

Pre-MSTP Summer Research Program
Life Sciences Summer Undergraduate Research Programs (LSSURP)
University of Minnesota
Summer 2020 Research Opportunities



[Joan Beckman, MD/PhD](#)

Assistant Professor of Medicine
Division of Hematology, Oncology, and Transplantation

Research in Dr. Beckman's lab in the University of Minnesota's Vascular Biology Center focuses on development of thrombosis in myeloproliferative neoplasms and patients with genetic mutations. We are modeling the vascular endothelium to determine how molecular mutations drive thrombosis development with the goal of identifying safer antithrombotic targets. Techniques a trainee would learn while doing research in Dr. Beckman's lab include flow cytometry, PCR, ELISA, standard histology, immunohistochemistry and immunofluorescence microscopy. Dr. Beckman is an adult hematologist. Students and residents interested in pursuing a career in this field or who are interested in small clinical projects (case reports, case series) related to hematology are also encouraged to contact Dr. Beckman for advice/guidance.

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[Brian Betts, MD](#)

Associate Professor of Medicine
Division of Hematology, Oncology and Transplantation

Allogeneic hematopoietic cell transplantation (HCT) can cure high risk leukemia, lymphoma, and marrow failure syndromes. However, graft-versus-host disease (GVHD) remains a life threatening side effect of this procedure. The Betts lab is interested in developing selective pharmacologic and cellular immunotherapy strategies to separate GVHD from beneficial graft-versus-leukemia (GVL) effects of the allograft. This includes small molecules targeting T cell costimulation and cytokine activation, dendritic cell ER stress response, and various pathways directing donor T cell differentiation. The lab also uses xenotransplantation models to test engineered human immune cells for GVHD and solid organ rejection prophylaxis; including Tregs, innate lymphoid cells, and chimeric antigen T cells (see work presented at ASH 2019 <https://ash.confex.com/ash/2019/webprogram/Paper124031.html>). Importantly, the lab is focused on translation and our work has directly led to innovative GVHD prevention trials.

Lab PI, Brian C. Betts MD, was chief resident at the University of Minnesota (internal medicine) and chief fellow at Memorial Sloan Kettering Cancer Center (medical oncology and hematology). He enjoys teaching and has mentored successful pre-med students, graduate students, and junior faculty. Under Dr. Betts' mentorship, it is expected that you will gain practical experience in human immune cell functional assays, multi-parameter flow cytometry and immunohistochemistry, and novel xenogeneic transplant models. You will also gain experience in selecting patients for allogeneic and autologous HCT, cell therapy including chimeric antigen T cells, managing transplant and cell therapy complications, using post-transplant maintenance strategies to prevent relapse, as well as how to identify and treat GVHD.

Complete List of Published Work in MyBibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/1DESb01Xvb6QI/bibliography/40972017/public/?sort=date&direction=ascending>

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[Bryce Binstadt, MD, PhD](#)

Associate Professor, Department of Pediatrics
MSTP Associate Director

The Binstadt lab studies the pathogenesis of autoimmune diseases in animal models. Current projects focus on 1) the contribution of macrophages to cardiovascular inflammation in a model of rheumatoid arthritis and 2) the contribution of specific T cell populations to the development of type 1 diabetes. The student would also spend one half-day per week shadowing Dr. Binstadt in the outpatient pediatric rheumatology clinic at the University of Minnesota Masonic Children's Hospital

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[Tyler Bold, MD/PhD](#)

Assistant Professor of Medicine

Division of Infectious Diseases and International Medicine

Using Salmonella to deliver TB antigens to CD4 T cells

An effective new vaccine is direly needed for tuberculosis (TB), the world's leading infectious cause of death. However, it remains unclear which of the >4,000 antigenic proteins potentially produced by the bacterial pathogen *Mycobacterium tuberculosis* (Mtb) can elicit the most effective CD4 T cell responses, and why. To answer these questions, we will establish a system to test Mtb genes of interest, in a way that provides a link between the efficacy of a T cell response and its antigenic target. We are developing a method to use *Salmonella*, a more tractable phagosomal pathogen, to deliver various TB antigens to CD4 T cells. The goals of this undergraduate research project would be to 1. construct a *Salmonella* phagosomal expression vector, 2. demonstrate expression of a test antigen of interest, 3. and determine whether this recombinant strain can trigger functional, antigen-specific CD4 T cell responses in vitro and in vivo.

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[Michael Georgieff, MD](#)

Professor, Department of Pediatrics and the Institute of Child Development
Executive Vice Chair, Department of Pediatrics
Head, Division of Neonatology
Director, Center for Neurobehavioral Development

My laboratory studies the effect of fetal and neonatal iron deficiency on the developing brain, and specifically the hippocampus, which underlies recognition memory processing. We investigate hippocampal development and memory function in humans and rodent models. We utilize genetic models of fetal /neonatal brain iron deficiency in order to elucidate the specific requirement of iron for brain development and to understand the lifelong consequences of early life iron deficiency. My expertise in basic laboratory science includes conditional knock-out technology, neurometabolism, neuronal structural analysis, electrophysiology, gene expression and animal and human behavior. My clinical research expertise is in Neonatal Follow-up. Current studies focus on defining the critical period for iron during hippocampal development, the role of iron in mitochondrial health and disease, and the role of iron in epigenetic programming of synaptic plasticity genes. Students in my laboratory would work in either wet lab (bench) research using animal models of early life nutritional deficiencies and their effect on hippocampal development or in clinical research studying populations of babies with perinatal risk factors to hippocampal development.

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[Alex Khoruts, MD](#)

Professor of Medicine

Division of Gastroenterology Hepatology and Nutrition

Our laboratory is developing novel therapeutics for several indications, including *Clostridium difficile* infection and inflammatory bowel disease. Specifically, we are focused on bile acid derivative compounds. Some of these are inhibitors of *C. difficile* spore germination or vegetative growth. Others have the potential to signal through the host bile acid receptor TGR5. We assay these compounds using in vitro methods, studying various aspects of *C. difficile* lifecycle. We also test them using in vivo models. This work is supported by the Department of Defense, which is interested in developing novel antimicrobial agents. Ours is a multidisciplinary group that combines expertise in microbial ecology, microbiome science, medicinal chemistry, and clinical gastroenterology.

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[Emil Lou, MD, PhD, FACP](#)

Assistant Professor of Medicine
Division of Hematology, Oncology and Transplantation
Medical Director, Clinical Trials Office

I am a lab-based physician-scientist and clinical investigator. I obtained the MD and PhD degrees in a combined program before training in Internal Medicine and Medical Oncology at Duke University and Memorial Sloan-Kettering Cancer Center, respectively. I am board-certified in Internal Medicine, Medical Oncology, and Neuro-Oncology. My primary clinical focus is the care of patients with advanced gastrointestinal cancers and neurologic malignancies.

The Lou Lab investigates tumor heterogeneity and intercellular communication in a spectrum of invasive and aggressive solid tumor malignancies. Projects in the lab focus on investigating the biology of cancer cells as they relate to cancer cell invasion, progression, tumor recurrence, and chemotherapy resistance. The Lou lab primarily focuses its work on studying intercellular communication via cellular extensions called tunneling nanotubes (TnTs, or TNTs, for short). These structures are long, thin, spontaneously forming actin-based cellular extensions that occur in a variety of cell types including inflammatory cells (e.g. B cells, macrophages), neurons, and more recently being examined in malignant cells. Our collaborative team believes that TNTs are an underexplored yet potentially important mode of intercellular communication in cancer and play a heretofore unassessed role in tumor-stromal cross-talk in the complex and heterogeneous tumor microenvironment.

A pre-MSTP experience with Dr. Lou would include learning cell and molecular biology techniques that are important to accomplishing the above work, as well as principles and application of advanced microscopy. There is also opportunity to shadow Dr. Lou in oncology clinic if interested. Outside of clinic and the lab, Dr. Lou is active on professional use of social media in oncology and research, and chairs the Social Media Working Group for the American Society of Clinical Oncology (@ASCO). (@cancerassassin1 on Twitter and IG).

Complete List of Published Work in MyBibliography:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Emil+Lou>

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[David Potter, MD, PhD](#)

Associate Professor, Department of Medicine

Our laboratory is engaged in the study of cytochrome P450 (CYP) arachidonic acid epoxygenase enzymes and their roles in breast cancer progression, with the goal of developing new and effective treatments for advanced stage hormone therapy resistant ER+HER2- breast cancer. Recently, our lab discovered that metformin suppresses breast cancer growth, in part, through the inhibition of arachidonic acid epoxidation by CYP3A4 and CYP2C8, which generates second messengers called epoxyeicosatrienoic acids (EETs). Furthermore, EETs

promote nuclear translocation of the estrogen receptor alpha and the mTORC1 component RagC and promote a gene expression signature associated with cell proliferation and treatment resistance. Using a co-crystal of metformin in the active site of CYP3A4, we have discovered novel derivatives of metformin that are several hundred-fold more active than metformin and inhibit oxidative phosphorylation in mammary tumors, thereby reversing tumor hypoxia. A summer research project will involve study of the impact of novel metformin derivatives on ER+HER2- breast cancer in vitro and in vivo with the goal of identifying novel metformin derivatives that can be brought forward to clinical development. The project will also involve the use of azido-EET derivatives to pull down targets in the nuclear pore complex to identify candidate EET targets.

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[Kurt Prins, MD/PhD](#)

Assistant Professor of Medicine
Cardiovascular Division

A pre-MSTP student working with Dr. Prins will investigate the link between interleukin-6 and right ventricular dysfunction in pulmonary arterial hypertension. In this project, the summer student would work to isolate right ventricular cardiomyocytes from rats. Then isolated cardiomyocytes would be treated as a sham, interleukin-6, and interleukin-6 with Stattic, a STAT3 inhibitor. Cardiomyocyte contractility and calcium handling will be examined. Furthermore, the relationship between STAT3 and the microtubule network will be examined under the same conditions.

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[Gregory Vercellotti, MD](#)

Professor, Department of Medicine

Despite more than 100 years of sickle cell disease (SCD) research, patients still suffer significant morbidity and early mortality due to the consequences of hemolysis and vaso-occlusion (VO). Sickle crises frequently occur with bacterial infections and enhanced hemolysis challenging the innate immune system. These insights point to the central role of hemolysis in the pathophysiology of SCD. However, in the absence of robust therapies to arrest hemoglobin S (HbS) polymerization, the clinician must deal with the consequences of hemolysis, including NO depletion, oxidative stress, inflammation, coagulation, complement activation, VO, ischemia-reperfusion, vascular dysfunction, and ultimately organ damage. To understand mechanisms that would lead us to effective therapies, we showed that heme derived from sickle red blood cells (SS-RBCs) acts as a damage-associated molecular pattern (DAMP) that can activate toll-like receptor 4 (TLR4) of the innate immune system, independently of its cognate ligand lipopolysaccharide (LPS), leading to oxidant production, inflammation, VO, ischemia, and tissue injury. We believe that hemolysis and the intravascular release of HbS and heme are central to the pathophysiology of SCD. We hypothesize that the innate immune system, including TLR4 and complement, is fundamental to understanding hemolysis-driven inflammation, coagulation, VO, and vasculopathy in SCD. We will define the role of innate complement activation in hemolysis, inflammation, and VO and its link to TLR4 in SCD. Present studies are focusing on development of gene therapy for sickle cell disease and are measuring biomarkers of endothelial activation/vasculopathy that could be used to monitor its success including circulating endothelial cells and endothelial microvesicles in sickle patients.

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[Masato Yamamoto, MD, PhD](#)

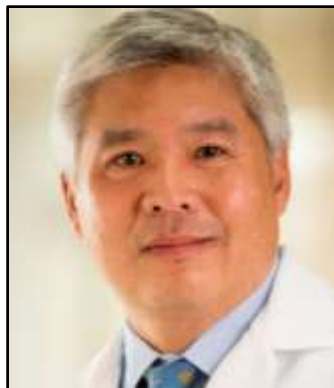
Eugene C. and Gail V. Sit Chair in Pancreatic and Gastrointestinal
Cancer Research

Vice-Chair of Surgical Science, Professor and Director, Division of
Basic and Translational Research

Department of Surgery

Dr. Yamamoto is a board certified gastroenterologist from Japan who leads surgical science in the Department of Surgery. The Yamamoto lab specializes in the design and engineering of adenovirus vector/virus for cancer treatment. The main subject of their research is oncolytic adenoviruses that selectively infect/replicate/kill cancer cells. They have developed a novel method to target the virus to the protein on the surface of the cancer cells. This technology enables treatment of cancers by systemic injection and thus permits treatment of advanced cancers that are no longer locally controllable. They are about to start a clinical trial of one of the viruses they have developed.

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[Doug Yee, MD](#)

Professor of Medicine and Pharmacology
John H. Kersey Chair in Cancer Research
Director, Masonic Cancer Center

The Yee laboratory focuses on growth regulatory pathways in breast cancer. Our aim is to develop new cancer therapeutic strategies based on a detailed understanding of the signaling pathways that regulate breast cancer survival, proliferation, motility, and metastasis. The work has focused on the function of the insulin-like growth factor (IGF) signaling system and the highly related insulin signaling pathway. We have shown that inhibitors of the IGF receptor are not effective in breast cancer because of their inability to block insulin signaling. Current projects in the lab focus on strategies to improve the targeting of this pathway. Laboratory projects include genetic and pharmacologic methods to block activation of a key adaptor protein (insulin receptor substrate-1) downstream of the receptors, defining regulatory pathways activated by IGF/insulin signaling to co-target the pathway, validation of an IGF gene expression signature in cell line models and human tumors, and development of insulin receptor targeting agents using monoclonal antibodies and insulin receptor isoform specific binding proteins identified from a yeast expression system. The student would also have the opportunity to participate in several clinically focused activities including the weekly breast cancer multi-disciplinary conference, the monthly breast cancer translational working group meeting, and shadowing Dr. Yee in his weekly medical oncology clinic. Trainees in the Yee laboratory will have exposure to laboratory, translational, and clinical research venues.