NIH NATIONAL CANCER INSTITUTE

iCURE

Intramural Continuing Umbrella of Research Experiences (iCURE) – 2020 Possible Projects

Possible Projects in the Center for Cancer Research (CCR)

Name	Scholar Level	Currently Available Research Areas and Projects	Location (In Maryland)
Jairaj Acharya, MBBS, PhD	All	Our long-term objective is to understand the complex interrelationship between phospholipid and sphingolipid metabolism and metabolic signaling in vivo. Intermediates of phospholipid (PL) and sphingolipid (SL) metabolism serve as second messengers for a number of signaling cascades. Sphingolipid composition in membranes influence a wide range of processes from protein secretion to activation of apoptosis. We have initiated studies to understand several aspects of lipid signaling in vivo using Drosophila and mouse models https://ccr.cancer.gov/Cancer-and-Developmental-Biology-Laboratory/jairaj-k-acharya	Frederick
Mirit I. 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	Bethesda
Suresh V. Ambudkar, PhD	All	P-glycoprotein (P-gp) and ABCG2 transporters also play an important role in drug-drug interactions, and in the bioavailability and pharmacokinetics of several drugs. Our long-term aim is to elucidate the role of ABC drug transporters in the development of multidrug resistance (MDR) in cancers and to aid the discovery of new therapeutic strategies to increase the efficiency of chemotherapy for cancer patients. We are elucidating molecular mechanisms of the ATP hydrolysis cycle and drug transport and the molecular basis of the polyspecificity of these transporters. For these studies we are employing innovative approaches including biochemical and biophysical techniques, cell-based transport assays, genetic manipulation and molecular modeling. https://ccr.cancer.gov/Laboratory-of-Cell-Biology/suresh-v-ambudkar	Bethesda
Terri S. Armstrong, PhD	Postdoctoral Fellow	The Armstrong lab is currently focused on developing models of cranial irradiation to explore associated toxicity. Preliminary data in the clinic suggests that SNPs in clock genes may be associated with increased risk of toxicity. The current project will include	Bethesda

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		development and testing of a model, and the use of transgenic mice to evaluate this effect. https://ccr.cancer.gov/Neuro-Oncology-Branch/terri-s-armstrong	
Joseph J. Barchi Jr., PhD	All	The Barchi lab studies the function of tumor-associated carbohydrate antigens (TACAs), aberrant glycan structures present on tumor cells that contribute to both the immune response to tumors and their aggressiveness. Organic synthesis is used to design probes and vaccine constructs of TACA-peptide conjugates as antitumor therapeutic agents. The vaccine constructs are comprised of TACA-based glycopeptides and molecular adjuvant molecules bound to gold nanoparticles. A current project is to design and find optimum conditions for the synthesis of novel nanoparticles that can activate antigen-presenting cells (APCs). https://ccr.cancer.gov/Chemical-Biology-Laboratory/joseph-j-barchi	Frederick
Pedro J. Batista, PhD	Post-baccalaureate, Postdoctoral Fellow	The goal of the lab is to understand how the epitranscriptome responds to changes in the cellular metabolic environment. We use genome engineering and cell lines derived from patient tumors as model systems to determine how RNA biogenesis and function is disrupted to facilitate the establishment and proliferation of cancer. Ultimately, understanding this process will uncover new targets for cancer therapy, as both metabolic pathways and RNA methylation dependent gene regulation can be targeted to sensitize cancer cells. https://ccr.cancer.gov/Laboratory-of-Cell-Biology/pedro-j-batista	Bethesda
John Brognard, PhD	All	The major focus of the research in the Signaling Networks in Cancer lab is to elucidate novel cancer-associated kinases in the unexplored kinome, guided by bioinformatics and functional genomic approaches. The research conducted by the fellow will focus on the development of proteolysis targeting chimeras (PROTACs) that target novel kinases in squamous cell carcinomas. The fellow will also focus on understanding the mechanisms that novel kinases are utilizing to promote tumorigenesis. https://ccr.cancer.gov/Laboratory-of-Cell-and-Developmental-Signaling/john-brognard	Frederick
Ira Daar, PhD	Post-baccalaureate	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 EphrinB transmembrane Eph ligand and Wnt pathway proteins. EphrinB and Wnt receptor mutants will be expressed in developing embryos to determine structural motifs that are important for EphrinB and Wnt receptor-induced developmental effects. EphrinB and Wnt pathway molecules will be co-expressed with proteins found to be associated with EphrinB. The ability of these	Frederick

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		proteins to physically interact and modulate EphrinB-induced developmental effects will also be assessed. https://ccr.cancer.gov/Cancer-and-Developmental-Biology-Laboratory/ira-o-daar	
Chengkai Dai, PhD	Graduate Student, Postdoctoral Fellow	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 under stress conditions. Contrasting with its dispensability for primary cells, cancerous cells become dependent on HSF1, a phenomenon referred to as “non-oncogene addiction”. Accordingly, HSF1 has been identified by Project Achilles as a common essential gene for a broad range of human cancer cell lines. https://ccr.cancer.gov/Mouse-Cancer-Genetics-Program/chengkai-dai	Frederick
Yamini Dalal, PhD	Graduate Student, Postdoctoral Fellow	The Dalal lab is interested in chromatin structure and epigenetic mechanisms that underpin normal and diseased states. Using high speed video nanomicroscopy (AFM) we would like to extend our interdisciplinary tools to visualize and quantify nanoscale looping and real-time changes in chromatin structure deriving from alterations in histone variants, chaperones, histone modifications, remodelers, and breaks. We are particularly interested in dissecting mutant forms of chromatin states found in cancer cells. https://ccr.cancer.gov/Laboratory-of-Receptor-Biology-and-Gene-Expression/yamini-dalal	Bethesda
Freddy E. Escorcia, MD, PhD	All	Our lab designs and evaluates proteins or small molecules with specificity to tumor-selective molecules for engineer radioisotope-derived imaging and therapeutic agents. Work ranges from bioconjugate chemistry and radiochemistry, molecular biology, and in vivo imaging. https://ccr.cancer.gov/Molecular-Imaging-Program/freddy-e-escorcia	Bethesda

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Jeffrey Gildersleeve, PhD	All	Cancer cells display a distinct set of carbohydrates on their surface relative to normal cells. Monoclonal antibodies that selectively target tumor-associated carbohydrate antigens are useful for diagnostic and therapeutic purposes as well as for basic research studies. Unfortunately, there are very few good monoclonal antibodies to carbohydrates. Our group is taking a multipronged approach to address this problem. Projects include engineering antibodies, high-throughput screening of human antibodies using our carbohydrate microarray, and studying the mechanisms by which the mammalian immune system produces carbohydrate-binding antibodies. https://ccr.cancer.gov/Chemical-Biology-Laboratory/jeffrey-c-gildersleeve	Frederick
Tim Greten, MD	All	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/thoracic-and-gi-malignancies-branch/tim-f-greten	Bethesda
Ramiro Iglesias-Bartolome, PhD	All	Our lab research focuses on elucidating the signaling mechanisms that control and drive tissue specific stem cell self-renewal and differentiation and their connections to tumor initiation and growth. In particular, our goal is to identify particular G-protein-coupled receptors (GPCRs) and their linked signaling partners that function as master regulators of epithelial stem cells during skin development, tissue homeostasis and cancer. https://ccr.cancer.gov/Laboratory-of-Cellular-and-Molecular-Biology/ramiro-iglesias-bartolome	Bethesda

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Peng Jiang, PhD	All	Dr. Jiang's research is focused on developing integrative frameworks that leverage the big-data resource in public domains to identify regulators of cancer therapy resistance. A general challenge in cancer research is the lack of data to understand the clinical efficacy of each treatment, while new drugs with distinct mechanisms of action get approved every year. To fill in the gap, we are developing statistical and machine learning infrastructures that transfer knowledge from a vast amount of previous data cohorts to the study of new cancer biology problems. Potential iCURE project: 1. Inference of cytokine activity through large-scale data integration. This project aims to create a computational framework to infer cytokine activities from the single-cell and spatial transcriptomics data through integrating data in the NCBI GEO and ArrayExpress databases. 2. Develop machine-learning frameworks to identify image features of cancer clinical outcomes. This project aims to develop feature selection algorithms for the deep neural networks to achieve knowledge discovery from cancer imaging data, especially high-content tissue imaging. https://ccr.cancer.gov/cancer-data-science-laboratory/peng-jiang	Bethesda
Peter F. Johnson, PhD	All	Our research focuses on mechanisms that regulate signal transmission from RAS oncoproteins to downstream targets in tumor cells and in cells undergoing oncogene-induced senescence (OIS, an intrinsic tumor suppression mechanism). We have found that subcellular localization of RAS effector kinases and mRNAs encoding their target proteins play a key role in determining cellular responses to oncogenic RAS. Our studies involve understanding how these spatial patterns are established and how they lead to oncogenic RAS-induced transformation in cancer cells or, alternatively, elicit OIS in normal cells expressing the same oncogene. The lab uses molecular and RNA biology techniques, biochemistry of signaling proteins, microscopic imaging of proteins and mRNAs, and mouse genetics to address these questions. Projects are available in each of these areas. https://ccr.cancer.gov/Mouse-Cancer-Genetics-Program/peter-f-johnson	Frederick
Anupama Khare, PhD	All	Our lab is interested in dissecting the molecular basis of complex microbial behaviors, with the ultimate goal of identifying novel targets for designing antimicrobial treatments. We are specifically interested in interactions between different bacterial species, and the evolution of antibiotic resistance. https://ccr.cancer.gov/Laboratory-of-Molecular-Biology/anupama-khare	Bethesda

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Shioko Kimura, PhD	Graduate Student, Postdoctoral Fellow	We study a novel cytokine called secretoglobin (SCGB) 3A2 on characterization and understanding of its anti-cancer activity. SCGB3A2 together with endotoxin (lipopolysaccharide, LPS) kills cancer cells through pyroptosis (swelling and rupture of cells). What exactly happening during pyroptosis of cancer cells at tissue/cellular level is not known. To this end, we do ex vivo culture of lung slices obtained from mice that were intravenously injected Lewis lung carcinoma cells, or co-culture the lung slices with macrophages, critical immune cells during carcinogenesis, with and without SCGB3A2 in the media. The cultured lungs are analyzed by using electron microscope and histopathological methods, and cellular and molecular biological techniques. https://ccr.cancer.gov/Laboratory-of-Metabolism/shioko-kimura	Bethesda
Daniel Larson, PhD	All	The primary goal of my laboratory is to understand gene expression in eukaryotic cells, starting from the mechanistic behavior of individual macromolecules and proceeding to their regulation in cells and tissue. Recently, we have begun to apply these experimental and theoretical approaches to the study of hematopoiesis. The differentiation of hematopoietic stem cells into committed lineages in the blood is the result of concerted regulation between transcription, splicing and translation, and a goal of the laboratory is to understand the dynamic interplay between these processes in space and time in single cells. https://ccr.cancer.gov/Laboratory-of-Receptor-Biology-and-Gene-Expression/daniel-r-larson	Bethesda
Andres Lebensohn, PhD	All	We study how cell signaling pathways produce different physiological outcomes in diverse biological contexts, such as during embryonic development and in adult tissue homeostasis. We focus on WNT signaling, a fundamental pathway that orchestrates patterning and morphogenesis during development and promotes tissue renewal and regeneration in adults. We use powerful genetic screens in human cells to discover new regulatory mechanisms and probe their molecular underpinning through biochemistry and cell biology to understand how they enable the pathway to generate distinct physiological outcomes. Based on this understanding we hope to devise more selective therapeutic strategies to target tumors driven by dysregulation of WNT signaling. https://ccr.cancer.gov/Laboratory-of-Cellular-and-Molecular-Biology/andres-m-lebensohn	Bethesda

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Kyung S. Lee, PhD	All	The architecture of a cell is established through varying degrees of hierarchical organizations from single molecules to macromolecular assemblies. Investigating how these molecules interact with one another to form a higher-order structural entity with a new biological function is a key step to unlocking the mystery of life. We are mainly interested in understanding the molecular bases of how the physicochemical properties of pericentriolar scaffold proteins drive the formation of micron-scale self-assemblies with distinct cellular functions. Recently, we found that human polo-like kinase 4, a key regulator of centriole duplication, forms a high M.W. complex with centrosomal scaffold proteins, which cooperatively self-assemble into a higher-order architecture around a centriole in a concentration-dependent manner. Notably, a failure in these events can result in abnormal centrosome numbers, improper spindle formation, and chromosome missegregation that ultimately lead to the development of various human diseases, including cancer, ciliopathy, and microcephaly. Thus, we aim to elucidate the molecular mechanism underlying the assembly of pericentriolar architectures to ultimately understand the etiology of centrosome-associated human diseases. https://ccr.cancer.gov/Laboratory-of-Metabolism/kyung-s-lee	Bethesda
W. Marston Linehan, MD	All	• The Urologic Oncology Branch conducts clinical and basic research designed to develop better methods for detecting, preventing, and treating patients with kidney cancer. • We aim to develop novel forms of targeted precision therapy for patients affected with renal cell carcinoma. We study the genetic and metabolic basis of renal cell carcinoma (RCC), including VHL, MET, FLCN, TFE3, fumarate hydratase and succinate dehydrogenase B pathways and have shown that renal cell carcinoma is fundamentally a metabolic disease. We identified the VHL clear cell renal cell carcinoma gene and are studying novel approaches to targeting the VHL/HIF2 pathway in in-vitro as well as in-vivo models. We are working on targeting the VHL/HIF2 pathway with a number of approaches both in in-vitro as well as in-vivo models. We have shown that fumarate hydratase-deficient type 2 papillary renal cell carcinoma is characterized by a Warburg metabolic shift to aerobic glycolysis with impaired oxidative phosphorylation and a dependence of glucose for its rapid proliferation and aggressive growth and that in FH-deficient RCC there is an accumulation of fumarate. We use quantitative, isotope-resolved metabolomics on tumor samples removed surgically and tumor derived renal cell carcinoma cell lines to characterize the metabolic basis of FH-deficient RCC which allows for identification and quantification of intermediary metabolites of intermediary metabolism in renal cell carcinoma. We conduct MIPE library screening of therapeutic agents to target RCC gene pathways to identify novel therapeutic agents and to evaluate for combinations of agents in synthetic lethal screens. Based on these findings	Bethesda

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		we have developed therapeutic approaches which are currently being evaluated in a clinical trial in patients with advanced RCC. https://ccr.cancer.gov/urologic-oncology-branch/w-marston-linehan	
Stan Lipkowitz, MD, PhD	Graduate Student, Postdoctoral Fellow	My laboratory investigates signal transduction pathways that regulate growth and programmed cell death in epithelial cancer cells. The ongoing projects in my laboratory are: 1) Regulation of signaling by Cbl proteins; 2) Activation of TRAIL death receptor pathways to kill breast cancer cells; and 3) CLPP agonists as treatment for breast cancer. Each project has basic and translational components. https://ccr.cancer.gov/Womens-Malignancies-Branch/stanley-lipkowitz	Bethesda

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Zheng-Gang Liu, PhD	All	TNF regulates many cellular processes including cell proliferation, differentiation and cell death and is involved in many types of diseases such as cancer. Inappropriate production of TNF plays a critical role in the pathogenesis of both acute and chronic inflammatory diseases. The deregulation of programed cell death such as apoptosis and necroptosis has been suggested to be pivotal for tumor development. Therefore, revealing the molecular mechanism of TNF signaling and the regulation of apoptosis and necroptosis will not only help to understand the biology of TNF function and programmed cell death but also provide insights for developing novel treatments of inflammatory diseases and cancer. Of particular significance is our work that helped to elucidate the molecular mechanism of TNF-induced necroptosis. Necroptosis, as apoptosis, is an important cell death mode that is both physiologically and pathologically relevant. However, the regulation of necrotic cell death is poorly understood. My lab has identified the most critical executor of necroptosis, MLKL, and demonstrated the mechanism of its function in necroptosis. Most recently, my lab demonstrated that necroptosis of tumor cells leads to tumor necrosis and promotes tumor metastasis. Currently, we are trying to understand how necroptosis promotes metastasis. https://irp.nih.gov/pi/zheng-gang-liu	Bethesda
Tom Misteli, PhD	All	The Misteli laboratory studies how genomes are organized and how they function inside of human cells. We use molecular techniques in conjunction with advanced high-throughput and high-resolution microscopy to map genomes in 3D space. Currently available projects include the assessment and identification of novel genome organization factors, whose function will be tested for their effect in cancer and other diseases and in aging or the development of synthetic cell biology approaches to study genome function. These studies will provide insights into basic principles of genome biology and they establish the foundation for novel diagnostic and clinical applications in cancer research. https://ccr.cancer.gov/Laboratory-of-Receptor-Biology-and-Gene-Expression/tom-misteli	Bethesda

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Beverly A. Mock, PhD	All	Project 1: Precision Medicine in Multiple Myeloma This project will utilize drug-response data we collected at NCATS on 45 multiple myeloma cell lines tested for 1900 compounds. We are in the process of developing a predictive pipeline for biomarker detection by combining single agent screen data with large-scale disease-specific data integration. The goal of this project is to develop a flexible precision medicine pipeline, capable of incorporating a wide range of data types and biological knowledge in the form of pathway and gene set annotations, related experimental datasets (including clinical trial data), and known drug-gene interactions to bear on the prediction outcome. We have been able to parse the 1900 compounds into roughly 27 drug clusters, (as defined by their similarity in dose response profiles across all cell lines). In the current iteration of the pipeline, we have observed strong enrichment for drugs with similar classes/mechanism in the detected drug clusters; the actual approach used to compute the clusters, however, is unaware of the drug classes. We will examine the top performing drug/biomarker combination in each of the drug clusters for which the pipeline is able to accurately predict cell line sensitivity. The iCURE scholar would be involved in assessing viability and target/biomarker responses in 14 myeloma cell lines treated with the candidate compounds: 6 myeloma cell lines ranked for their overall sensitivity (3 cell lines)/resistance (3 cell lines) to the 1900 compounds, and MM cell line pairs (4 parental and 4 drug resistant lines) which were selected in vitro for their resistance to proteasome inhibitor or dexamethasone treatment, two agents used in myeloma standard of care. Project 2: Analysis of HEAT Repeat Mutations in Mtor (mammalian target of rapamycin) Signaling We are in the process of examining a series of 12 different cancer-associated HEAT domain mutations which encompass a region of Mtor implicated in tumor susceptibility; we now have preliminary evidence that some HEAT domain mutations directly affect signaling, while others do not, and the iCURE scholar would be involved in evaluating these in the context of their altered signaling and disease involvement. https://ccr.cancer.gov/Laboratory-of-Cancer-Biology-and-Genetics/beverly-mock	Bethesda
Jagan Muppidi, MD, PhD	All	The Muppidi lab studies the intersection of the immune response and generation of malignancies derived from B cells. The lab uses genetically engineered animal models to define how genetic changes found in B cell lymphomas contribute to altered B cell behavior within the microenvironment and the subsequent development of malignancy. https://ccr.cancer.gov/Lymphoid-Malignancies-Branch/jagan-r-muppidi	Bethesda

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Shalini Oberdoerffer, PhD	All	Research in my laboratory broadly examines how epigenetics alters genomic function. At root, we are interested in the mechanisms by which a static DNA template gives rise to cellular and organismal complexity. We examine the role of DNA and RNA modifications in determining: 1) how a single gene generates multiple protein-coding splice variants, and 2) how a single messenger RNA molecule dictates distinct protein fates during translation. The enzymes we study are frequently mutated in human cancers. We ultimately aim at understanding how nucleic acid modifications contribute to the etiology of disease with a focus on novel therapeutic interventions. https://ccr.cancer.gov/Laboratory-of-Receptor-Biology-and-Gene-Expression/shalini-oberdoerffer	Bethesda
Hyun Park, PhD	All	The Park lab seeks to understand the role of cytokine receptor expression and signaling in T cell development, differentiation and homeostasis. Specifically, we aim to decipher the transcriptional and post-transcriptional mechanisms of cytokine receptor expression and downstream signaling in T cells that controls their survival and effector function. The lab has generated a series of mouse models using CRISPR/Cas9 technology and conventional gene targeting that replicate human diseases and immune deficiencies. In this context, we generated new mouse strains that links aberrant cytokine receptor signaling to inflammation and autoimmune diseases. The lab utilizes cutting-edge techniques such as RNA-seq, multi-color flow cytometry but also high-dimension analytic tools, such as CyTOF and single cell RNA sequencing (scRNA-seq), to understand the molecular mechanisms in these processes. https://irp.nih.gov/pi/jung-hyun-park	Bethesda
Natalie Porat-Shliom, PhD	Graduate Student, Postdoctoral Fellow	Cellular organelles are membrane bound compartments where enzymes catalyze metabolic reactions. In response to changes in nutrient availabilty cellular organelles change their morphology, localization and contact with one another. However, very little is known about the physiological roles of these dynamic rearrangement in organ physiology and disease. We utilize light microscopy and particularly intravital microscopy to understand these events in the intact liver. We aim to target organelle dynamics and contact sites as an approach for liver cancer therapy. https://ccr.cancer.gov/thoracic-and-gi-malignancies-branch/natalie-porat-shliom	Bethesda

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Kumaran Ramamurthi, PhD	All	Our laboratory studies how cells divide and differentiate to understand how these processes may go awry during diseases like cancer. We focus on how proteins localize in a cell and assemble into large structures during cell division and morphogenesis using bacteria (such as the spore-forming Bacillus subtilis or the human pathogen Staphylococcus aureus) as relatively simple model systems. We employ a wide variety of approaches, such as classical genetics and biochemistry, fluorescence microscopy, and biophysics and computational techniques to address our scientific questions. Students from our lab have gone on PhD programs, medical and veterinary school, and industry; postdocs have started jobs in academia and industry. For more information on projects and our publications, please see: https://ccr.cancer.gov/Laboratory-of-Molecular-Biology/kumaran-s-ramamurthi	Bethesda
Paul Randazzo, MD, PhD	Post-baccalaureate, Postdoctoral Fellow	Our group studies the biochemistry and biology of the Arf family of GTPases and their regulators. Our recent focus has been on the Arf GTPase-activating protein ASAP1, which has been implicated in cancer invasion and metastasis. Currently, we have projects examining the regulation of the enzymatic activity of ASAP1 and mechanisms by which ASAP1 affects the actin cytoskeleton and cell behaviors including cell migration, proliferation and differentiation. https://ccr.cancer.gov/Laboratory-of-Cellular-and-Molecular-Biology/paul-a-randazzo	Bethesda
Eytan Ruppin, MD, PhD	All	The Ruppin lab is focused on developing and harnessing data science approaches for the integration of multi-omics data to better understand the pathogenesis of cancer, its evolution and treatment. We collaborate with many experimental cancer labs, aiming to develop and utilize computational approaches to jointly gain a network-level integrative view of the systems we study. From a translational perspective, together with our collaborators, we aim to predict and test novel drug targets and biomarkers to treat cancer more effectively. https://ccr.cancer.gov/cancer-data-science-laboratory/eytan-ruppin	Bethesda
Martin Schnermann, PhD	All	Our group uses modern organic chemistry to develop approaches for cancer imaging and drug delivery. We are actively exploring the development of novel antibody drug conjugates, an emerging modality to selectively deliver small molecule payloads to a range of tumor types. We are particularly focused on the development novel molecules and linker methods that are designed for use in challenging solid tumor settings, such as metastatic liver cancer and non-small cell lung cancer. Trainees on this project will be exposed a range of techniques, including organic synthesis, antibody design, and in vitro and in vivo characterization of novel molecular entities. https://ccr.cancer.gov/Chemical-Biology-Laboratory/martin-j-schnermann	Frederick

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DeeDee Smart, MD, PhD	Post-baccalaureate, Postdoctoral Fellow	Metabolic regulators of the radiation response and brain radiosensitivity. This is a collaborative project with Dr. Ravinder Reddy of the University of Pennsylvania Department of Radiology and Dr. Alan Koretsky of the National Institute of Neurologic Diseases and Stroke 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 as well as investigational therapeutic interventions. https://ccr.cancer.gov/Radiation-Oncology-Branch/deedee-k-smart	Bethesda
Esta Sterneck, PhD	All	Mechanisms of Breast Cancer Cell Plasticity in Metastasis / Novel Therapeutic Options: Our laboratory conducts basic research using breast cancer cell lines, xenograft mouse models, genetic models, and PDX models to characterize the molecular signaling pathways that regulate breast cancer cell biology. In ongoing studies involving inflammatory breast cancer and organoid culture systems, we have discovered a signaling pathway involving E-cadherin, COX-2, AKT and GSK3beta that is implicated in cluster dissemination and metastasis (Balamurugan et al., under revision). The iCURE-sponsored trainee will participate in ongoing projects to (1) identify the molecular pathways that lead to hybrid epithelial-mesenchymal cell states, with focus on gene regulation, and/or (2) determine the drug-sensitivities of cancer cells and the underlying mechanisms of response/resistance depending on cell state. Immune-oncology: Analysis of the myeloid lineage response to tumor development in mice: The importance of the immune system in modulating tumor initiation, development, progression, as well as response to therapeutics, is well established. In addition, exploitation of the host defense system for novel therapeutic strategies is one of the most promising frontiers in cancer management. My laboratory conducts basic research on the molecular mechanisms underlying tumor biology. Specifically, we study the functions of the transcription factor CEBPD. To dissect the cell-type specific roles of C/EBPδ, we generated mice with a floxed allele of Cebpd. Because C/EBPδ is expressed in mature myeloid cells and myeloid-derived suppressor cells (MDSCs), we chose the LysM-Cre mouse to delete Cebpd in these cell types. The goal of this Project is to charactgerize myeloid-lineage specific functions of C/EBPδ that modulate tumor biology and thereby advance our mechanistic understanding of the tumor-host interactions that control tumor progression. This project will involve extensive molecular and functional analysis of the myeloid cell lineage in the context of mouse tumor models. State of the art core support including imaging and	Frederick

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		singe-cell sequencing will be part of the analysis. The project will be in collaboration with Dr. J. Keller (MCGP, CCR, NCI) and other investigators at NIH. https://ccr.cancer.gov/Laboratory-of-Cell-and-Developmental-Signaling/esta-sterneck	
Yousuke Takahama, PhD	All	Our laboratory is interested in understanding molecular mechanisms that: 1) build functionally competent thymus microenvironments, which are capable of supporting the production and selection of T cells, 2) govern thymic selection to establish a functionally competent and self-tolerant repertoire of T cells, 3) position developing T cells to localize within the thymus microenvironments for production and selection of T cells. https://ccr.cancer.gov/Experimental-Immunology-Branch/yousuke-takahama	Bethesda

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Lino Tessarollo, PhD	All	My laboratory is using the mouse as a genetically amenable in vivo tool to address the physiological roles of neurotrophins and their receptors. Drugs to target neurotrophin signaling are already in clinical trials for cancer treatments but their long-term effects in mammalian physiology is unknown. We are interested in dissecting the cell specific neurotrophin signaling pathways and their role in the nervous and cardiovascular system. Our effort is aimed at understanding the specific roles of neurotrophins during development and in the mature organism and the impact that disruption of these signaling pathways may have in mammals. https://ccr.cancer.gov/Mouse-Cancer-Genetics-Program/lino-tessarollo	Frederick
Kylie Walters, PhD	All	Research in our group is focused on molecular characterization and targeting of the ubiquitin-proteasome and protein quality control pathways. Dysfunction of these processes is associated with human diseases including cancer. We apply modern structural biology techniques to solve 3-dimensional atomic resolution structures of constituents of these pathways and use cell biology techniques to dissect functional significance. Projects are available to study molecular interactions and to use this knowledge for structure-based molecular targeting. https://ccr.cancer.gov/Structural-Biophysics-Laboratory/kylie-j-walters	Frederick
Xin Wei Wang, PhD	Postdoctoral Fellow	Dr. Wang's research centers on functional genomics of liver cancer using genome-scale technologies paired with several national/international collaborative initiatives and clinical studies. His lab focuses on basic/translational research by building a comprehensive global liver cancer data ecosystem and employing integrated genomics to address liver cancer heterogeneity. His lab emphasizes new molecular approaches such as genomics, transcriptomics, metabolomics, microbiomics, viromics and single cell analysis to define tumor subtypes and identify biomarkers for early detection, diagnosis, prognosis and prediction, and to delineate the molecular mechanisms of liver cancer initiation and metastasis with applications towards precision oncology. https://ccr.cancer.gov/laboratory-of-human-carcinogenesis/xin-wei-wang	Bethesda
Roberto Weigert, PhD	All	Our lab has developed an imaging approach called Intravital Subcellular Microscopy (ISMic) that enables the visualization of cellular and subcellular processes in live animals with an unprecedented resolution. We have developed a model system that permits to image the initiation, progression and metastasis of tumors generated by carcinogen exposure, and at the same time, to investigate the contribution of the tumor micro-environment. This model will be exploited to investigate, at a molecular level, the role of membrane remodeling, cellular metabolism and the immune system during tumor progression, with the potential of unraveling novel cellular mechanisms that will lead to more effective therapies for cancer treatment.	Bethesda

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		https://ccr.cancer.gov/Laboratory-of-Cellular-and-Molecular-Biology/roberto-weigert	
Allan M. Weissman, MD	All	Our laboratory is focused on the ubiquitin-proteasome system in cancer and other diseases. We have determined that gp78, which is a ubiquitin ligase of the endoplasmic reticulum, plays a causal role in cancer aggressiveness and is expressed at higher levels in breast cancers from African-Americans than European-Americans. Studies utilize human tissue samples, our mouse models, genetically manipulated cell lines, and biochemical approaches. Using these, a recruit will have the opportunity to undertake a project to assess molecular mechanisms of gp78-mediated cancer aggressiveness and participate in development of therapeutic interventions to manipulate the function of gp78 and related molecules in cancer. https://ccr.cancer.gov/Laboratory-of-Protein-Dynamics-and-Signaling/allan-m-weissman	Frederick
Christopher Westlake, PhD	Post-baccalaureate, Postdoctoral Fellow	Most eukaryotic cells have a single primary cilium required for developmental and cancer-associated signaling, including Hedgehog, Notch and Wnt pathways. Defects in the formation and function of cilia have been linked to a number of human genetic diseases, referred to as ciliopathies, and cancer. My laboratory has shown that cilia assembly initiates inside the cell via a vesicular transport-dependent mechanism controlled by PI3K-Akt signaling. Our goal is to understand the basic fundamental membrane trafficking processes required for ciliogenesis using advanced cellular imaging, genetics and biochemistry approaches. We are also examining ciliogenesis dysfunction in cancer cells resulting from upregulated PI3K-Akt signaling. https://ccr.cancer.gov/Laboratory-of-Cell-and-Developmental-Signaling/christopher-j-westlake	Frederick
Sandra Wolin, MD, PhD	All	The Wolin lab studies how noncoding RNAs function, how cells recognize and degrade defective RNAs, and how failure to degrade these RNAs contributes to human disease. One pathway that we study involves noncoding RNA-protein complexes known as Ro60 ribonucleoproteins (RNPs). In all studied organisms, Ro60 binds noncoding RNAs called Y RNAs. Current projects include uncovering new roles for Ro60 and Y RNAs in mammalian cells and bacteria and identifying new RNA surveillance pathways in mammalian cells. https://ccr.cancer.gov/RNA-Biology-Laboratory/sandra-l-wolin	Frederick
Chuan Wu, MD, PhD	All	The neuroimmune interactions within the gut involve the actions of neurotransmitters, neuromodulators and cytokines that carry signals, often bidirectionally, between enteric neurons and immune cells. Our lab focuses on understanding how the interactions between immune system, nervous system and microbiome regulate intestinal and systemic homeostasis. https://ccr.cancer.gov/Experimental-Immunology-Branch/chuan-wu	Bethesda

Name	Scholar Level	Currently Available Research Areas and Projects	Location (In Maryland)
Euna Yoo, PhD	All	The Yoo group focuses on the development of chemical strategies to study and manipulate the human immune system. We use natural product screening and synthetic chemistry to develop chemical probes that specifically detect and perturb key regulators and functional enzymes involved in immune activation and tolerance. One of the main focuses is the design and synthesis of novel covalent ligands for cysteine proteases in tumor-associated immune cells. By applying and advancing chemoprotomics approach, our studies aim to understand the biological mechanisms of immunomodulators in the treatment of cancer and uncover new therapeutic avenues. https://ccr.cancer.gov/Chemical-Biology-Laboratory/euna-yoo	Frederick

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

Name	Scholar Level	Currently Available Research Areas and Projects	Location (In Maryland)
Sonja Berndt, PharmD, PhD	All	I conduct both population-based epidemiologic research as well genetic research. My research focuses on hematologic malignancies, prostate cancer, and obesity. Some potential projects available include: 1. Racial differences in myeloid malignancies in the U.S. 2. Racial differences in distribution of multiple primaries in the U.S. 3. Impact of race on changes in obesity over time. 4. Prevalence and differences in chromosomal integrated HHV6 across racial and ethnic populations. 5. Racial differences in genetic architecture of lymphoma and other cancers. https://dceg.cancer.gov/about/staff-directory/berndt-sonja	Shady Grove
Michael Dean, PhD	All	Our group is interested in the role of both inherited genetic variation and somatic variation in tumors determines cancer risk and tumor evolution. We primarily study cervical cancer, but also work with investigators studying breast, bladder, liver cancer and pediatric cancer. We have a strong focus on cancer in Latin American populations and underserved populations. https://dceg.cancer.gov/about/staff-directory/dean-michael	Shady Grove

Name	Scholar Level	Currently Available Research Areas and Projects	Location (In Maryland)
Eric A. Engels, MD, MPH	Graduate Student, Postdoctoral Fellows	My research is informed by my clinical training as an infectious diseases physician and my experience caring for HIV-infected patients. When I came to NCI in 1998, my background led me to focus on immunosuppression associated with HIV infection as a major cancer risk factor. Since 2005, I have also studied solid organ transplant recipients, who suffer from similar T-cell immune deficits due to the use of immunosuppressant medications to prevent rejection. Immunosuppression affects cancer in several ways. Loss of T-cell mediated immune control of oncogenic viral infections leads to an increased incidence for a characteristic spectrum of cancers. In my research on immunity and cancer, I address important etiologic and public health questions. My work often incorporates a “big data” approach, applying sophisticated analytic methods to large linked databases. These projects measure the population-level impact of cancer, including recent trends; assess etiologic questions; and evaluate outcomes after cancer diagnosis. I also use tools of molecular epidemiology to address selected hypotheses suggested by these analyses. https://dceg.cancer.gov/about/staff-directory/engels-eric	Shady Grove
Hormuzd Katki, PhD	All	Developing individualized lung cancer risk calculators that accurately estimate risks for minorities and subgroups, for use in selecting people for screening: Individualized lung cancer risk calculators are being used to recommend ever-smokers for lung cancer screening. However, current individualized lung cancer risk calculators do a poor job of estimating risk for minorities, women, and other subgroups (Katki et al, Ann Intern Med 2018). We propose to combine big data from nationally-representative surveys, cancer registries, trials, and epidemiologic cohorts, to develop calculators that accurately estimate risk for minorities, women, and other subgroups. The project will be heavily statistical and data-science oriented, and epidemiology training would also be valuable. (Postdoctoral Fellow Specific Project Idea) Quantifying disparities in lung cancer screening:Current lung cancer screening guidelines account for smoking history, but not race/ethnicity/gender, and thus under-select African-Americans and women for screening. However, some of the under-selection is due to African-Americans and women smoking less than other groups. I propose using the Peters-Belson method for quantifying the contributions of known factors towards explaining an observed disparity. This project will identify the reasons for the observed disparities in screening eligibility, to help suggest guidelines that mitigate the disparities. The ideal candidate would have knowledge of R computer programming, statistics, and epidemiology, but a willingness to independently learn these on-the-job would suffice. https://dceg.cancer.gov/about/staff-directory/katki-hormuzd	Shady Grove

Name	Scholar Level	Currently Available Research Areas and Projects	Location (In Maryland)
Lindsay M. Morton, PhD	All	Advances in childhood cancer treatment is one of the greatest successes in oncology in recent decades. However, survivors face a number of treatment-related adverse effects, including the development of second cancers. We are conducting large-scale genomics studies to identify whether some childhood cancer survivors are susceptible to radiotherapy- and chemotherapy-related second cancers. The combination of SNP-array genotyping and whole exome sequencing data enable us to evaluate both rare and common genetic variants. Detailed phenotype data, including radiation dose reconstruction, provide distinctive opportunities to employ novel methods for quantifying joint gene-treatment effects. https://dceg.cancer.gov/about/staff-directory/morton-lindsay	Shady Grove
Ludmila Prokunina-Olsson, PhD	All	Genetics and translational genomics of cancer and immune response. We start from germline variations identified by GWAS and perform computational and laboratory investigations to identify molecular phenotypes and translational applications of these findings. https://dceg.cancer.gov/about/staff-directory/biographies/K-N/prokunina-olsson-ludmila	Shady Grove
Meredith Shiels, PhD	Graduate Student, Postdoctoral Fellow	My research largely uses surveillance and descriptive epidemiology to quantify trends in cancer incidence and mortality and premature mortality, and to understand the drivers behind these trends. Potential projects could focus on the following areas: 1) quantifying the role of major risk factors on changing national cancer rates over time; 2) estimating changing cancer risk and burden among HIV-infected people; and 3) conducting detailed analyses of rising premature death rates in the United States. https://dceg.cancer.gov/about/staff-directory/shiels-meredith	Shady Grove
Mary H. Ward, PhD	All	Dr. Ward's research focuses on environmental causes of cancer, with emphasis on drinking water contaminants, pesticides, and other chemicals in relation to childhood cancers and adult gastrointestinal and thyroid cancers. Dr. Ward uses geographic information systems (GIS) to develop new methods for exposure assessment. In cohort and case-control studies, drinking water nitrate increased the risk of thyroid, bladder, kidney, and ovarian cancers. Following up upon these findings, Dr. Ward is using GIS-based models to estimate nitrate levels in drinking water supplies for the Agricultural Health Study, a cohort of pesticide applicators and their spouses with high exposure to nitrate through their private wells. Dr. Ward and her colleagues are also evaluating residential exposures to agricultural pesticides and animal operations in studies of childhood cancers in California and Denmark. https://irp.nih.gov/pi/mary-ward	Shady Grove

Name	Scholar Level	Currently Available Research Areas and Projects	Location (In Maryland)
Rose Yang, PhD, MPH	All	My research has focused on the molecular epidemiology of breast cancer and gene identification in cancer-prone families. Breast cancer: I am currently leading breast cancer studies in several Asian populations with the main goals of identifying distinct genomic alterations in tumors and adjacent normal tissues among Asian women and examining the associations of these changes with risk factors, breast tissue composition and density, and breast cancer subtypes. Melanoma and chordoma: The goals of these studies are to identify novel high-penetrance genes or genetic/ epigenetic factors that modify susceptibility in familial melanoma and chordoma. In addition, in collaboration with a neurosurgery hospital in Beijing, China, we are characterizing the genomic landscape of chordoma tumors using whole genome sequencing and RNA sequencing https://dceg.cancer.gov/about/staff-directory/biographies/O-Z/yang-rose	Shady Grove