Nguyen, PhD	All	Head and Neck Cancer (HNC) is the 6th most common cancer globally, but the 5-year survival rates have not changed. HPV- HNC accounts for 38%-80% of all HNC globally. Organismal growth relies on conserved nutrient signaling pathways, such as mechanistic Target of Rapamycin (mTOR), that converge amino acids and growth factors to regulate cellular metabolism. Dysregulation of mTOR signaling can result in diseases, such as head and neck cancer (HNC), type II diabetes, and neurological disorders. mTOR signaling has been implicated as a major driver for HNC, accounting for >80% of all HNC, in both HPV+ and HPV- HNC 4-6. mTOR signaling is divided into unique macromolecular protein complexes, Raptor (mTORC1), Rictor (mTORC2), and most recently, mEAK-7 (mTORC3). Even though mTOR signaling has been identified as a major driver of a diverse array of	CCR Bethesda

		cancers worldwide, few therapeutics have shown true efficacy in the suppression of long-term disease. Since my discovery of a third mTOR complex, there has been an increasing probability of the existence of novel mTOR complexes. This would suggest that identifying novel mTOR complexes and understanding the role of mTORC3 signaling in HNC would result in future targets for drug development. These studies would allow for the investigation of mTORC3 signaling on the tumor-immune microenvironment (TIME) through 1) transgenic mice harboring wild-type, heterozygous meak7 knockout, and homozygous meak7 knockout, 2) analyzing the role of diet and caloric restriction (CR), 4) spatial multiomic analysis of patient derived premalignant and malignant oral lesions, and 4) drug development targeting mEAK-7 for specific therapeutics for translational investigation. My goal is to understand the TIME in HNC regarding mTORC3, evaluate metabolic modulation, and finally, to develop inhibitors of mTORC3 signaling for therapeutic use in HNC patients. https://ccr.cancer.gov/surgical-oncology-program	
Rosa Nguyen, MD, PhD	Graduate Student, Postdoctoral Candidate	Project 1: We designed new immunocytokines for the therapy of several childhood solid tumors including neuroblastoma. The project will focus on a head-to-head comparison of the new immunocytokine with existing ones (Nguyen et al., 2022, Clin Cancer Res). Preclinical studies will incorporate, for example, in vitro cytotoxicity assays, cytokine multiplex analysis, multi-color flow, animal modeling of antibody/cytokine therapy, and applications of genome-wide CRISPR screens and Cellular indexing of transcriptomes and epitopes by single-cell RNA-seq (CITE-seq). Project 2: We are interested in understanding the impact of age on adoptive T-cell therapy. Using clinically relevant syngeneic CAR T-cell and TCR T-cell models, the aim of this project is to evaluate the efficacy and molecular differences in aged and young adoptive T-cells and recipient animals of varying ages and how disparate therapy responses can be overcome by the use of transgenic cytokines. Techniques and assays applied to achieve these goals are, for example, small animal imaging, single-cell multiome analysis, in vitro cytotoxicity assays, cytokine multiplex analysis, multi-color flow, animal modeling of CAR T-cell therapy, and spatial analysis methods. The goal of both projects is to forge a path to clinical translation. https://ccr.cancer.gov/staff-directory/rosa-nguyen	CCR Bethesda

Terren Niethamer, PhD	Postdoctoral Candidate	The Niethamer lab studies the contributions of endothelial cells to development and regeneration of the lung. We focus especially on the signaling between endothelial cells and other cell types that shapes tissue morphogenesis to build and rebuild three-dimensional structures for gas exchange. Our recent unpublished work has identified several signaling pathways more classically associated with axon guidance that may play a role in endothelial-epithelial communication during regeneration. I am currently recruiting a postdoctoral fellow to use three-dimensional imaging techniques, mouse genetics, and ex vivo organoid culture studies to determine the role of these signaling pathways in establishing and regenerating the gas exchange interface in the lung alveolus. By defining the impact of the endothelium on lung alveolar tissue organization, we will better understand the normal mechanisms the lung uses to repair itself and how these may go awry in disease states or cancer. Our ultimate goal is for this work to contribute to the development of new regenerative therapies in the lung. https://ccr.cancer.gov/staff-directory/terren-k-niethamer	CCR Frederick
Andre Nussenzweig, PhD	All	Chemotherapy is the mainstay in the treatment of various cancers and continues to extend life for millions of patients. With the rapid increase in survivorship, neurological injury from chemotherapy has become an urgent but unmet clinical need. However, little is known about the biological mechanisms by which different chemotherapies lead to neurological deficits nor about preventive measures that might alleviate debilitating side effects. In this project, we will examine the impact of widely used anti-neoplastic chemotherapies on post-mitotic cells in the nervous system. We will determine the extent of DNA damage across the nervous system, changes in gene expression, and determine which cell types are most vulnerable. For these studies both mouse models and iPSC derived neurons and microglia will be used. These mechanistic insights into the side effects of chemotherapy may offer therapeutic solutions that could prevent neurotoxicity. https://ccr.cancer.gov/staff-directory/andre-nussenzweig	CCR Bethesda
Barry O'Keefe, PhD	Post-Baccalaureate, Postdoctoral Candidate	The Molecular Targets Program (MTP) of the National Cancer Institute's Center for Cancer Research (NCI's CCR) has postdoctoral positions available in its Protein Chemistry and Molecular Biology Section (PCMBS). The PCMBS uses its expertise in protein chemistry, biophysics, enzymology, molecular biology and screening to adapt CCR basic science laboratory findings into high throughput cell-free screens for the interrogation of pure compound and pre-fractionated natural product libraries. In addition, we use these same skills to discover and characterize novel bioactive proteins from natural product extracts that increase our knowledge of protein structure and function, address diseases and molecular targets of interest, and potentially lead to clinical development.	CCR Frederick

		1. The first position is for a scientist with experience in biochemistry and enzymology. The selected candidate will be expected to conduct investigations into adapting laboratory cancer biology discoveries on molecular targets of interest for cancer into bioassays and high-throughput screens for the discovery of novel natural products. The candidate will also be involved in mechanism of action studies on natural products that display inhibitory activity against targets of interest. 2. The second position is for a researcher with experience in molecular biology and protein chemistry. Applicants should be interested in the isolation, physical and functional characterization of proteins and in the genetic engineering of proteins for expression in E. coli systems. The successful candidate will engage in efforts to isolate or engineer new bioactive proteins and peptides with activity against cancer, HIV, and SARS-CoV-2. https://ccr.cancer.gov/staff-directory/barry-r-okeefe	
Francis O'Reilly, PhD	All	Project Title: Comprehensive Mapping of the Protein-Interactome of the Nucleus with Structural Proteomics Currently, structural data is sorely lacking across much of the nuclear protein interactome. The nucleus is a dynamic environment where proteins interact in complex networks to control gene expression, replication, and repair. Understanding these interactions is crucial for unraveling the molecular underpinnings of various diseases. Our lab combines structural biology approaches with proteomics to map the structure of protein complexes in the nucleus of the cell and identify how these change during the development of cancer. We then seek to develop drugs to that target these protein-protein interactions to act as cancer therapeutics. Our lab also does significant technical development in the field of crosslinking mass spectrometry. This and other approaches that you will learn and develop as a member of our group in structural biology and proteomics are highly sought-after in academia and industry. Our lab is young and collaborative, with projects spanning molecular biology, proteomics, and informatics. You will be instrumental in developing and applying advanced proteomic technologies to systematically identify and quantify protein-protein interactions. We invite applications from motivated students or postdocs who are ready to contribute to this cutting-edge exploration in a multidisciplinary environment. There is excellent support for professional development in the vibrant research community of the NCI. https://ccr.cancer.gov/staff-directory/francis-j-oreilly	CCR Frederick
Kumaran Ramamurthi, PhD	All	Delivery of cancer therapeutics to non-specific sites decreases treatment efficacy while increasing toxicity. Our lab has reported the assembly of nanoparticles, termed "SSHELs," that mimic bacterial spores. SSHELs are built using a tiny porous silica	CCR Bethesda

		bead (whose diameter may be tuned), covered with a membrane and two bacterial spore surface proteins. The surface of SSHELs can be modified to display multiple different molecules, including proteins that target specific cell surface markers that are overexpressed on cancer cells. Additionally, we are able to load SSHELs with multiple different types of cargo, including small molecules, proteins, and RNA. We recently reported that we could modify SSHELs with an affibody that recognizes a cell surface marker (HER2) that is overexpressed on a subset of ovarian cancer cells. Modified SSHELs loaded with a chemotherapeutic agent (doxorubicin) effectively and specifically killed HER2-positive ovarian cancer cells in vitro. In a mouse model of ovarian cancer, we showed that SSHELs more effectively delivered doxorubicin to ovarian tumors compared to the leading FDA-approved nanoparticle used in the clinic to deliver doxorubicin, and with reduced toxicity (our publication: https://pubmed.ncbi.nlm.nih.gov/36640333/). Current projects in the lab include 1) using SSHELs to deliver peptide vaccines, 2) comparing the efficacy of SSHELs to several FDA-approved antibody-drug conjugates, and 3) testing the efficacy of SSHELs in delivering RNA to specific cell types. https://ccr.cancer.gov/staff-directory/kumaran-s-ramamurthi	
Nitin Roper, MD	All	The Roper laboratory is focused on studying neuroendocrine tumors, particularly small cell lung cancer. The laboratory is engaged in translational research aimed at understanding the relationship between Notch signaling and immunologic, epigenetic, and molecular aspects of neuroendocrine tumors. We use multipronged experimental approaches, including in vivo approaches, to address clinically relevant research questions. In particular, the laboratory seeks to develop new immuno-oncology focused therapeutic strategies for these cancers. The Developmental Therapeutics Branch offers a highly collaborative and interactive research environment with opportunities available to interact with members of a multidisciplinary research community. We are committed to creating an inclusive research environment and to supporting the successful research careers of all trainees. https://ccr.cancer.gov/staff-directory/nitin-roper	CCR Bethesda
Sergio Ruiz Macias, PhD	All	Our program within the Laboratory of Genome Integrity is interested in understanding the molecular mechanisms driving cell fate decisions. For this, we use human and mouse embryonic stem cells (ESCs) as well as mouse embryos to study cell plasticity, pluripotency and differentiation. We leverage the use of these in vitro and in vivo models to get a better comprehension of embryonic development, cell transformation and cancer. In the last few years we focused our efforts to study the molecular determinants of totipotency, the cell state of maximum developmental plasticity on which a single cell can originate a whole organism and is associated to early blastomeres in the embryo, mainly those found in the 2-cell embryo in mice. Our current projects examine the role of new regulators involved in the acquisition	CCR Bethesda

		and the exit from totipotency and the relevance of the genome architecture in these transitions. https://irp.nih.gov/pi/sergio-ruiz-macias https://ccr.cancer.gov/staff-directory/sergio-ruiz-macias	
Martin Schnermann, PhD	All	This project will apply in vivo optical imaging to the design of new ADC chemistry. While the potential of ADCs has been validated, existing agents have proven much more toxic than anticipated. Critically, much of this toxicity is mAb target-independent and due to deleterious effects of the payload and linker. Our approach applies new imaging probes to the development of strategies addressing questions in the field of ADC design. These include: 1) What role do payload properties and labeling chemistries have on tumor and off-target distribution? 2) Are linkers activated by the tumor microenvironment preferred to those cleaved after internalization? We are translating efforts from these imaging studies into the design, synthesis and testing of novel linker-payload combinations. These studies will combine insights and techniques ranging from natural products and fluorophore synthesis to cellular and in vivo characterization. We are creating novel hydrophilic ADC payloads designed to maintain mAb tumor-targeting properties, but then be converted to cell-permeable active species following tumor localization. These will be applied with the novel linkers and optimized conjugation chemistry that will be defined through our imaging studies. Overall, our goal in these studies is to establish an “imaging-first” workflow for the design and testing of novel targeted drug delivery agents. https://ccr.cancer.gov/staff-directory/martin-j-schnermann	CCR Frederick
Nirali Shah, MD, MHSc	Post-Baccalaureate	Clinical Research project/retrospective analysis for patients enrolled on CAR T-cells to evaluate for risk factors and outcomes related to toxicity. https://ccr.cancer.gov/staff-directory/nirali-n-shah https://ccr.cancer.gov/pediatric-oncology-branch/leukemia-lymphoma-transplant-cell-therapy-clinical-team	CCR Bethesda

Shyam Sharan, PhD	Postdoctoral Candidate	Among the various risk factors responsible for the development of breast cancer, the best-established indicator is inheritance of a mutant BRCA1 or BRCA2 gene. Individuals with a personal or family history of early onset and/or bilateral breast and/or ovarian cancer, or a history of male breast cancer are offered sequencing-based genetic tests to screen for mutations in BRCA1 and BRCA2. Sequencing-based genetic tests have resulted in the identification of many unique variants in these genes. There is clearly a need to develop new approaches to determine the pathogenicity of variants and clinically annotate and classify them. To address this, several in silico prediction models as well as functional assays have been developed. We have developed a functional assay based on the critical role of BRCA2 in the survival and proliferation of Brca2-null mouse embryonic stem cells (mESC). Variants are generated in human BRCA2 cloned in a bacterial artificial chromosome (BAC) by recombineering-based gene editing method. These variants are expressed under the control of their own promoter in mESC, which ensures expression at physiological levels. We have identified many BRCA2 variants that disrupt the protein function. We plan to further characterize these pathogenic variants to understand how a single amino acid alteration renders the protein nonfunctional. https://ccr.cancer.gov/staff-directory/shyam-k-sharan	CCR Frederick
Dinah Singer, PhD	Post-Baccalaureate	Our lab is focused on understanding the molecular mechanisms that regulate gene expression across diverse cellular and tissue environments. The biological processes of chromatin organization, transcription and translation have been extensively and have provided a deep understanding of the mechanisms that regulate each independently. Because these processes do not function independently, but rather must be coordinately regulated to maintain or restore cellular homeostasis, understanding the mechanisms that coordinate gene expression is essential. It has been known for some time that many proteins have pleiotropic functions, also known as “moonlighting” functions. The wide-spread occurrence of pleiotropy has led us to postulate that the pleiotropic functions of individual proteins allow them to coordinate biological processes. Indeed, we discovered that the two transcription factors we study – TAF7 and BRD4 - have pleiotropic functions. Our long-term goal is to understand how these proteins coordinately regulate gene expression to establish appropriate levels of expression. Two projects focus on this goal: 1) Determining the mechanisms by which the pleiotropic transcription factor, TAF7, coordinately regulates transcription, RNA export and translation. We hypothesize that post-translational modifications play a crucial role in mediating TAF7’s transitions between functional states. This hypothesis will be tested by a) mapping	CCR Bethesda

		the potential sites of TAF7 post-translation modification and determining whether mutation of those sites affects TAF7's stability and functions. 2) Determining the mechanisms by which the pleiotropic functions of the transcription factor, BRD4, serve to integrate chromatin structure, transcription, and RNA splicing. Due to its pleotropic functions, BRD4 dysregulation has been linked to numerous disorders and it is an important target in cancer and other diseases. However, its precise and effective targeting has been challenging due to its unknown full-length structure. While the BRD4 apoprotein is mostly disordered, it is predicted to undergo binding-induced folding. We are currently screening a small molecule library to identify molecules that could stabilize BRD4 structure. This project includes the testing of small molecules in in-vitro functional assays, in-vivo cellular toxicity assays and several biophysical assays. The lead compounds will be used to solve the structure of BRD4. https://ccr.cancer.gov/staff-directory/dinah-s-singer	
DeeDee Smart, MD,PhD	Post-Baccalaureate, Postdoctoral Candidate	Metabolic regulators of the radiation response and brain radiosensitivity. This is a collaborative project and is focused on defining changes in metabolism in the normal brain from radiation treatment using chemical exchange saturation transfer (CEST) MRI imaging techniques, and correlating observed metabolic changes with clinical outcomes in patients as well as therapeutic interventions which are under investigation to prevent/treat radiation-induced neurologic injury and radiation-induced memory disruptions. In addition to radiographic imaging, project may involve animal models, in vitro and bench-based laboratory models and assays, and clinical information from human research subjects. https://ccr.cancer.gov/Radiation-Oncology-Branch/deedee-k-smart	CCR Bethesda
Adam Sowalsky, PhD	Postdoctoral Candidate	The Sowalsky lab studies mechanisms of treatment response in prostate cancer. We have recently identified biomarkers and opportunities for drug sensitivity in high risk localized prostate cancer based on tissue samples acquired from NCI clinical trials. We are now interested in studying the mechanistic relationships between pathways we have identified using different cell culture models and methods in molecular biology and biochemistry. For example, we have found that tumors in patients who exhibit recurrence after receiving radiation and hormone therapy for prostate cancer express greater levels of TGF-beta signaling before receiving therapy. These tumors also show mutations to PTEN and p53, so we are interested in the biochemical nexus of TGF-beta, PTEN, p53, radioresistance and androgen independence. The ideal postdoctoral candidate is interested in studying a cancer type that has profound effects on a large number of people annually, knowing that they can make	CCR Bethesda

		a significant contribution to our knowledge of this disease. Postdoctoral candidates in the Sowalsky lab receive training in bioinformatics/computational biology, but no computational background is required. All postdocs will also receive additional training in the design and execution of new translational studies around additional or ongoing clinical trials. https://ccr.cancer.gov/staff-directory/adam-g-sowalsky/lab	
Ramaprasad Srinivasan, MD, PhD	Post-Baccalaureate, Postdoctoral Candidate	The primary goal of our laboratory is to develop new therapeutic strategies for evaluation in patients with kidney cancer. Over the past three decades, it has become increasingly clear that kidney cancer encompasses a disparate group of malignancies that arise in the kidney but are characterized by distinct genetic, molecular, and clinical features. Our research seeks to provide a better understanding of the biological underpinnings of individual subtypes of kidney cancer in order to facilitate the development of new therapeutic approaches. Our work has led to the identification of novel standards of care for treating VHL-associated tumors and tumors associated with fumarate hydratase alterations (NEJM 2021). Major projects in the lab focus on evaluating the role of metabolic alterations and DNA damage in distinct forms of kidney cancer by determining the effects of inhibiting specific enzymes necessary for energy metabolism and DNA repair. Our lab is also interested in testing the impact of agents targeting HIF2 in various forms of kidney cancer and identifying rational drug combination strategies with the potential to enhance the activity of these agents. iCURE scholars will have access to state-of-the-art equipment and core facilities, and will work in a dynamic, interdisciplinary research environment with the opportunity to directly impact patient care. https://ccr.cancer.gov/staff-directory/ramaprasad-srinivasan	CCR Bethesda

Gabriel Starrett, PhD	Graduate Student, Postdoctoral Candidate	Polyomaviruses are ubiquitous non-enveloped double stranded DNA viruses that can cause cancer in humans, especially those that are immune suppressed. Merkel cell polyomavirus is the best studied as the etiologic agent of most cases of Merkel cell carcinoma, a rare, aggressive, neuroendocrine skin cancer. However, a growing body of evidence supports the idea that BK polyomavirus plays (BKPyV) a causal role in bladder cancer carcinogenesis. These viruses are wholly dependent on host DNA damage response machinery and usurp these processes for their own replication. Our lab is interested in understanding how polyomavirus infection can result in host genome mutagenesis, genome instability, and ultimately virus integration that frequently precedes tumorigenesis. To do so we develop and implement a variety of sequencing approached to measure mutation rates, chromatin alterations, and gene expression changes in clinical specimens. We then use this information to build cellular model systems to further dissect polyomavirus-mediated mechanisms of tumorigenesis with the goals of preventing disease and improving therapies in immunosuppressed patients and the general population. https://ccr.cancer.gov/staff-directory/gabriel-j-starrett	CCR Bethesda
Esta Sterneck, PhD	All	This laboratory conducts basic research using cell culture and a variety of mouse models to elucidate the molecular mechanisms that determine cancer cell biology and metastasis including the role of tumor-immune cell interactions. **Project 1:** Targeting of breast cancer cell plasticity in metastasis. Through studies of inflammatory breast cancer and a novel 3D culture systems, we investigate how cell-cell adhesion and fluid mechanics influence the metabolism and metastatic propensity of breast cancer cells. Using a variety of molecular tools and experimental paradigms the project aims to (1) provide insights into the molecular pathways that lead to hybrid epithelial-mesenchymal cell states and cell-cell adhesion; (2) determine pharmacological means to disrupt cell-cell adhesion, metabolism, and metastasis; (3) perform genetic screens to identify important pathways in cancer cell survival and metastasis. **Project 2:** Mechanisms of tumor-induced hematopoiesis and role of neutrophils in metastasis. In this project, we utilize mice with a myeloid-lineage specific deletion of the transcription factor C/EBPdelta (Cebpd) to understand tumor-induced myelopoiesis and development of myeloid-derived suppressor cells. In this project, a variety of mouse models and ex vivo assays will be used to study neutrophil development and function in the cancer context. Sex-specific aspects of hematopoiesis and immunotherapy approaches may be explored. Th group is affiliated and extensively collaborates with the Mouse Cancer Genetics Program at NCI Frederick, and the Women's Malignancies Brach at NCI Bethesda. https://ccr.cancer.gov/staff-directory/esta-sterneck	CCR Frederick

Carole Thiele, PhD	All	The Cell & Molecular Biology Section of the Pediatric Oncology Branch studies genetic and epigenetic changes in the pediatric peripheral nervous system tumor Neuroblastoma. By identifying changes that affect the biology of the neuroblastoma tumor cells enabling them to proliferate and evade normal anti-cancer immune surveillance mechanisms we can develop new therapeutic insights. We use state-of-the-art molecular genetic and immunologic approaches to develop new treatments. We then test them in pre-clinical patient-derived xenograft and immunologically competent mouse models to evaluate the most rational approach to move to the clinic to treat children/young adults with high-risk neuroblastoma tumors. Projects include (see also website and recent publications): -Using “Omic”approaches how MYCN oncogene amplification alters transcriptional programs governing growth and differentiation oncogene MYCN are determined at a genome level. -The development and evaluation of small molecule inhibitors targeting MYCN or its interacting proteins. -Using bioinformatic and genomic approaches to identify how retrotransposons are activated in neuroblastoma tumors -Understanding tumor heterogeneity using bar-coded single-cell sequencing to identify the genetic basis of cellular plasticity -Using Proteomics and Mass Spec analysis to identify unique tumor associated cell surface markers that may serve as immune targets Trainees with an interest in translational research will have the ability to interact with basic research scientists as well as physician-scientists to both understand tumor pathogenesis and therapeutic development. The scientists in the Cell & Molecular Biology Section participate in the “bench to bedside and back to the bench” research which is a hallmark of the NCI’s Pediatric Oncology Branch. https://ccr.cancer.gov/staff-directory/carol-j-thiele#news	CCR Bethesda
Anish Thomas, MBBS, MD	All	We work on the most aggressive type of lung cancer, small cell lung cancer. SCLC is a model disease to better understand the three key features of cancer: tumor plasticity, chemo/immunotherapy resistance, and metastases. We have a few spanning basic, translational, and clinical focusing on SCLC. On the basic side we investigate novel drugs aiming to understand their mechanisms and determinants of response with the goal of clinical translation. On the translational side, we seek to understand and define subtypes of tumors that are most likely to respond to specific therapies, using tools such as WGS, RNA-seq, methylation, scRNA etc on tumor and ctDNA datasets. On the clinical side, we conduct clinical trials of cutting-edge	CCR Bethesda

		therapeutics with a focus on agents targeting DNA replication, repair, and chromatin remodeling. https://ccr.cancer.gov/staff-directory/anish-thomas#research	
Kylie Walters, PhD	Graduate Student, Postdoctoral Candidate	Our group studies naturally existing pathways for protein quality control and degradation and engineer chemical tools to induce the degradation of cancer-associated proteins through these pathways. We pursue our research goals by integrating structural, chemical, and cellular biology approaches, allowing trainees to learn multiple techniques and disciplines. We have focused on the ubiquitin-proteasome pathway, which performs regulated protein degradation. Inhibition of the proteasome is standard of care for treating hematological cancers and PROTACs, which induce the degradation of proteins of interest by usurping ubiquitination machinery, are in clinical trials for breast and prostate cancer. In our previous studies, we have discovered two of the proteasome ubiquitin receptors and a binding site in the proteasome for an E3 ligase. These discoveries have inspired new therapeutic approaches and provide fundamental insights into how protein lifespans are regulated. We have open projects to apply structural techniques to newly discovered proteasome-associating proteins and to other cancer targets. https://ccr.cancer.gov/staff-directory/kylie-j-walters	CCR Frederick
Roberto Weigert, PhD	Graduate Student, Postdoctoral Candidate	Tumor cells evade the immune system and understanding this process is fundamental to design new and more effective therapies to cure cancer. One mechanism of immune evasion is based on the aberrant expression on the surface of the tumor cells of specific glycans, such as the sialic acids (SAs). SAs bind to a specific class of molecules, the Siglecs, that are expressed on T-cells and other immune cells. The interaction between Siglecs and SAs blocks the activity of the immune cells leading to tumor growth. Siglecs have been explored as therapeutic targets primarily for leukemia with various degree of success. On the other hand, targeting the expression of sialic acids has not been fully exploited due to the lack of a detailed understanding of the regulation of this process. We have recently discovered a novel mechanism, called GlycoSwitch, which rapidly controls surface sialylation in response to activation of growth factor receptors, such as EGFR, that are highly expressed in most cancers. In this project, to unravel the role of the dysregulation of sialoglycans and GlycoSwitch pathway during the immune modulation of tumor progression, we will use a combination of intravital microscopy (IVM) in live animals, genetic engineering, and correlative spatial glycomics and transcriptomics to: i) define the precise changes in the sialic acid landscape at a cellular level during tumor initiation, progression, and transition to malignancy in live animals; ii) establish the role of the GlycoSwitch in the immune modulation of tumor progression; and iii) validate our findings in a clinical setting. https://ccr.cancer.gov/staff-directory/roberto-weigert	CCR Bethesda

Christopher Westlake, PhD	All	This project will investigate regulation of cellular membrane transport critical in development and normal homeostasis. Specifically, we are investigating the role of membrane trafficking regulators in ciliogenesis and ciliary signaling. This project will utilize advanced cellular imaging (super resolution and volume electron microscopy), biochemistry and proteomics, and genetics systems (human cell, mouse and zebrafish models) important for understanding ciliogenesis in ciliopathy-related disease and cancer. https://ccr.cancer.gov/staff-directory/christopher-j-westlake	CCR Frederick
Urbain Weyemi, PhD	Graduate Student, Postdoctoral Candidate	Non-small cell lung cancer (NSCLC) is the second most common cancer and the leading cause of cancer-related deaths worldwide, with a 5-year survival of patients with advanced disease below 20%. Unfortunately, many forms of NSCLC are highly refractory to current therapies, including radiotherapy and chemotherapy targeting DNA damage response (DDR). The most common DDR inhibitors, such as those targeting PARP, ATM, and ATR, have advanced in clinical trials, and many of these drugs were approved for treating other types of cancer. However, cancer treatments targeting the DDR often encounter drug resistance, particularly in NSCLC cells. When used as single agents, DDR inhibitors often yielded non-satisfactory outcomes in NSCLC patients. This acquired drug resistance is often caused by alternative metabolic pathways that help cancer cells counteract a drug's most damaging effects. Evidence shows that these DNA repair genes and pathways are intrinsically involved in regulating bioenergetic metabolic pathways such as mitochondrial respiration, glycolysis, pentose phosphate pathway, and redox homeostasis. Utilizing a metabolism-centered CRISPR-Cas9 genetic screen, we reported the discovery that Kelch-like ECH-associated protein 1 (KEAP1), an oxidative stress sensor, is a critical driver for resistance to Ataxia-telangiectasia mutated (ATM) kinase inhibition in breast and lung cancer cells (Li et al, PNAS 2023, PMID: 36724254) We hypothesize that cancer cells exploit energetic metabolism to overcome drug treatments targeting the DDR and that inhibiting the DDR concomitantly with a required metabolic gene will synergistically increase cell death. Using CRISPR screens and mouse models, we aim to elucidate the significance of the synthetic lethality between inhibition of DDR kinases ATR and ATM, and deficiencies in redox homeostasis genes in cancer cells. https://ccr.cancer.gov/staff-directory/urbain-weyemi	CCR Bethesda
Brigitte Widemann, MD Co-PI's: Karlyne Reilly, PhD John Glod, MD, PhD	All	Project 1: Determining Population Estimates of Rare Pediatric Cancers and Ultra-Rare Cancers in the US Population To understand the needs of rare cancer patients, it is important to understand who is affected; however, for many rare cancers there are few published studies looking at their incidence and whether they affect people equally across demographic groups	CCR Bethesda

Mary Frances Wedekind, DO Marc Sitbon, PhD Andrea Gross, MD		(sex, race, ethnicity, etc.). Due to variable mechanisms of health care delivery, more accurate data is available from groups such as Orphanet in Europe, compared to the US. Data collected from US state cancer registries can give a relatively unbiased view of demographics of rare cancer diagnoses. In this project, the fellow will work with the director of the Rare Tumor Initiative and clinicians in the My Pediatric Adult and Rare Tumor network (MyPART; https://www.cancer.gov/pediatric-adult-rare-tumor) in collaboration with curators of the Surveillance, Epidemiology, and End Results Program (SEER; https://seer.cancer.gov/) and the National Childhood Cancer Registry (NCCR; https://nccrexplorer.ccdi.cancer.gov/about/nccr.html) to develop methods to the following questions: 1. What is the incidence of different “rare” pediatric cancers in the US, and what is the distribution by sex and race? 2. Which cancer across all age groups are “ultra-rare” (incidence of <1 in 1 million people per year or <300 cases) in the US and how does this compare to data collected from other countries? Project 2: Studying Mechanisms of Drug Response and/or Resistance in New Models of Rare Pediatric Cancer Based on current results of ongoing experiments at the time the fellow starts, the fellow will use a cell- or mouse-based model of a pediatric rare tumor in the Rare Tumor Initiative section to examine tumor growth/death response to select FDA-approved or late-phase investigational drugs. The fellow will use molecular biology techniques to probe the mechanism of drug response or resistance. Previous lab experience in molecular biology, cell biology, and/or mouse models is strongly preferred for this project. The project may also involve characterization of new models of rare tumors for how well they represent patient tumors. Project 3: Correlation of clinical characteristics and course with histopathology and genomic findings using chordoma and hereditary medullary thyroid carcinomas. Very recent work using artificial intelligence approaches has demonstrated the utility of histopathologic features based on H&E slides only to subclassify solid tumors including rare sarcomas and to predict on clinical aggressiveness and response to therapy. On the natural history study for rare solid tumors, we have two clinically well characterized cohorts of patients with chordoma and MTC, respectively, for which we have sufficient numbers and pathology slides to explore this approach. This project includes working with the clinical team, with the lab of pathology and with our computational experts.	

		Project 4: Longitudinal analysis of brain MRIs in children and adults with neurofibromatosis type I to assess how imaging features such as the volume of brain structures correlate with clinical manifestations. NF1 is a genetic tumor predisposition syndrome characterized by RAS pathway activation and manifestations in every organ system including the central nervous system (CNS). These include development of gliomas, but also neurocognitive and developmental issues and autism spectrum manifestations. Recent work from our collaborator at UCSF has demonstrated that sophisticated analyses of brain MRIs in RAS pathway disorders including NF1 and Rasopathies are correlated with clinical features. The NCI Pediatric Oncology Branch NF1 team has collected hundreds of MRIs in children and young adults with NF1 and for many also corresponding neurocognitive evaluations. Of note, the POB has longitudinal MRIs for many patients. This provides the unique opportunity to analyze these brain MRIs in collaboration with our extramural collaborator and to characterize findings for this unique population. This project will involve data analysis for more than 100 patients with longitudinal MRI including clinical variables In addition, the student will learn image analysis and longitudinal analyses. Project 5: Obtaining medical and family history on a natural history study for patients with rare solid tumors (NCT03739827): Comparison of information obtained from forms completed by patients and data extracted from medical records. The natural history study for rare solid tumors collects all available medical records as well as detailed medical information and family history by patient report for each enrolled participant. Extraction of medical information and completion of detailed questionnaires by patients is time consuming. The goal of this project will be to compare information obtained from medical records and completed questionnaires. The focus will be on feasibility of obtaining completed questionnaires from participants as well as identification of discrepancies. This analysis will aid the future direction of the natural history study and also the development of new observational studies. Project 6: Using bioinformatics, we have identified about 160 new human genes that derive from ancient retroviral infections, and which are related to retroviral envelopes glycoproteins (Envs) that bind nutrient transporters of the SLC family. Using newest protein structure prediction tools (Alphafold, Foldseek, and Metafold), we found that	

		at least 50 of these new genes, which we coined as endoRBDs, match structures that have already been described for the receptor-binding domains (RBDs) of bona fide retroviral Envs. Most interestingly, RBDs of this family for which a receptor has been identified bind to metabolic transporters of the SLC family that play key roles in cellular differentiation, inflammation, and oncogenic processes, such as transporters of glucose, lactate, amino acids, phosphate, vitamins, etc. Moreover, our group has shown that RBDs can specifically modulate nutrient transports by cognate SLCs. The candidate, who will be thoroughly familiar with molecular and cellular biology approaches will work in conjunction with a bioinformatician and already established intramural and international collaborations. The project will consist in: 1- assessing expression of putative SLC-binding endoRBDs in different contexts related to cancers and differentiation processes studied in the Pediatric Oncology Branch and the Rare Tumor Initiative program 2- identifying the precise form of endoRBD mRNAs expressed in different cellular contexts 3- test the endoRBD forms found to be expressed for potential metabolic impact 4- deriving new ligands from these endoRBDs to monitor expression profiles of corresponding SLC receptors 5- identifying the cognate SLC receptors We will thus assess the role of these new endoRBDs as a new network of metabolic regulators and potential druggable targets. Project 7: Assessing the natural history of poorly differentiated chordoma using volumetric MRI analysis Poorly differentiated chordoma is a very rare sarcoma (less than 30 cases in the US per year), which occurs more frequently in children than adults and is characterized by INI1 deficiency. In a national and international collaboration, we have collected the clinical characteristics and imaging studies for patients with poorly differentiated chordoma. A subset of the patients has been enrolled on our natural history for rare solid tumors study. As interventional clinical trials for poorly differentiated chordoma are ongoing and in development the establishment of an external control will be needed. The goal will be to describe the longitudinal natural history of poorly differentiated chordoma including clinical characteristics and use of volumetric MRI analysis to reproducibly and sensitively monitor chordoma growth rare. This information will help understand the natural history of these tumors and inform the design of interventional trials. https://ccr.cancer.gov/staff-directory/brigitte-c-widemann	
Xin Wei Wang, PhD	Postdoctoral Candidate	Wang lab focuses on functional genomics of liver cancer using genome-scale technologies including single cell analyses paired with several national/international collaborative initiatives and clinical studies. Dr. Wang oversees a basic/translational	CCR Bethesda

		research program emphasizing new molecular approaches to define tumor subtypes and identify biomarkers for early detection, diagnosis, prognosis, and prediction, to delineate the molecular mechanisms of liver cancer with applications towards precision medicine. Select publications include: Budhu et al Cell Reports Medicine, 2023; Ma et al Nature Communications, 2022; Liu et al, Cell 182, 317-28, 2020, Ma et al, Cancer Cell 36: 418-30, 2019; Chaisaingmongkol et al, Cancer Cell 32: 57-70, 2017; Ji et al, N Engl J Med 361: 1437-47, 2009; Dang et al, Cancer Cell 32: 101-14, 2017; Ye et al, Cancer Cell 30: 444-48, 2016; Ye et al, Nature Medicine 9: 416-23, 2003. The fellow will have opportunities to conduct cutting-edge cancer research with plenty of interactions with top-notch research groups at the NIH. Examples of opportunities: • Exciting research that spans cancer biology, mathematical modeling, and translational science with the goal of improving early detection and therapeutics for cancer. • Applying cutting-edge technologies including single-cell sequencing and spatial sequencing to profiling patient derived tumor samples. • Various collaboration opportunities. • Interaction opportunities with exceptional basic scientists, computational biologists, and clinicians at NIH. • Numerous opportunities for exposure at NIH and international conferences. https://ccr.cancer.gov/staff-directory/xin-wei-wang	
Matthew Wolf, PhD	Post-Baccalaureate, Postdoctoral Candidate	This project is in the Cancer Biomaterials Engineering Section at the National Cancer Institute. My lab investigates immunomodulatory biomaterials for use in next-generation cancer immunotherapies. We aim to integrate immunomodulatory biomaterials with immune oncology – the study of the immune system's role in recognizing and fighting cancer. This project aims to study how biomaterial scaffold properties such as architecture and composition affect immune cell recruitment and activation. These findings are applied in a cancer immunotherapy delivery and tissue repair, in vivo. This project has a strong emphasis on cancer immunology, using techniques such as FACS, confocal imaging, and gene expression analysis. https://ccr.cancer.gov/staff-directory/matthew-t-wolf	CCR Frederick
Sandra Wolin, MD, PhD	All	We study how noncoding RNAs function, the RNA surveillance pathways that remove defective and harmful RNAs and the mechanisms by which defects in these pathways contribute to diseases such as cancer and autoimmunity. Our approach is multidisciplinary, as we combine molecular biology, genetics, biochemistry and structural biology to discover novel functions for noncoding RNAs and to identify novel RNA surveillance pathways. Projects include deciphering the functions of novel noncoding RNAs and determining how RNA chaperones recognize their RNA targets and assist their correct folding.	CCR Frederick

		https://ccr.cancer.gov/RNA-Biology-Laboratory/sandra-l-wolin	
Colin Wu, PhD	All	tRNAs are central players in protein synthesis because they are essential for accurate decoding of the genetic code embedded in the mRNAs. Post-transcriptional modifications of tRNAs are crucial in maintaining proper structure and functions. tRNA modifications are epigenetic and can fine-tune the protein synthesis rate to meet the needs of the cell. Modifications such as methylation, acetylation, hydroxylation, and deamination can impact the decoding capacity of a tRNA by changing the Watson-Crick base-pairing rules. While a loss-of-function mutation in tRNA-modifying enzymes often leads to neurological diseases and cancer, we are interested in studying Ten-Eleven Translocation (TET) family enzymes that catalyze the oxidation of 5'-methylcytosine (5mC) to 5'-hydroxymethylcytosine (5hmC). Among the mammalian TET family enzymes (TET1, TET2, and TET3), TET2 is one of the most frequently mutated gene in diverse lymphoid and myeloid cancers. In myeloid neoplasms, TET2 accounts for more than 50% of all TET oxidation activities. Recent biochemical studies showed that TET2 acts on both DNA and RNA, and a recent study supports a role for TET2-catalyzed modification of tRNA at m5C sites in regulating protein synthesis. In this project, we seek to systematically dissect the function of TET family enzymes in modifying tRNAs and determine the extent to which they impact protein expression in myeloproliferative neoplasms. To study the molecular function of TET family proteins, we use TET2, TET1/2, and TET2/3 knockouts in K562 immortalized chronic myelogenous leukemia cells generated by CRISPR Cas9-mediated gene editing. By sequencing total tRNA, we observed that several arginine, proline, and asparagine tRNA isodecoders are significantly down-regulated in the knockout cell lines. We are currently applying this line of mechanistic investigation to samples from acute myeloid lymphoma (AML) patient with TET2 mutations. https://ccr.cancer.gov/staff-directory/colin-wu	CCR Frederick
Changqing Xie, MD, PhD	All	Cholangiocarcinoma is an aggressive liver malignancy with poor prognosis. The efficacy of current available treatment options is suboptimal. Cancer stemness/ cancer stem-like cells play a critical role on tumor initiation, metastasis, recurrence, and therapy resistance. However, the mechanism has been largely unknown. My group is focusing on dissecting the relationship of cancer stem-like cells with surrounding immune cells/stromal cells in cholangiocarcinoma microenvironment with the assistance of single cell RNA sequencing, spatial transcriptomics as well as other regular research tools. Our ultimate goal is to develop novel cancer stemness/cancer stem-like cell directed therapy and improve the efficacy of immunotherapy/chemotherapy in cholangiocarcinoma, which may also be beneficial to other cancer types.	CCR Bethesda

		https://ccr.cancer.gov/staff-directory/changqing-xie https://www.ncbi.nlm.nih.gov/myncbi/changqing.xie.1/bibliography/public/	
Euno Yoo, PhD	Post-Baccalaureate, Postdoctoral Candidate	The goal of our research project is to study functional proteases that play important roles as instigators and regulators of immune responses and understand how they shape the tumor microenvironment and dictate the fate of tumor cells. Our research focuses on the development of chemical strategies and tools that allow kinetic and dynamic measurement of the network of protease activities. We use our expertise in synthetic chemistry to synthesize small molecules and peptidomimetics to probe and inhibit the activity of proteases and utilize biochemistry, structure biology, and chemical proteomics to characterize the protease-ligand interactions. https://ccr.cancer.gov/Chemical-Biology-Laboratory/euna-yoo	CCR Frederick
Ying Zhang, PhD	All	Cytokines of the TGF-beta superfamily like BMPs and TGF-betas regulate development, differentiation, cell proliferation and cell death, cell motility, matrix production, wound healing and tumor growth. The canonical TGF-beta signaling responses are mediated by Smad proteins through regulation of transcription and alternative splicing. We are interested in the understanding of molecular mechanisms of Smad proteins in these regulations during cancer progression, such as epithelial to mesenchymal transition, cell migration and invasion using approaches of molecular biology, cell biology and high-throughput genome-wide sequencing analysis. https://ccr.cancer.gov/staff-directory/ying-e-zhang	CCR Bethesda
Zhi-Ming Zheng, MD, PhD	Graduate Student, Postdoctoral Candidate	Our lab has been studying protein-RNA interactions and their consequences in various infections with tumor viruses, including high-risk human papillomaviruses and Kaposi's sarcoma-associated herpesvirus. This study aims to understand how RNA splicing and non-coding RNAs regulate the expression of viral and host genes in viral carcinogenesis. The long-term goal is to develop a series of therapeutic approaches to control viral or cellular gene expression for cancer or AIDS treatments and to identify biomarkers for clinical diagnosis and prognosis. https://ccr.cancer.gov/staff-directory/zhi-ming-zheng	CCR Frederick

Possible Projects in the Center for Global Health (CGH)

Investigator	Scholar Level	Currently Available Research Areas and Projects	Location (In Maryland)
Satish Gopal, MD, MPH	Post-Baccalaureate,	As Adjunct Investigator in the CCR Lymphoid Malignancies Branch, I continue clinical/translational studies of lymphoid malignancies in Africa working primarily with collaborators in Malawi and Kenya. This includes a new CCR-sponsored phase 2	Shady Grove

	Postdoctoral Candidate	clinical trial of atezolizumab for relapsed/refractory EBV+ lymphoma in Malawi and Kenya for which protocol development and site preparation will be occurring throughout 2024 for anticipated opening to accrual in early 2025. As Director of CGH, I also collaborate on global policy and public health-oriented research (e.g. portfolio analyses, registry and health system data analyses generated by countries) typically utilizing real world data sources, with collaborators at NIH/NCI, NCI-designated cancer centers, and other partners like WHO.	

Possible Projects in the Division of Cancer Control and Population Sciences (DCCPS)

Investigator	Scholar Level	Currently Available Research Areas and Projects	Location (In Maryland)
Amy Davidoff, PhD	Post-Baccalaureate, Postdoctoral Candidate	The scholar/fellow will work on projects that support the mission of the Healthcare Assessment Research Branch (HARB), which is to promote high-quality population-based research on demographic, social, economic, and health system factors as they relate to providing screening, treatment, and survivorship services for cancer. HARB engages in developing, improving, and disseminating data resources and is about to release several new or updated datasets, which will expand study populations, and add information concerning healthcare provider characteristics, and characteristics of the environment in which individuals live and work that may affect cancer risk and treatment. The scholar/fellow will have opportunities to use these data to collaborate on analyses and manuscripts, including leading their own research projects under the mentorship of NCI scientists. Day-to-day activities may include literature reviews, development of research plans, data abstraction, data analysis, dissemination activities (scientific abstract, presentation and manuscript preparation), portfolio analysis, and support of other branch research initiatives as needed. A successful post-doctoral fellow applicant will have completed their doctoral training in health economics, health policy or health services, epidemiology, public health, or a related discipline, and have very strong data management and quantitative analysis skills. A successful post-baccalaureate applicant will have completed undergraduate training or a master's degree in one of these fields, with intermediate-level skills using statistical packages (SAS, Stata, R), experience working with ancillary programs (Excel, Powerpoint, EndNote), and interest in learning new research skills. https://healthcaredelivery.cancer.gov/about/harb/	Shady Grove
Michelle Doose, PhD, MPH	Post-Baccalaureate, Postdoctoral Candidate	The NCI Office of Cancer Survivorship (OCS) works to enhance the quality and length of survival of all persons diagnosed with cancer and to prevent, minimize, or manage adverse effects of cancer and its treatment. My research is centered on advancing health equity in cancer survivorship by studying structural/institutional determinants and the mechanisms that contribute to disparities in healthcare and health outcomes among cancer survivors. I have applied epidemiological methods to study care coordination within and across healthcare teams and health system boundaries using primary and secondary data sources, including surveys, interviews, medical records, claims data, and cancer registries. I am interested in developing new projects and collaborating on ongoing projects related to healthcare delivery models, care coordination, quality of care for multiple chronic conditions, and the integration of social care into clinical care. https://cancercontrol.cancer.gov/ocs	Shady Grove

William Klein, PhD	Postdoctoral Candidate	I am collaborating with DCEG to facilitate the use of the lung screening tool they have developed based on the results of the National Lung Screening Trial. As a risk communication researcher, I am interested in applying risk communication and health communication literatures to develop a clear and usable tool for potential patients and providers. The fellow would help lead several research projects designed to test ideal factors to use in this and other risk tools. There will also be opportunities to engage in other risk communication projects in our program including several addressing public awareness of the link between alcohol and cancer. I would serve as primary mentor but the fellow would also have the chance to work with other scholars in the Behavioral Research Program. Our program has a strong mentorship culture with several fellows (e.g., CPFP, CRTA, iCURE, PMF), and we prioritize the professional advancement of our fellows (e.g., first authorship on manuscripts, training opportunities, working group participation). Based on interest, the fellow could also work with me on several genetic testing projects in collaboration with DCEG and NHGRI, focusing mostly on decision making and communication about genetic testing results. https://staffprofiles.cancer.gov/brp/prgmStaffProfile.do?contactId=480126&name=William%20-Klein&bioType=stf	Shady Grove
Rick Moser, PhD	Post-Baccalaureate, Postdoctoral Candidate	This is an opportunity for someone with interests in behavioral research including health communication, survey and research methods, statistical analysis, and data harmonization. One set of projects would involve joining a team that administers the Health Information National Trends Survey (HINTS), a population-based survey of US adults. This would involve doing data management, running statistical analyses, creating reports based on these analyses, helping to prepare documents to support researchers to use the data, and contributing to publications created by the team, and leading your own analyses, related presentations, and publications. Also, you would be part of a working group with Healthy People 2030 as HINTS supports 5 objectives and you could be part of this trans-HHS initiative. In addition, you would be involved with developing the GEM portal, to promote and disseminate the use of common measures for prospective research to increase data harmonization for merging and comparability. https://hints.cancer.gov/	Shady Grove
Annie Noone, PhD	Postdoctoral Candidate	A fellow could choose to work on several projects. The research question could be as described or there is flexibility. 1. SEER trends/descriptive epidemiology. There is flexibility if there is interest in a particular cancer site. a. Update on breast cancer trends Breast cancer incidence rates are increasing among Asian women faster than any other race group. Analyze trends by race-ethnicities, age, and biomarkers (eg. triple negative, hormone-positive breast cancer) to understand the drivers behind this increasing trend.	Shady Grove

		b. Analyze trends for vulva and/or vaginal cancer Incidence rates for vulva cancer among white women over age 50 have been increasing and mortality rates for women age 65+ have been increasing 2.9% per year since 2013. This analysis would provide an updated review of incidence, mortality and survival. c. Impact of COVID on cancer rates and trends Due to the pandemic, there were substantial delays in cancer diagnosis and receipt of timely treatment. To what extent delay in diagnosis impacted outcomes is unknown. Using SEER data, assess if cancer patients were more likely to die from their cancer vs. other causes during the pandemic time. How does this vary by different subgroups of the population by race and SES status? 2. Using SEER-Medicare data to examine comorbidity status a. Pre- and post- diagnosis comorbidities. Comorbidity severity impacts treatment decisions as well as survival after a cancer diagnosis. In addition, cancer treatment may exacerbate comorbid conditions. This project would examine comorbidities before and after cancer diagnosis. b. Post-comorbidities related to treatment. This project would focus on comorbidities likely to be associated with treatment. 3. Disaggregated trends for Asian-Pacific Islander (API) groups Usually cancer trend data are shown with API as one group. However, this group is comprised of several distinct ethic populations with unique cancer trends. The SEER program is updating the populations https://surveillance.cancer.gov/branches/	
Jill Reedy, MPH, RDN	Post-Baccalaureate, Postdoctoral Candidate	The Risk Factor Assessment Branch in NCI's Epidemiology and Genomics Research Program develops, supports, and stimulates assessment of modifiable risk factors among individuals and diverse populations across the cancer continuum to inform and advance health promotion. Research areas include diet, physical activity, and sleep methods, the integration of risk factors, and novel assessment with digital technologies of risk factors. Multiple projects are available for an individual with a strong interest in monitoring cancer-related risk factors in the population and improving methods of assessing those factors. The trainee will work collaboratively in a support role with scientific staff at the NCI and other Institutes at the NIH in the design, development, and analysis of research projects. This position provides an exciting	Shady Grove

		and unique opportunity to work with leaders in the field of population monitoring and assessment of modifiable risk factors, particularly diet, physical activity, sedentary behavior, sleep, and weight. https://epi.grants.cancer.gov/risk/	
Carolyn Reyes-Guzman, PhD, MPH	Postdoctoral Candidate	Characterizing nondaily cigarette smokers could aid tobacco prevention efforts, thereby reducing downstream tobacco-related morbidity and mortality. Research shows that racial/ethnic minority populations are more likely to smoke cigarettes in a nondaily frequency compared to their White counterparts, while co-using other types of tobacco products at the same time. Further evaluation of these differences translates to closing the gap on tobacco use and health disparities among these populations given their disproportionate burden of tobacco use. https://cancercontrol.cancer.gov/brp/tcrb	Shady Grove
Robin Vanderpool, DrPH	Post-Baccalaureate, Postdoctoral Candidate	The National Cancer Institute's (NCI's) contact center, known as NCI's Cancer Information Service (CIS), was established in 1975 as an essential part of NCI's communication infrastructure and information dissemination efforts. For over 40 years, NCI's CIS has been providing compassionate and scientifically based information to patients, their families and friends, health providers, researchers, and the general public about all aspects of cancer including: cancer clinical trials, cancer prevention, risk factors, symptoms, early detection, diagnosis, treatment, and survivorship. CIS also provides tobacco and cessation counseling and information. The CIS documents each interaction across its contact points (i.e., telephone, LiveHelp, email, social media) using an OMB-approved coding schema, resulting in a rich database profiling active information-seekers that can be used to inform NCI's research priorities. As collaborative partners, DCCPS – specifically the Health Communication and Informatics Research Branch (HCRIB) – and the CIS have established an agenda focused on secondary data analyses of CIS contact data for research and programmatic planning purposes; increasing CIS connections throughout NCI Divisions, Offices, and Centers; and disseminating findings through reports, manuscripts, and presentations. We are looking for a fellow to assist with execution of data management protocols, including quarterly data updates from the CIS Contact Center, and ongoing data cleaning and preparation for analytic activities as well as provision of quantitative analytic support to understand cancer information-seeking on topics that address NCI initiatives and research priorities. This project would result in numerous publication and presentation opportunities; therefore, high quality writing and presentation skills are also required. The fellowship would be based in DCCPS/HCIRB and the fellow would also work with the CIS program and Westat, a research services contractor. https://cancercontrol.cancer.gov/brp/hcirb ; https://www.cancer.gov/contact	Shady Grove

Possible Projects in the Division of Cancer Epidemiology and Genetics (DCEG)

Investigator	Scholar Level	Currently Available Research Areas and Projects	Location (In Maryland)
Jonas Almeida, PhD	All	epiVerse - Functionalized language models (funLLM) for data-intensive epidemiology research **Synopsis** EpiVerse is a data science and engineering project seeking contributors with an interest in Artificial Intelligence and portable WebComputing. We seek contributions from computationally minded researchers wanting to develop portable analytical solutions that can be delivered at the point of consumption (the code, not the data, does the traveling). Experience with JavaScript, or willingness to develop it is a major selection criterion. **Objective** To develop a distributed web computing infrastructure using language models functionalized for epidemiology applications. A prototypal playground implementation, where feasibility/scope of application is being tested, is available at https://epiverse.github.io. **Context** With the advent of Large Language Models using Transformers, popularized by ChatGPT almost a year ago, a new approach to operating FAIR Data ecosystems became possible. Some long-standing challenges of processing biomedical data, such as schema harmonization and translation between coding systems, could suddenly be handled programmatically with relative ease using GPT's completion APIs. However, a key piece of language-based interoperability remained unavailable for a while: the LLM functionalization of calls to external resources, such as those made available by both institutional data APIs like data.cdc.gov, and by the broader mandate for real-time structured data of data.gov. Two other sets of data-intensive resources have matured to the FAIR Data API level: BigData integrators like the Genomic Data Commons (gdc.cancer.gov), and direct engagement of user-facing care provision such as Electronic Health Records, wearable sensors and consumer genomics via FHIR API (hl7.org/fhir). Tellingly, substantial efforts at NIH seek to advance such computational solutions also in EHR environments (datascience.nih.gov/fhir-initiatives/researchers-training). https://dceg.cancer.gov/about/organization/tdrp/dserg https://dceg.cancer.gov/about/staff-directory/almeida-jonas	Shady Grove

Laufey Amundadottir, PhD	Post-Baccalaureate	My lab focuses on understanding inherited risk of pancreatic cancer through multiple genomic and wet-lab approaches. We are currently working on several large scale genomic screens (e.g. CRISPRi and Massively Parallel Reporter Assays) across multiple risk loci identified through Genome Wide Association Studies. In addition, we are doing in-depth analyses at several pancreatic cancer risk loci with the aim of identifying functional risk variants and their target genes, and understand the biology underlying risk. The postbac candidate we are looking for would work with one of the postdocs in my lab using methods related to assessment of gene regulation, enhancer/promoter activity, transcription factor binding to DNA, gene function, iPSC cells, and the role of inflammation underlying molecular events that influence pancreatic cancer risk. https://dceg.cancer.gov/about/organization/tdrp/ltg/amundadottir-lab	Shady Grove
Laura Beane Freeman, PhD	Postdoctoral Candidate	Studies around the world have observed that farmers and other agricultural workers are at elevated risk of several specific cancers, despite lower overall mortality and,in particular, cancer mortality. In this occupational group, excess risks are observed for Hodgkin lymphoma, non-Hodgkin lymphoma, leukemia, multiple myeloma, and cancers of the brain, skin, lip, stomach, and prostate. Exposures suspected of contributing to the excesses include pesticides, viruses, mycotoxins, well-water contaminants, and a variety of other agents encountered in the agricultural environment. There are a variety of projects related to these exposures and cancer primarily conducted within the context of the Agricultural Health Study cohort, www.aghealth.nih.gov. Current projects involve epidemiologic evaluations of occupational and non-occupational pesticide exposure, and early life agricultural exposures. https://dceg.cancer.gov/about/staff-directory/beane-freeman-laura	Shady Grove
Sonja Berndt, Pharm.D., PhD	All	Genome-wide association studies (GWAS) have been successful in discovering many genetic loci associated with cancer risk, but more research is needed to identify functional variants, understand biological mechanisms, and translate the findings to clinical practice. My group is focused on implementing and testing new bioinformatic and genetic methods to help refine and understand discovered genetic loci. Potential projects include conducting genetic analyses (e.g., fine-mapping, trans-ancestry analyses), implementing new bioinformatic methods (e.g., colocalization, omics data), evaluating the contribution of epigenetic markers to risk, and investigating polygenic risk scores and cancer progression. https://dceg.cancer.gov/about/staff-directory/berndt-sonja	Shady Grove

Li Cheung, PhD	Post-Baccalaureate	I would like to develop methods to accurately estimate the years of life lost due to cancer and the years of life gainable by secondary prevention. Current estimation of the years of life lost are biased as they compare ages of cancer death against either a specific attained age or to actuarial tables estimates of life expectancy, but this approach does not account for differences between those who acquire cancer and the general population. Similarly the years of life-gainable is often estimated as the difference in death age between those diagnosed with localized, distant, and regional stage cancers, but the two populations may not be directly comparable. https://dceg.cancer.gov/about/staff-directory/cheung-li	Shady Grove
Ji Yeon Choi, PhD	Graduate Student, Postdoctoral Candidate	The main goal of our research is to understand the genetic susceptibility to common cancers focusing on lung cancer. Although smoking is a well-known environmental risk factor for lung cancer, 10-15% of lung cancer also arises in never-smokers, and genetic factors contribute to lung cancer in both smokers and never-smokers as shown by family and population-based studies. Genome-wide association studies (GWAS) have identified multiple genomic loci contributing to lung cancer risk in diverse populations, including those specific to lung cancer histological types, ancestry, and smoking status. To understand what genes and pathways underlie these genomic loci, we adopt functional genomics approaches including massively parallel reporter assays (MPRA), CRISPR-based screening, and chromatin interaction studies. We further profile heritable gene expression regulation patterns by building expression quantitative loci (eQTL) datasets from diverse ancestries and contexts, including underrepresented populations and cell-type-specific datasets using single-cell sequencing technologies. These functional genomics approaches could collectively prioritize candidate susceptibility genes and functional variants from multiple GWAS loci. We further characterize prioritized genes individually using cell-based systems. Our projects are highly collaborative involving both experimental and computational approaches adopting cutting-edge genomics tools. https://dceg.cancer.gov/about/organization/tdrp/ltg/choi-lab	Shady Grove
Shahinaz Gadalla, MD, PhD	Graduate Student, Postdoctoral Candidate	Two projects are available, the first is a study comparing cancer profile/characteristics in patients with myotonic dystrophy to the general U.S. population with cancer. The second is a genetic epidemiology study evaluating genetic markers of risk and prognosis in patients with hematological malignancies. https://dceg.cancer.gov/about/staff-directory/gadalla-shahinaz	Shady Grove

Mia Gaudet, PhD Co-PI's: Marie-Josèphe Horner, PhD	Post-Baccalaureate, Graduate Student	The Connect for Cancer Prevention Study ("Connect") welcomes iCURE scholars at different stages throughout their career. Connect is a new prospective cohort designed to investigate the etiology of cancer and its outcomes by capitalizing on research innovations to advance the field of cancer epidemiology and prevention. As one of the largest modern cohorts of its kind, the study is recruiting 200,000 participants from across 10 large, integrated health care systems throughout the United States. For more information on Connect study design, visit: https://www.cancer.gov/connect-prevention-study and https://youtu.be/axFBegy3FUI We invite iCURE scholars to collaborate on evidence-based and data-driven engagement, recruitment and retention strategies for diverse and underrepresented populations. Fellows will also gain professional experience with real-time study operations including, but not limited to, quantitative evaluation of recruitment metrics, design of biospecimen collection, and questionnaire development. Situated in the Trans-Divisional Research Program of the Division of Cancer Epidemiology and Genetics, Connect also encourages fellows to explore different areas of scientific expertise within the division. We support opportunities to build multidisciplinary collaborations on emerging topics such as new digital technologies for exposure assessment (e.g. sensor tracking), design of prospective transcriptome, proteome, microbiome, and genome-wide association studies, data science and data ecosystem design based on FAIR principles (Findable, Accessible, Interoperable, Reusable). https://dceg.cancer.gov/research/who-we-study/cohorts/connect	Shady Grove
Gretchen Gierach, PhD, MPH	All	The position is seeking a Master's-level individual with experience in epidemiology or biostatistics interested in breast cancer survivorship to work on studies from the DCEG-Kaiser Permanente Breast Cancer Survivors Cohort, which is a retrospective record-linkage cohort study of over 19,000 women diagnosed with breast cancer. The study aims are to evaluate the impact of breast cancer treatment on risk of second cancers, cardiovascular disease, and mortality. Recent efforts include increasing the racial diversity of the cohort. The candidate would assist with statistical analyses, manuscript preparation, and program management related to the addition of new study centers, and to learn the impact of study findings on clinical care and risk-benefit assessment. The candidate would be co-mentored by Gretchen Gierach, Ph.D., M.P.H., and Jacqueline B. Vo, Ph.D., R.N., M.P.H., who are co-PIs of the study. https://dceg.cancer.gov/about/staff-directory/gierach-gretchen https://dceg.cancer.gov/about/staff-directory/vo-jacqueline	Shady Grove

Jonathan Hofman, PhD, MPH	All	The objective of my research is to understand the role of agricultural exposures, per- and polyfluoroalkyl substances (PFAS), and other risk factors in the development of various malignancies, focusing in particular on multiple myeloma and kidney cancer. Specifically, I am conducting classical and molecular epidemiology studies in the following three areas: 1) agricultural exposures and cancer; 2) PFAS and cancer risk; and 3) the biological mechanisms of multiple myeloma development and progression. In particular, there are opportunities for projects within the Biomarkers of Exposure and Effect in Agriculture (BEEA) study, a molecular epidemiologic subcohort within the Agricultural Health Study. The BEEA study is designed to facilitate investigations of the potential biological mechanisms through which pesticides and other agricultural exposures influence cancer risk. I am also exploring opportunities to follow up on findings from BEEA in other agricultural populations. In addition, there would be opportunities for classical, molecular, and genetic epidemiologic studies of multiple myeloma and kidney cancer, including investigations of racial and ethnic disparities in these malignancies. Ultimately, the goal of this work is to better characterize the carcinogenic potential of these high priority and widespread environmental and occupational exposures, and to generate new insights into the etiology of multiple myeloma, kidney cancer, and other cancers. https://dceg.cancer.gov/about/staff-directory/hofmann-jonathan	Shady Grove
Sarah Jackson, PhD, MPH	Post-Baccalaureate, Postdoctoral Candidate	This fellowship will involve work on sex differences in cancer incidence and survival and/or cancer among sexual and gender minority (SGM) adults. The selected fellow could work on one or both of these topics depending on their interests and qualifications. Research projects related to sex differences would entail conducting research on the role of sex differences in the immune response to viruses and cancer, as well as examining the role of sex hormones in the development of cancer. Research projects related to SGM populations would include a range of topics related to screening, risk factors, incidence, and outcomes of cancer among transgender and gender diverse adults. All these projects will involve analyses of data from surveys, registries, cohort studies, and electronic health records. The fellow will develop and enhance their analytic skills in SAS or R, and their scientific writing and presentation skills. Postbac fellows will be given increasing independence as the fellowship progresses. Postdoc fellows will be encouraged to develop their own collaborations and resources. For projects related to SGM populations, a demonstrated experience working with the LGBTQ+ community is preferred. https://dceg.cancer.gov/about/staff-directory/jackson-sarah	Shady Grove

Rena Jones, PhD, MS	All	I work on studies to investigate the association of environmental contaminants with cancer risk in both adults and children. Main areas of my research program include air pollution and drinking water contaminants. I also study industrial exposures (e.g., fracking and oil refineries) and agricultural exposures, including pesticides and concentrated animal feeding operations. The application of geospatial methods and data is a major component of this work. There are opportunities for the iCURE scholar to learn how to incorporate survey, regulatory, environmental and biological monitoring and other data to construct environmental exposure assessments for epidemiologic studies, and evaluate their associations with cancer risks in both case-control and cohort study designs. They can also expect to develop analytic skills in SAS, R, and Excel, work with GIS-based exposure data and linkages, and also develop their scientific writing and presentation skills. I have a broad research program that focuses on exposures that are widespread and have important public health impacts. Our team is diverse, close-knit, and fun to work with. Come join us! https://dceg.cancer.gov/about/organization/tdrp/oeeb https://dceg.cancer.gov/about/staff-directory/jones-rena	Shady Grove
Alexander Keil, PhD	All	I conduct research into the epidemiologic and causal inferential methods underlying studies of health effects of exposure mixtures. I have several possible projects at multiple levels: Environmental epidemiology has increasingly taken a mixtures-based approach to estimating health effects of the environment in which many exposures are measured simultaneously. Routinely, analyses are performed on these data using default statistical approaches. Alternatively, methods are available to tailor mixtures' analyses directly to urgent categories of public health questions, such as identifying joint effects of receiving many harmful exposures at once and quantifying whether environmental exposure disparities could be contributing to health disparities. I could greatly use your help in these projects, where you could learn a) how to organize data for epidemiologic analyses using open source statistical software like R or Julia and perform basic data summarization; b) the use of publicly available data to characterize how effectively the exposures we face can be used to estimate effects of independent or joint exposure to multiple chemicals; or c) how to assist with and carry out simulation studies on new methods for estimating health effects of exposure mixtures. Applicants at the post-doctoral level are also welcome to help me brainstorm new ideas on integrating causal inference approaches with exposure mixtures using the wealth of epidemiologic data here in DCEG. Applicants at all levels will be encouraged to help or lead the writing-up of study results with the goal of scientific publication. Existing skills in programming, environmental epidemiology, and causal	Shady Grove

		inference are most welcome, but I am also seeking candidates who are enthusiastic about learning in these areas and have not yet had the chance to do so. https://dceg.cancer.gov/about/staff-directory/keil-alexander	
Maria Teresa Landi, MD, PhD	Post-Baccalaureate, Postdoctoral Candidate	Project 1 - Sherlock-Lung study aims to characterize the genomic and evolutionary landscape of lung cancers in never smokers (LCINS) and to develop an integrated molecular, histological, and radiological classification of these tumors. The target sample size is 2,000 multi-ethnic and geographically diverse LCINS. Currently, we are analyzing deep whole-genome sequencing data from >1,200 tumor/normal samples and RNA-seq and methylation tumor/normal data from >1,800 samples in collaboration with genomics leaders worldwide. To further characterize LCINS tumor evolution and cell-of-origin, we are also conducting long-read Nanopore DNA sequencing, single-cell sequencing, and spatial transcriptomics. We are also developing genomic analysis algorithms, pipelines and web-based interactive tools for genomics analyses and data visualization. We have many genomic and clinical results and are seeking junior investigators who are interested in participating in writing related manuscripts. Project 2 - Melanoma studies: a. Acral lentiginous melanoma (ALM) is a rare subtype of melanoma occurring in typically non sun-exposed anatomical sites. We are collecting >1000 biospecimens from diverse populations, particularly from various Latin American countries to perform the largest investigation of ALM to date to define molecular and immune landscape, and the association of host factors with molecular and clinical features of ALM. b. We are collaborating with others, especially those from Latin America, to join the effort for the Phase III melanoma GWAS meta-analysis, with large sample size (>100,000) and controls. These data will increase power for subtype specific analysis of genetic loci predisposing to melanoma. c. We are leading MelaNostrum, a consortium that conducts familial cutaneous melanoma studies using homogeneous procedures for data and sample collection, and the largest WES analysis of >3,000 melanoma-prone families. We have identified new genes responsible for melanoma. https://dceg.cancer.gov/about/staff-directory/landi-maria	Shady Grove
Choonsik Lee, PhD	Post-Baccalaureate, Graduate Student	There has been a increasing interest and number in proton therapy for pediatric cancer patients. At the same time, increasing concerns are also growing about potential late effects from the treatment modality compared to the conventional x-ray radiotherapy. Radiation Epidemiology Branch (REB) is working to establish an epidemiological cohort of 20,000 pediatric proton and photon therapy patients extracted from multiple radiotherapy centers in the U.S. The medical physicists in	Shady Grove

		the Dosimetry Unit, REB is developing methods to accurately calculate the patient-specific radiation exposure to normal tissues for those patients by using a series of technologies: processing electronic therapy records (images, treatment plans, etc.), simulating proton and photon therapy machines, and calculating organ-level radiation doses using computer simulations running on the NIH supercomputing servers. A successful candidate will participate in the method development and dose calculation process as well as presentation/publicaiton of the outcomes from the research. https://dceg.cancer.gov/about/staff-directory/lee-choonsik	
Mitchell Machiela, ScD, MPH	Graduate Student, Postdoctoral Candidate	Germline variation and somatic mutations are important contributors to cancer risk. My research program focuses on integrative analysis of germline and somatic data to better understand the etiology of cancer, with a focus on germline-somatic interactions that could elevate risk. My group utilizes population-based data from large, international biobank studies (>100K participants) and applies integrative methods to help disentangle the genetic etiology of cancer. Most projects focus on hematologic cancer risk, but opportunities are available to investigate solid tumors and infection-related malignancies as well. Trainees will gain experience with a variety of genomic approaches including genome-wide association studies, whole-genome sequencing, whole-exome sequencing, targeted sequencing, long-read sequencing, RNA sequencing, DNA methylation, telomere length assays, and single-cell technologies. https://dceg.cancer.gov/about/staff-directory/machiela-mitchell	Shady Grove
Jessica Madrigal, PhD, MS	Post-Baccalaureate, Graduate Student	In collaboration with Dr. Rena Jones, I work on studies using geographic information systems for environmental exposure assessment and to identify determinants of environmental exposures and their association with cancer risk in adults and children. A large part of my work focuses on carcinogenic industrial air pollutant exposures. In particular, there are opportunities to describe underlying patterns of exposure to environmental pollutants, the non-chemical environment, and social-structural factors among diverse population groups within the US and conduct multifactorial studies of cancer etiology among these participants from various US-based cohorts. There are also opportunities to use national surveys like the NHANES to conduct exposure validation studies of linked exposure data. The iCURE scholar can expect to develop analytic skills in SAS, R, and Excel, work with GIS exposure datasets that are linked to cohort data and develop their scientific writing. Ultimately, the goal of this work is to characterize environmental causes of cancer disparities among different population groups in the US and to generate new insights into the etiology of multiple cancer types. https://dceg.cancer.gov/fellowship-training/fellowship-experience/meet-fellows/oeeb/madrigal-jessica	Shady Grove

Lisa McReynolds, MD, PhD	Post-Baccalaureate, Postdoctoral Candidate	My research group is focused on characterizing the genetics of inherited bone marrow failure and myeloid malignancy predisposition. My group uses a combination of family studies and large population cohorts to investigate these germline syndromes. Pathogenic variants (mutations) in two closely related genes SAMD9 and SAMD9L lead to MIRAGE and ataxia-pancytopenia syndromes respectively. These disorders account for at least 10% of all pediatric myelodysplastic syndromes. Mutations in these genes are unique amongst the inherited bone marrow failure syndromes (IBMFS) in that they are gain-of-function, rather than the typical loss-of-function mutations seen in other IBMFS. The population prevalence of mutations in these genes is not known, nor is the penetrance of disease amongst individuals with a mutation. Additionally, the phenotypes associated with the syndrome have been described in clinically identified families, likely leading to an over estimation of severity. For this project, the population-level prevalence of SAMD9 and SAMD9L mutations will be investigated using three large cohorts of individuals with exome sequencing completed and linked electronic health records (EHR)- the Geisinger DiscovEHR, the UK BioBank and the All of Us cohort. Frist, we will devise a system for categorizing mutations that is applicable for these gain-of-function genes. Next we will then determine the penetrance of several phenotypes including cytopenias, cancers and congenital abnormalities using the linked EHR. Lastly, we will look to see if other associated phenotypes can be uncovered through these genetically ascertained individuals. https://dceg.cancer.gov/about/staff-directory/mcreynolds-lisa	Shady Grove
Ludmila Prokunina-Olsson, PhD	Post-Baccalaureate, Postdoctoral Candidate	We study human genetics. Specifically, we are interested in understanding how human genetic variants affect molecular mechanisms and increase cancer risk or alter the immune response, in interaction with various environmental and infectious exposures. The spectrum of interests in the lab includes urinary bladder cancer, other cancers and genetically regulated immune response (check our high-impact publications on each of the topics on the lab website). We are looking for new team members who are willing to share their knowledge and experience and learn and apply new skills. Our ultimate goal is to understand the biological mechanisms of genetic associations we detect by studying large sets of patients and controls and then translate our findings to the clinic and healthcare practice. We value creativity, dedication and strive for self-growth. We offer a stimulating, collaborative, multicultural, inclusive, and fun environment, multiple bioinformatics, genomics and laboratory methods to try and master, a real possibility to contribute to high-impact publications and solve critical medical questions. https://dceg.cancer.gov/about/staff-directory/prokunina-olsson-ludmila	Shady Grove

Mark Purdue, PhD	Graduate Student, Postdoctoral Candidate	In my research I use classical and molecular epidemiologic methods to investigate cancer associations with occupational and environmental exposures, and to better understand the causes of kidney cancer. Some project opportunities I have available include: - analyses of data from studies investigating early-life risk factors of childhood cancers; - cancer associations with exposure to per- and polyfluoroalkyl substances (PFAS); - racial-ethnic and exposure-related differences in tumor molecular characteristics of kidney cancer; and - inherited genetic variants associated with kidney cancer (the largest genome-wide association study of its kind in the world). There will also be opportunities to help develop new research ideas to pursue. https://dceg.cancer.gov/about/staff-directory/purdue-mark	Shady Grove
Rachel Stolzenberg-Solomon, PhD, MPH, RD	All	Fellows will work with a multidisciplinary team that includes epidemiologists, statisticians, and/or bioinformaticians. There are several potential project(s) that fellows can work on. Opportunities include 1) evaluating nutrition and dietary disparities across race and ethic groups within the National Health and Nutrition Examination Survey (NHANES), 2) dietary pattern analyses within prospective cohorts with pancreatic cancer as an outcome, and 3) molecular epidemiologic studies that utilize omics (metabolomic, lipidomic, and genomic) data for cancer risk factors and/or pancreatic cancer outcomes employing novel statistical approaches. The applicants ideally should have training in epidemiologic methods and statistics, strong quantitative skills, and an understanding of biological and molecular processes. Training in nutrition or population genetics is beneficial. Good writing skills are also desirable. https://dceg.cancer.gov/about/staff-directory/stolzenberg-solomon-rachael	Shady Grove
Emily Vogtmann, PhD	Graduate Student, Postdoctoral Candidate	Microbes, including bacteria and fungi, are essential for numerous physiological processes and likely play multiple roles in health and disease. However, the relationship between the microbiome and cancer remains understudied. My research focuses on 1) understanding the relationship between the oral and fecal microbiome with cancer risk; and 2) methodologic studies of the microbiome to evaluate optimal methods to collect, store, and process oral and fecal samples for microbiome analyses. Data include newly generated 16S rRNA gene data and shotgun metagenomic sequencing data from samples analyzed in DCEG and large, existing datasets of the microbiome and microbiome-related exposures with various outcomes. https://dceg.cancer.gov/about/staff-directory/vogtmann-emily	Shady Grove

Rose Yang, PhD MPH	All	Dr. Yang at the Integrative Tumor Epidemiology Branch is seeking applicants with training in epidemiology, computational biology, genetics/genomics, or a related field to conduct molecular/genetic epidemiologic research. Dr. Yang's research focuses on investigating the etiologic and molecular heterogeneity of breast cancer, finding novel susceptibility genes for familial melanoma and chordoma, and characterizing the somatic genomic landscape of chordoma, by integrating molecular and genomic technologies as well as digital pathology to well-characterized tissues in epidemiologic studies. Projects may include analysis of histologic/radiologic images and omics data for molecular and spatial characterization of tumor and TME, next-generation sequencing analysis to identify germline susceptibility genes, and statistical analysis of risk factor and clinical data. Various approaches may be used to test hypotheses, including epidemiologic/statistical, computational pathology, and integrative genomic analyses. https://dceg.cancer.gov/about/staff-directory/yang-rose	Shady Grove
Haoyu Zhang, PhD	All	Large-scale multi-ancestry genetic, genomic, and multi-omics studies are showing unprecedented promise in revealing disease mechanisms, identifying novel drug targets, and developing personalized prevention and treatment plans. However, methodologies focusing on large multi-ancestry datasets are still in the early stages of development. My lab is interested in developing scalable statistical methods and software for analyzing large-scale multi-ancestry genetic data in order to answer questions about health disparities and advance genetic research in diverse populations. The majority of methodology projects are motivated by real-world challenges. The lab, in particular, has three major directions: 1. Genetic association testing in multi-ancestry genome-wide association studies (GWAS). 2. Developing polygenic scores (PRS) to predict risk in diverse populations 3. Using Mendelian randomization (MR) methods to identify causal risk factors for diseases. The lab collaborates closely with a number of large genetic consortiums, including the Breast Cancer Association Consortium (BCAC), the Polygenic Risk Method in Diverse Populations Consortium (PRIMED), and the International Lung Cancer Consortium (ILCCO). The successful candidates have prior experience in a quantitative field, such as statistics or biostatistics, bioinformatics, or computer science, as well as proficiency in commonly used software (e.g., R or Python). https://dceg.cancer.gov/about/staff-directory/zhang-haoyu	Shady Grove
Tongwu Zhang, PhD	All	Our research group specializes in investigating cancer genetics and genomics using advanced computational methods and diverse sequencing technologies. Our primary focus is on understanding tumor heterogeneity and evolution in the context of specific genetic backgrounds and causative factors. We delve deep into the	Shady Grove

		intricacies of tumor heterogeneity and evolution, exploring how they vary across diverse populations, exposures, and genetic interactions. Our projects also delve into cutting-edge cancer genomic features, including mutational signatures, retrotransposable elements, and extrachromosomal DNA (ecDNA). To achieve our goals, we employ intensive computational resources and diverse cancer genomic approaches. We utilize pan-cancer genomic datasets from prominent international studies such as TCGA, PCAWG, ICGC, Genomics England, Hartwig Medical Foundation, ALCHEMIST, and AACR GENIE, as well as internal cancer genomic datasets from underrepresented populations within DCEG. In addition to our research endeavors, we are committed to developing innovative computational methods, interactive visualization tools, and data portals. These resources facilitate a deeper understanding of complex cancer genomic features, enabling researchers to explore and analyze data comprehensively. As a member of our team, you will have the opportunity to lead or co-lead international collaborative projects focused on cancer genomics analyses and studies. You will receive mentorship to acquire new methods and approaches for analyzing large-scale and high-dimensional genomic data. Moreover, you will have the chance to develop new projects and collaborate closely with experts in diverse fields, including bioinformatics, data science, biostatistics, epidemiology, cancer genomics, and genetics. This collaborative environment extends beyond NIH, allowing you to work with experts outside the organization. https://dceg.cancer.gov/about/staff-directory/zhang-tongwu	