UC DAVIS

GRADUATE GROUP IN IMMUNOLOGY

Research Retreat Weekend

February 24 & 25, 2023

Graduate Group in Immunology

Research Retreat Weekend

February 24 & 25, 2023

Index

Friday, February 24 Schedule

8:30 a.m.	The Hilton Garden Inn Lobby, 110 F Street, Davis (transportation provided to Gladys Valley Hall)
9:00 a.m.	Convene in 1023 Gladys Valley Hall, UC Davis Campus (light breakfast served)
9:15 a.m.	Welcome with Dr. Chuck Bevins, GGI Chair
9:30 a.m.	Program Overview with Dr. Chuck Bevins, GGI Chair
10:15 a.m.	Immunology Research at UC Davis with Dr. Judy Van de Water, GGI Academic Adviser
10:45 a.m.	Break
11:00 a.m.	10-min Research Talk with Dr. Ryan Snodgrass, GGI Faculty Member
11:15 a.m.	10-min Research Talk with Dr. Allison Ehrlich, GGI Faculty Member
11:30 a.m.	10-min Research Talk with Dr. Jogender Tushir-Singh, GGI Faculty Member
11:45 a.m.	10-min Research Talk with Dr. Colin Reardon, GGI Faculty Member
12:00 p.m.	Lunch Break at Scrubs Café, 976 Garrod Drive (Aggie Cash Cards will be provided)
1:45 p.m.	Drive to the California National Primate Research Center Meet in Vet Med 3B parking lot.
2:00 p.m.	California National Primate Research Center Tram Tour *No photos allowed while at the Primate Center
3:00 p.m.	Break (return to hotel)
5:45 p.m.	Drive to dinner (vans depart Hilton Garden Inn, 110 F Street)
6:00 p.m.	Dinner with GGI students and faculty (Vet Med 3B Lobby, 1089 Veterinary Medicine Drive)
8:00 p.m.	Return to Hotel (drivers depart from Vet Med 3B parking lot)

Saturday, February 25 Schedule

8:00 a.m. Vans depart the Hilton Garden Inn, 110 F Street, Davis
*Please be sure to check out of the hotel before departing (they will hold your luggage or you can bring it with you)

8:15 a.m. Breakfast with GGI Students and Faculty
Walter A. Buehler Alumni Center

8:55 a.m. Welcome with Dr. Athena Soulika, GGI Recruitment Event Co-Chair

GGI Student Presentation

9:00 a.m. Sonny Elizaldi, 5th year GGI student
"Alpha 4 Integrin: The Driving Force Behind CCR5+ CD4 T Cell Migration to the Brain Parenchyma"

GGI Alumni Presentations

9:20 a.m. Dr. Alan Nguyen, Associate Scientist at Sutro Biopharma, Inc.
"From wound healing to cancer: How the GGI prepared me for industry"

9:55 a.m. Dr. Anthony Zamora, Assistant Professor, Department of Medicine, Medical College of Wisconsin
"From Natural to Engineered: Hacking T cells to Detect and Eliminate Tumors"

GGI Faculty Presentation – Keynote Speaker

10:30 a.m. Dr. Maryam Afkarian, Depner Endowed Professor, Division of Nephrology, Department of Medicine
"Dissecting role of inflammation in one other chronic human disease- diabetic kidney disease"

Poster Session

11:00 a.m. Viewing of GGI student posters (group A)

12:00 p.m. Viewing of GGI student posters (group B)

1:00 p.m. Closing Remarks with Dr. Chuck Bevins, GGI Chair

Picnic Lunch for Recruitment Committee & Prospective Students

1:15 p.m. Meet hosts Ali Arizzi and Brianna Ramirez in Alumni Center Lobby

1:20 p.m. Picnic Lunch - prospective students and current students
UC Davis Arboretum

2:30 p.m. Vans return to the Hilton Garden Inn

Yasmin Azzam
Seattle University
Biochemistry

Mollie Black
University of Tennessee, Knoxville
Animal Science

Aiquan Chang
University of California, Berkeley
Molecular and Cell Biology
Harvard University
Immunology (M.S.)

Spencer Danner-Bocks
University of Nevada, Reno
Biotechnology

Alva Duenas Alvarez
California State University, Fullerton
Biological Sciences

Kimberly Gardner
Howard University
Nutritional Sciences

Jack Goon
University of California, Davis
Biochemistry and Molecular Biology

Aaron Graber
Goshen College
Molecular Biology/Biochemistry

Ivan Lu
University of California, San Diego
Biochemistry and Cell Biology

Sophie Maxfield
Mount Holyoke College
Biological Sciences and Art History

Annette Mercedes
University of Washington
Biology and Anthropology
University of California, Berkeley
Infectious Diseases and Vaccinology (M.S.)

Jordan Pavlic
Oregon Institute of Technology
Biology – Health Sciences
California State University, Sacramento
Biological Sciences: Stem Cell (M.S.)

Bridgett Rios
University of North Carolina, Chapel Hill
Biology

Anson Seow
University of California, Merced
Biological Sciences: Microbiology & Immunology

Kelly Weldon
University of California, San Diego
Biochemistry/Chemistry
University of California, Davis, School of Medicine
MD (in progress)

Dear prospective students:

The Graduate Group in Immunology (GGI) is excited to share with you all that our campus has to offer and show you the many distinct ways that UC Davis is able to foster a highly collaborative and excellent educational environment. While exploring our campus, please note the following schools and centers which sponsor collaborative research endeavors with our graduate students and that consistently keep UC Davis ranking among the top graduate schools in the nation.

UC Davis is home to the California National Primate Research Center (CNPRC). The CNPRC is one of seven such centers supported by the National Institutes of Health (NIH). The National Primate Research Centers are a unique resource for investigators studying human health and disease, offering the opportunity to assess the causes of disease, and new treatment methods in nonhuman primate models that closely resemble humans.

The UC Davis School of Veterinary Medicine is located on the main Davis campus and has shaped the field of veterinary medicine, from developing dynamic education programs to uncovering solutions for emerging diseases of animals and humans to sharing knowledge with communities worldwide. The school trains tomorrow's small and large animal veterinarians and develops leaders in veterinary medical practice, higher education, public health, research, disease control, food safety, environmental protection and biotechnology. Established in 1946 and opened in 1948, the school consistently has been ranked first among all veterinary schools in North America by US News and World Report.

The UC Davis School of Medicine has been named by U.S. News & World Report among the top 20 schools for primary care training and the top 50 schools for research. The school is affiliated with the UC Davis Medical Center, one of the nation's best teaching hospitals, and is located at our Sacramento campus. Additionally, in 2012 the UC Davis Cancer Center achieved the highest distinction as one of only 41 National Cancer Institute Comprehensive Cancer Centers.

Our Sacramento campus is also home to the UC Davis MIND Institute (*Medical Investigation of Neurodevelopmental Disorders*). The MIND Institute is a collaborative international research center, committed to the awareness, understanding, prevention, care, and cure of neurodevelopmental disorders.

Our campus offers more than 20 distinct core facilities to support research endeavors as well as provide pilot study grants. In the following pages we highlight a few of these core facilities and invite you to search the UC Davis website for more information.

We hope you enjoy your visit!


Douglas Akahoshi


Alessandra Arizzi


Nicholas Bates


Katelien Blumenthal


Ryan Bruneau


Antonio Cembellin-Prieto


Craig Collins


Michael Cremin


Claire Depew


Sonny Elizaldi


Mindy Fernandez


Arthur Flores


Kevin Fong


Marissa Franke


Katie Griffin


Rian Harriman


Chase Hawes


Stephanie Henson


Chin-Wei Hsu


Daniela Jimenez


Janna Johnson

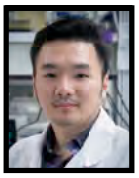

Chelsea Kelland


Danielle Kim


Amanda Kirane


Alvin Lam


Marshall Lammers


Jaewon Lee


Susan Lei


Madison Luker


Julianna Madigan


Nicolle Martin


Clarisa Martinez


Love Moore


Rachel Moreno


Dhiraj Nallapothula


Hadley Osman


Rama Ouattara


Morgan Poindexter


Brianna Ramirez


Aryana Razmara

Jordan Rixon

Felipe Rodriguez

Jamin Roh

Sara Rosero

Sharmila Sambanthamoorthy

Tina Sanchez

Sharon Sanghar

Michael Sheng

Noah Siegel

Juan Tamayo

Immunology Graduate Group

2022-2023

Natasha Tanner

Kayla Thomas

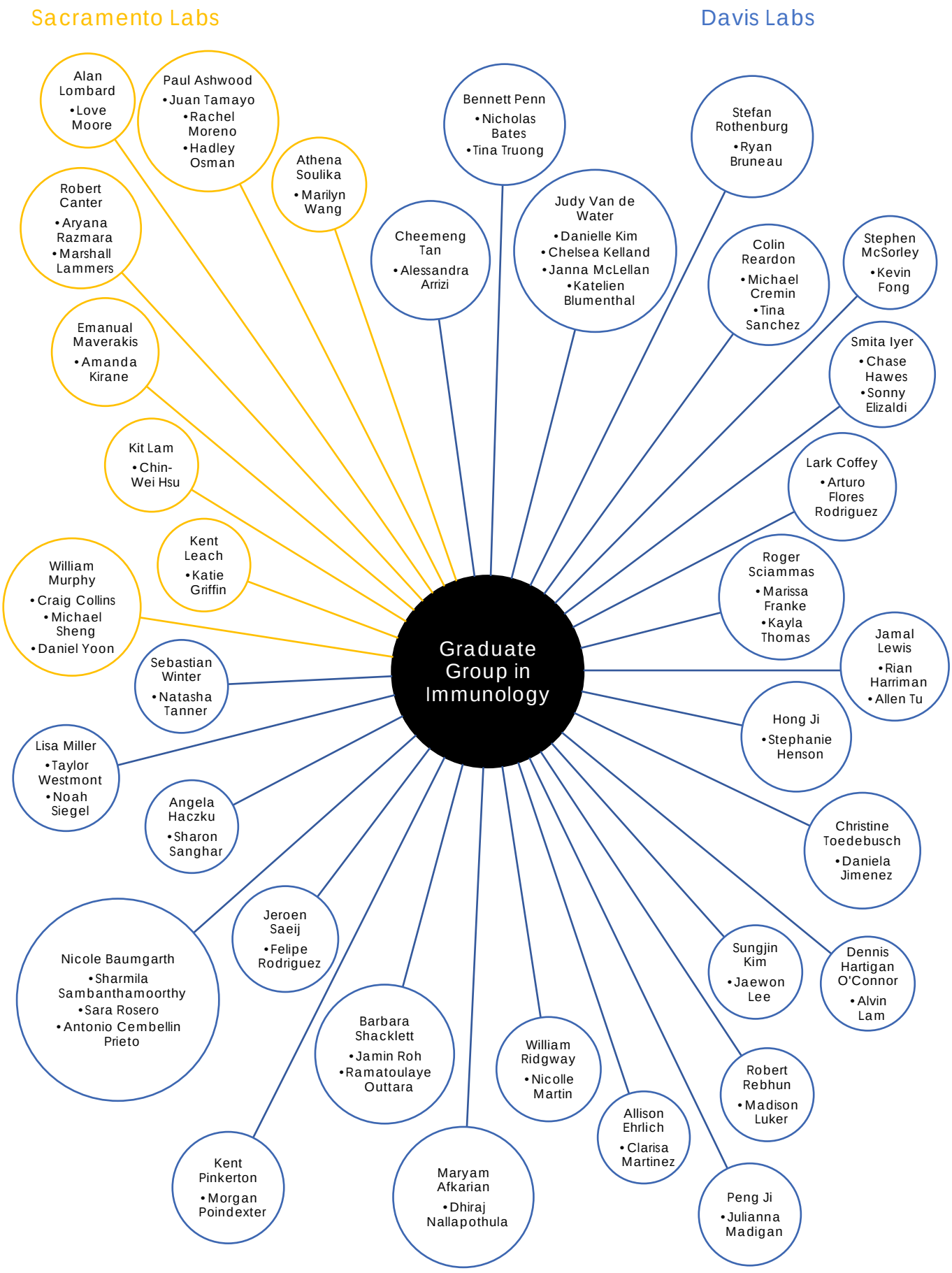
Tina Truong

Allen Tu

Marilyn Wang

Taylor Westmont

Daniel Yoon


Sacramento Labs
Davis Labs
Graduate Group in Immunology
Alan Lombard
• Love Moore
Paul Ashwood
• Juan Tamayo
• Rachel Moreno
• Hadley Osman
Athena Soulika
• Marilyn Wang
Bennett Penn
• Nicholas Bates
• Tina Truong
Stefan Rothenburg
• Ryan Bruneau
Robert Canter
• Aryana Razmara
• Marshall Lammers
Cheemeng Tan
• Alessandra Arrizi
Judy Van de Water
• Danielle Kim
• Chelsea Kelland
• Janna McLellan
• Katelien Blumenthal
Colin Reardon
• Michael Cremin
• Tina Sanchez
Stephen McSorley
• Kevin Fong
Emanual Maverakis
• Amanda Kirane
Smita Iyer
• Chase Hawes
• Sonny Elizaldi
Kit Lam
• Chin-Wei Hsu
Lark Coffey
• Arturo Flores Rodriguez
Kent Leach
• Katie Griffin
William Murphy
• Craig Collins
• Michael Sheng
• Daniel Yoon
Roger Sciammas
• Marissa Franke
• Kayla Thomas
Jamal Lewis
• Rian Harriman
• Allen Tu
Sebastian Winter
• Natasha Tanner
Hong Ji
• Stephanie Henson
Lisa Miller
• Taylor Westmont
• Noah Siegel
Angela Haczku
• Sharon Sanghar
Christine Toedebusch
• Daniela Jimenez
Nicole Baumgarth
• Sharmila Sambanthamoorthy
• Sara Rosero
• Antonio Cembellin Prieto
Jeroen Saeij
• Felipe Rodriguez
Sungjin Kim
• Jaewon Lee
Dennis Hartigan O'Connor
• Alvin Lam
Barbara Shacklett
• Jamin Roh
• Ramatoulaye Outtara
William Ridgway
• Nicolle Martin
Robert Rebhun
• Madison Luker
Allison Ehrlich
• Clarisa Martinez
Kent Pinkerton
• Morgan Poindexter
Maryam Afkarian
• Dhiraj Nallapothula
Peng Ji
• Julianna Madigan

Ask the Aggies: Why did you choose UC Davis?

I love UC Davis both for the community of the town as well as the community that GGI brings. Moving away from friends and family can be stressful, but I immediately felt at home in the program.

-Natasha Tanner, 1st Year

UC Davis is a beautiful campus that has a little something for everyone to enjoy nearby – be it major cities or beautiful hikes and campgrounds. The faculty are collaborative and outstanding with a variety of research interests and the university provides access to incredible facilities that not all campuses have access to. GGI is an incredible program that supports and values each of its graduate students, and I'm happy I made the decision to attend here.

-Nicolle Martin, 2nd Year

One of the reasons I picked UC Davis for graduate school is because our institution has its own veterinary school and a connected medical center that serve as great resources for conducting research. As someone who has lived in Davis for almost 6 years now, I can also attest to the pleasant and progressive community here.

-Sharon Sanghar, 2nd Year

"I've really enjoyed my time at UC Davis, mostly because of its dedicated, collaborative faculty and staff, who have prioritized the student experience amidst the pandemic and overall transition to graduate school." - Kristina Sanchez, 3rd year

"I knew UC Davis would be a lovely place to attend graduate school after spending a few days here. The campus is beautiful and downtown is quaint, but it wasn't until I met GGI at recruitment that I was sold. I felt supported and prioritized as a potential student before I was even admitted, and I was incredibly excited about the research and facilities here. I also had a good feeling about a city where biking is the primary mode of transportation for many!" - Julianna Madigan, 4th year

How does UC Davis compare?

3rd for global research impact in Life and Earth Sciences

Centre for Science and Technology Studies at Leiden University 2015-2017

2nd in Agriculture and Forestry Globally

QS World University Rankings 2022

1st in Veterinary Medicine in the Nation

QS World University Rankings 2022

2nd among Affordable Elite Colleges

Washington Monthly Affordable Elite Colleges 2021

1st in the nation for Diversity Inclusiveness and Internationalization

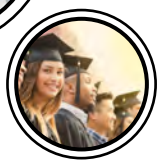
QS World University Rankings, 2022

1st nationally in biological and agricultural engineering

U.S. News & World Reports "Americas" Best Graduate Schools" 2022

5th globally Most Sustainable Universities

Ul Green City Metric, 2022



2nd Best Public University in the Nation

Washington Monthly Magazine 2022

For additional listings by schools, or to see how we have established a history of being among the top rated schools, please refer to the Office of Graduate Studies website that can be found at: (https://www.ucdavis.edu/about/rankings/)

Our award-winning faculty

Autoimmunity Cancer Immunity Comparative Immunity Host-Pathogen Interaction

Mucosal Immunology Nutritional Immunology Immune Signaling Neuroimmunology

Maryam Afkarian

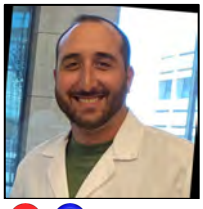
MD, PhD
Professor
Internal Medicine, Nephrology
mafkarian@ucdavis.edu

Keywords: inflammation, diabetic kidney disease
Research Interests: Mechanistic understanding of inflammation in chronic diseases; specifically understanding the innate and adaptive immune response in diabetic kidney disease (DKD) and characterizing the role of the immune response on DKD pathogenesis. First group to identify an association between urine complement components and progression of diabetic kidney disease (DKD).

Paul Ashwood

PhD
Professor
Medical Microbiology & Immunology,
The MIND Institute
pashwood@ucdavis.edu

Keywords: autism, neuroimmunology, neurodevelopment
Research Interests: We are interested in how the immune system influences the development of autism, with several ongoing projects focusing on the microbiota, maternal allergies and asthma, and the innate and adaptive immune system. We use a variety of research models, including mouse models, organoids and human specimens, to address our hypotheses.



Tom Ambrosi

PhD
Assistant Professor
Orthopedic Surgery
thambrosi@ucdavis.edu

Keywords: skeletal stem cell biology, immune cell output
Research Interests: Our lab studies the interactions of skeletal and hematopoietic cellular lineages in postnatal bones of mice and humans using a stem cell-centric approach. Interrogating skeletal stem cell biology during development, aging and cancer/disease allows us to dissect the cellular niches and molecular signals maintaining hematopoietic stem cells and regulating immune cell output. Our long-term goal is to leverage our discoveries to develop strategies to prevent and target skeletal stem cell-based bone aging and hematopoietic malignancies.

Andreas Bäumler

PhD
Professor & Vice Chair
Medical Microbiology & Immunology
ajbaumler@ucdavis.edu

Keywords: enteric pathogens, their host and its microbiota
Research Interests: Our research shows that enteric pathogens (Salmonella and Citrobacter) use their virulence factors to disrupt over the gut ecosystem by the host immune system, thereby engineering environmental changes that trigger dysbiosis and facilitate pathogen expansion. Virulence factors of enteric pathogens are therefore useful tools for identify immune functions that govern microbial growth on body surfaces. In turn, this knowledge informs strategies to remediate dysbiosis in a broad range on human diseases by restoring the functionality of immune functions that balance the microbiota.

Charles Bevins

MD, PhD
Professor and Chair of the Immunology Graduate Group
Medical Microbiology & Immunology
clbevins@ucdavis.edu

Keywords: innate and mucosal immunology

Research Interests: My group is interested in defining mechanisms that mediate homeostasis between host and microbes at mucosal surfaces. With a main focus on the gastrointestinal tract, our research seeks to provide a better understanding of numerous human diseases, including inflammatory bowel disease, infectious enteritis, necrotizing enterocolitis and others.

Robert Canter

MD
Professor
Surgery
Comprehensive Cancer Center
rjcanter@ucdavis.edu

Keywords: cancer immunology and immunotherapy, natural killer cell immunotherapy, canine immunotherapy, soft tissue sarcomas

Research Interests: Translational research in cross-species phenotype and function of NK cells and NK targeting of cancer stem cells.

Sean Collins

PhD
Associate Professor
Microbiology & Molecular Genetics
srcollins@ucdavis.edu

Keywords: neutrophils, chemotaxis, signal transduction, degranulation

Research Interests: Mechanisms of signal transduction and information processing by single cells (using a human neutrophil model), cell migration, chemotaxis, neutrophil extracellular trap formation, phagocytosis.

Lillian Cruz-Orengo

PhD
Associate Professor
Anatomy, Physiology, & Cell Biology
cruzorengo@ucdavis.edu

Keywords: blood-brain barrier, neuroimmune interactions, autoimmunity

Research Interests: My research focuses on sexual dimorphism of the blood-brain barrier (BBB) microvasculature as a relevant contributor to MS neuropathogenesis with the purpose of developing sex-specific therapeutic targets. Using the chemokine ligand CXCL12, a key regulator of immune trafficking into the central nervous system (CNS) as a biomarker, we hope to understand how BBB polarity is differentially regulated in females during CNS autoimmunity.

Satya Dandekar

PhD
Professor & Chair
Medical Microbiology & Immunology
sdandekar@ucdavis.edu

Keywords: mucosal immunology, viral infections

Research Interests: Molecular pathogenesis of Human Immunodeficiency Virus (HIV) and Simian Immunodeficiency Virus (SIV) infections with special emphasis on gastrointestinal mucosal lymphoid tissue (GALT) as a major target organ of the viral Infection, and as a viral reservoir. Repair and renewal of gut mucosal immune system during therapy.

Maneesh Dave

MD, MPH
Associate Professor
Internal Medicine
mdave@ucdavis.edu

Keywords: Regenerative medicine, microbiome, inflammatory bowel disease

Research Interests: Regenerative medicine, microbiome studies, clinical trials, and developing next-generation tools that can predict/assess response to IBD therapies.

Allison Ehrlich

PhD
Assistant Professor
Environmental & Molecular Toxicology
akehrlich@ucdavis.edu

Keywords: aryl hydrocarbon receptor, type 1diabetes, CD4+ T cells, mucosal immunology

Research Interests: My research aims to identify the mechanisms by which AhR activation leads to divergent CD4+ T cell fates, regulates gut mucosal immune responses, and alters microbiome-immune system crosstalk during the development of type 1 diabetes.

Melanie Gareau

PhD
Associate Professor
Anatomy, Physiology, & Cell Biology
mgareau@ucdavis.edu

Keywords: microbiota, behavior, innate immune, neuroinflammation

Research Interests: Characterizing the microbiota-gut-brain axis in models of inflammatory bowel disease and following infection with an enteric bacterial pathogen. Determining the mechanisms involved in the development of the microbiota-gut-brain axis in early life.

Angela Haczku

MD, PhD
Professor & Associate Dean of Research
Pulmonary & Critical Care Medicine
haczku@ucdavis.edu

Keywords: lung immunity, allergy, asthma, COPD, wildfire smoke, COVID-19

Research Interests: Airway inflammation caused by environmental exposures (allergen, cigarette smoke, ozone and wildfire smoke inhalation, psychosocial stress) in asthma and COPD. Innate and adaptive immune crosstalk and mechanisms of corticosteroid resistance. SARS-CoV-2 infection and vaccine development. Lung physiology and a wide spectrum of immunological cell and molecular biology techniques.

Dennis Hartigan O'Connor

MD, PhD
Associate Professor
Medical Microbiology and Immunology
dhartigan@ucdavis.edu

Keywords: cancer, cell trafficking

Research Interests: Research focuses on the development of the human immune system and interaction of that system with agents of chronic infection such as the human immunodeficiency virus (HIV) and hepatitis C virus (HCV). Most recently studies focus on the development of Th17 cells, regulatory T cells (T-regs), and antigen-presenting cells in the mucosal immune system. He is interested in the relationship between variable development of such immune cells and variable control over chronic infectious diseases.

Rivkah Isseroff

MD
Professor
Dermatology
Institute for Regenerative Cures
rrisseroff@ucdavis.edu

Keywords: tissue repair, wound healing, bioengineered tissue, adrenergic receptor, MSC, wound microbiome

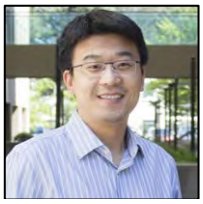
Research Interests: We study wound repair, using in vitro, animal, and human ex vivo models. Current work: catecholamines, adrenergic receptor signaling and neuroimmune modulation of the wound and its microbiome, generation of an MSC-bionegineered tissue to improve healing. Bench-to-beside translation in our wound clinic.

Hong Ji

PhD
Assistant Professor
Anatomy, Physiology and Cell biology
School of Veterinary Medicine
hgji@ucdavis.edu

Key words: epigenetics, environment exposures, air pollution, asthma

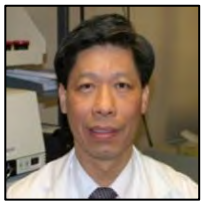
Research Interests: Dr. Ji's research group is focused on elucidating the epigenetic regulation of chronic diseases such as childhood asthma and examining how epigenetic mechanisms mediate the impact of environmental exposures during critical developmental windows (e.g., infancy) on increased disease susceptibility.



Peng Ji
PhD
Assistant Professor
Nutrition
penji@ucdavis.edu

Keywords: nutrition, enteric infections, host resistance

Research Interests: Evaluation of early-life nutrition on development and host resilience to infectious diseases. We use animal models and a systems biology approach to determine the development outcomes of nutrient deficiency and excess and their impact on host vulnerability to infections during the critical window of development. Recent work focuses on micronutrient deficiency and excess and dietary bioactive compounds. We have developed pathogen-challenged piglet models to mimic certain enteric bacterial pathogen infections in humans with the highest prevalence in infants and young children.



Kit Lam
MD, PhD
Professor & Chair
Biochemistry & Molecular Medicine
Hematology & Oncology
kit.lam@ucdmc.ucdavis.edu

Keywords: nanotherapeutics, drug discovery, chemistry

Research Interests: Application of combinatorial library methods for basic research and drug discovery, nanotherapeutics, immunotherapeutics, peptide targeted therapy for cancer, peptide immunochemistry, proteomics, chemical biology, bioconjugate chemistry, substrates and inhibitors for tyrosine kinase, tyrosine sulfotransferases and proteases, development of anti-microbial agents.

Sungjin Kim
PhD
Associate Professor
Medical Microbiology & Immunology
Center for Immunology & Infectious Diseases
sjikim@ucdavis.edu

Key words: NK cells, anti-viral activity, anti-tumor activity

Research Interests: We study innate immune cell responses to infectious disease and malignancy, with a particular focus on natural killer (NK) cells, the third major population of lymphocytes.

J. Kent Leach
PhD
Professor
Orthopedic Surgery
Biomedical Engineering
jkleach@ucdavis.edu

Keywords: tissue engineering, immunomodulation for tissue repair

Research Interests: The Leach Lab uses various materials, mechanical stimulation, and advanced manufacturing methods to generate platforms with engineered properties that meet the functional and biological demands of native tissue. The team aims to discover new strategies for accelerating the repair and regeneration of lost or diseased tissues and translate these findings to help animal and human patients in need.

Marcelo Kuroda
MD, PhD
Professor
Anatomy, Physiology, and Cell Biology
Center for Immunology and Infectious Diseases
mjkuroda@ucdavis.edu

Keywords: aging, monocyte/macrophages, HIV/SIV, TB

Research Interests: 1) Determining the role of monocyte/macrophages in the pathogenesis of infectious diseases, chronic inflammation and aging; 2) Examining the immunology of aging, and 3) Assessing the roles of macrophages in the pathogenesis of TB using the macaque model of TB/SIV.

Patrick Leung
PhD
Adjunct Professor
Rheumatology, Allergy & Clinical Immunology
psleung@ucdavis.edu

Keywords: biliary cirrhosis, food allergies

Research Interests: Molecular basis and Immunotherapy of primary biliary cirrhosis. Molecular immunology of food allergens and immunotherapy of seafood allergy.

Chengfei Liu

MD, PhD
Assistant Professor
Urologic Surgery
cffliu@ucdavis.edu

Keywords: urologic oncology, therapy resistance
Research Interests: Bridging basic and clinical research that ultimately yields novel translational efforts in urologic oncology, yielding new paradigms for protein post translational modification and drug resistance in cancer cells, advance the understanding of cancer biology and providing opportunities for innovative cancer therapeutics.

Alan Lombard

PhD
Assistant Professor
Urologic Surgery; Biochemistry and Molecular Medicine
aplombard@ucdavis.edu

Keywords: prostate cancer, immunotherapies
Research Interests: My research centers on the study of prostate cancer and mechanisms underlying its progression and both response and resistance to therapy. The lab's current focus is on the integration of PARP inhibitor treatment strategies into clinical care and the design of novel combination therapies which will enhance PARP inhibitor efficacy.

Emanual Maverakis

MD
Professor
Dermatology; Medical Microbiology & Immunology
Institute for Regenerative Cures
emaverakis@ucdavis.edu

Keywords: autoimmunity, immunotherapy, glycoimmunology
Research Interests: Dr. Maverakis' basic science research is focused on autoimmunity, basic T cell biology, and cancer immunology. Many of his projects look at the role of glycans in these areas of interest. Other projects focus on utilizing T cell repertoire analysis as a tool to study immune responses.

Steven McElroy

MD
Professor & Division Chief of Neonatology
Pediatrics
sjmcelroy@ucdavis.edu

Keywords: intestinal tract, host immunology
Research Interests: Understanding injury and repair mechanisms in the immature intestinal tract. Our research has deep roots in epithelial biology, microbial host interactions, and host immunology (both innate and adaptive).

Stephen J. McSorley

PhD
Professor
Anatomy, Physiology & Cell Biology
Center for Immunology & Infectious Diseases
sjmcsorley@ucdavis.edu

Keywords: CD4 T cells, bacterial infections
Research Interests: Our laboratory focuses on examining T cell response to mucosal pathogens with a view to deepening our understanding of protective immunity and vaccine development.

Lisa Miller

PhD
Professor
Anatomy, Physiology & Cell Biology
California National Primate Research Center
lmiller@ucdavis.edu

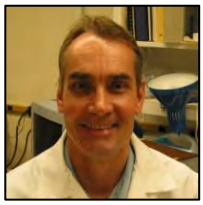
Keywords: lung, development, nonhuman primate
Research Interests: My laboratory is focused on investigating the impact of environmental exposures (air pollution, allergens, microbes) on development of mucosal immunity in the lung. We use murine and nonhuman primate models to understand the immune determinants of susceptibility that initiate airways disease and lead to chronic pulmonary disorders.

William Murphy

PhD
Professor & Vice Chair
Dermatology; Internal Medicine
Institute for Regenerative Cures
wmjmurphy@ucdavis.edu

Keywords: immunotherapy, viral, NK cells, stem cell transplants

Research Interests: Use of immunotherapy in cancer, particularly in the context of bone marrow transplantation and using models of metastatic disease. How the immune system normally suppresses itself and how the tumor further suppresses attempts by the immune system to attack it.



Kent Pinkerton

PhD
Professor & Director
Pediatrics, Anatomy, Physiology & Cell Biology
Center for Health and the Environment
kepinkerton@ucdavis.edu

Keywords: inhalation toxicology, perinatal development, asthma

Research Interests: Immunotoxicology of the respiratory system. The effects of environmental air pollutants (gases, vapors, and particles) on lung inflammation and disease. The role of cytokines and growth factors in lung maturation and development. The impact of aerosolized nanomaterials on health and disease. E-cigarette vaping on lung function/structure, as well as early life transgenerational impacts.

Robert O'Donnell

MD, PhD
Professor
Hematology & Oncology
UCD Comprehensive Cancer Center
rtodonnell@ucdavis.edu

Keywords: radioimmunotherapy, cancer, apoptosis

Research Interests: Radioimmunotherapy using radionuclide-labelled, cancer-specific monoclonal antibodies for treatment of patients with metastatic breast or prostate cancer, and lymphoma. Use of nude mouse models to explore synergy between this radioimmunotherapy and other drugs. Molecular, genetic changes caused by therapy and their effects on apoptosis. Molecular engineering of new antibody fragments capable of targeting malignant cells.

David Pleasure

MD
Professor & Director of Research
Neurology & Pediatrics
Shriner's Hospital
depleasure@ucdavis.edu

Keywords: myelin, oligodendroglia, astroglia, multiple sclerosis, leukodystrophy

Research Interests: I am a clinical neurologist with a research focus on glial development and glial diseases. My currently funded research centers on Canavan disease, a vacuolar leukodystrophy of infancy and childhood.

Bennett Penn

MD, PhD
Associate Professor
Infectious Diseases Medicine
bhpenn@ucdavis.edu

Keywords: TB, tuberculosis, macrophage, CRISPR

Research Interests: Dr. Penn's research focuses on understanding the immune response to *Mycobacterium tuberculosis*, the bacteria that causes the human disease tuberculosis, using cutting-edge genetic and proteomic tools.

Katherine S. Ralston

PhD
Assistant Professor
Microbiology & Molecular Genetics
ksralston@ucdavis.edu

Keywords: host-pathogen interactions, cell death, survival pathways

Research Interests: Interactions between the eukaryotic pathogen *Entamoeba histolytica* and the human host. The pathogen was named "histolytica" for its ability to destroy host tissues, which is driven by direct killing of human cells. We study how *E. histolytica* kills cells and invades tissue

Colin Reardon

PhD
Associate Professor
Anatomy, Physiology & Cell Biology
creardon@ucdavis.edu

Keywords: inflammatory bowel disease, neuro-immune, optogenetics

Research Interests: My research is focused on understanding the role of the nervous system and neurotransmitters in the modulation of the immune system and inflammation.

Robert Rebhun

DVM, PhD
Professor
Surgical & Radiological Sciences
rbrebhun@ucdavis.edu

Keywords: translational oncology, canine immunotherapy
Research Interests: I am a veterinary medical oncologist interested in comparative and translational oncology. Recent work has focused on canine cancer immunotherapy including defining the tumor microenvironment, generating reagents for diagnostic and clinical cancer immunotherapy studies, and testing novel immunotherapies in pet dogs with naturally occurring advanced metastatic cancer.

William Ridgway

Professor, Division Director
Rheumatology, Allergy & Clinical Immunology
wmridgway@ucdavis.edu

Keywords: immunogenetics, autoimmunity, T cells, tolerance, T1D, PBC

Research Interests: Genetics of autoimmunity and autoimmune phenotypes. The primary emphasis is on investigating mouse models of spontaneous polygenic autoimmune syndromes including type one diabetes and primary biliary cirrhosis.

Grace Rosenquist

PhD
Assistant Adjunct Professor
Neurobiology, Physiology & Behavior
rosenqui@yahoo.com

Keywords: protein post-translational modification

Research Interests: Post-translational modification of proteins, particularly tyrosine sulfation. Proteins of interest include glycoprotein viral coats, ionotropic and metabotropic glutamate receptors, and G-coupled protein receptors. Collaboration with laboratories which can validate predictions.

Stefan Rothenburg

MD, PhD
Associate Professor
Medical Microbiology & Immunology
rothenburg@ucdavis.edu

Keywords: virology, innate immunity, host-virus interactions, host-virus evolution

Research Interests: We are studying the molecular mechanisms that determine the host range and virulence of viruses by analyzing the interactions of viruses with the host innate immune system. Our long-term goal is to better predict the emergence and threat of newly evolving viruses.

Jeroen Saeij

PhD
Associate Professor
Pathology, Microbiology & Immunology
jeroensaeij@gmail.com

Keywords: host-parasite interactions, innate immunity, virulence

Research Interests: Our focus is the identification of genes of the obligate intracellular parasite Toxoplasma gondii that modulate the host cell and/or determine virulence, host genes and pathways that determine resistance/susceptibility, and to characterize their specific interactions.

Roger Sciammas

PhD
Associate Professor
Anatomy, Physiology & Cell Biology
Center for Immunology & Infectious Diseases
rsciammas@ucdavis.edu

Keywords: B cells, antibody, transcription factors

Research Interests: Our lab focuses on a better understanding of the control of antibody by investigating transcription factor activity and the architecture of gene regulatory networks in which they are embedded.

Ryan Snodgrass

PhD
Assistant Adjunct Professor
Nutrition
rgsnodgrass@ucdavis.edu

Keywords: monocytes, nutrition

Research Interests: Innate immunity and focus primarily on monocyte and macrophage biology. Regarding monocytes, I am interested in how ageing and nutritional status (fasting vs postprandial) modulates circulating monocyte subsets and their respective phenotypes. With respect to macrophages, I am interested in the role of intestinal macrophages in maintaining gut homeostasis; more specifically, how microbiota-derived metabolites, which can be influenced by our diet, contribute to macrophage function in the gut.

Barbara Shacklett

PhD
Professor
Medical Microbiology & Immunology
blshacklett@ucdavis.edu

Keywords: HIV, AIDS, mucosal immunity, T-cells

Research Interests: My laboratory studies cell-mediated immune responses to HIV and other viruses in mucosal tissues, and immune cell trafficking, to the gastrointestinal and reproductive tracts and the central nervous system. Current projects focus on tissue-resident memory T-cells, the functionality of cytotoxic T-cells, and chronic cytomegalovirus infection in the context of HIV disease.

Athena Soulika

PhD
Assistant Professor
Dermatology
Shriner's Hospital
asoulika@ucdavis.edu

Keywords: neuroimmunology, glial cells, innate immunity, skin immunology

Research Interests: Inflammatory neurological disorders, innate immunity responses within the CNS and how these affect the disease course. Local immune responses in the skin and their effects on injury.

Scott Simon

PhD
Professor & Vice Chair
Biomedical Engineering
sisimon@ucdavis.edu

Keywords: mechanosignaling, integrins, selectins, microfluidics

Research Interests: Inflammation in response to acute infection (Staph aureus and MRSA) and chronic disease (Atherosclerosis). Innate immunity of host response. In particular, how neutrophils and monocytes travel from blood out into tissue where they fight infections but can also contribute to disease.

Ellen E. Sparger

DVM, PhD
Associate Adjunct Professor
Medicine & Epidemiology
eesparger@ucdavis.edu

Keywords: molecular determinants of FIV pathogenesis

Research Interests: Conducting studies to identify molecular determinants of pathogenesis of feline immunodeficiency virus (FIV) infection in cats and to characterize FIV mutant viruses as attenuated virus vaccines.

Charles Stephensen

PhD
Adjunct Professor
USDA Western Human Nutrition Research Center
charles.stephensen@ars.usda.gov

Keywords: nutrition, T-cells, gut microbiome

Research Interests: My research focuses on the effects of diet and nutritional status on immune function. Current work focuses on the effect of diet (e.g., dietary fiber or human milk oligosaccharides found in breastmilk) on the intestinal microbiome and, in turn, the effect of the microbiome on immune function, including inflammation, immune cell activation and response to immunization. Other projects have focused on the direct effects of vitamin A and other nutrients on immune function.

Cheemeng Tan

PhD
Associate Professor
Biomedical Engineering
cmtan@ucdavis.edu

Keywords: immunotherapy, artificial cellular systems

Research Interests: The Tan Lab uses a holistic approach, which integrates synthetic biology and systems biology, to engineer synthetic vesicles, cell-free systems, and synthetic cells. Our work will lead to effective and safe artificial cellular systems for broad biotechnological applications, including immunotherapy of cancer cells and bacterial infection.

Suzanne Teuber

MD
Professor
Rheumatology, Allergy & Clinical Immunology
ssteuber@ucdavis.edu

Keywords: food allergies, cross-reactivity

Research Interests: Molecular characterization of food allergens associated with life-threatening anaphylactic reactions. Effect of seed polyphenolics on immune response and the possible role in development of food allergy to peanuts and tree nuts. Cross-reactivity of a food allergy.

Christine Toedebusch

DVM, PhD
Assistant Professor
Surgical & Radiological Sciences

Keywords: Neuroimmunology, tumorigenesis

Research Interests: Neuroimmunology and the role of microglia in canine and feline CNS health and disease, with a specific focus on the role of microglia in primary brain tumorigenesis.

Jose Torres

PhD
Professor
Medical Microbiology & Immunology
jvtorres@ucdavis.edu

Keywords: cancer immunology, immunotherapy

Research Interests: Our laboratory is dedicated to the study of tumors that avoid recognition and elimination by the human immune system. We combine modulation of the immune system in the tumor environment with active immunization to treat metastatic cancer. This work involves design, development and testing of peptide immunogens from tumor specific and tumor associated antigens.

Renée Tsolis

PhD
Professor
Medical Microbiology & Immunology
rmtsolis@ucdavis.edu

Keywords: innate immunity, phagocytes, bacterial infections

Research Interests: My research group studies how bacterial pathogens breach mucosal surfaces and interact with macrophages and neutrophils. We utilize both cellular and animal infection models to study on the one side how phagocytes control bacterial infections, and on the other side how bacterial pathogens evade the host's control mechanisms to cause persistent infection.

Joseph Tuscano

MD
Professor
Hematology and Oncology
UCD Comprehensive Cancer Center
joseph.tuscano@ucdmc.ucdavis.edu

Keywords: immunotherapy, B cells

Research Interests: Development of immune-based therapeutics for B cell malignancies. B lymphocyte signal transduction abnormalities; their role in human disease.

Natalia Vapniarsky,

DVM, PhD
Assistant Professor
Pathology, Microbiology & Immunology
vapniarsky@ucdavis.edu

Keywords: engineered tissues, immunomodulation
Research Interests: Tissue engineering of immuno-universal tissues and implants. I am investigating how the recipient perceives engineered tissues and how this immunity can be modulated via the implant. I am also studying immunomodulation by mesenchymal stem cells.

Jogender Tushir-Singh

PhD
Associate Professor
Department of Microbiology & Immunology
JTSigh@ucdavis.edu

Keywords: cancer immunology, viruses, CAR based immunotherapies

Research Interests: Therapeutic Antibodies, Cancer Immunotherapy, Tumor Cell-death, Antibody-directed SARS-CoV2 targeting.

Xiao-Jing Wang

MD, PhD
Professor
Pathology and Laboratory Medicine
drxwang@ucdavis.edu

Keywords: cancer immunology, microenvironment
Research Interests: The lab studies a) Role of immune microenvironment in cancer progression and metastasis; b) Mechanisms of immune evasion of cancer and cancer immunotherapy; c) mechanisms of inflammatory skin diseases, chronic inflammation affecting wound healing and tissue remodeling; d) therapeutic interventions in chronic wounds, radiation toxicities, inflammatory disease and fibrosis in oral cavity and skin.

Judy Van de Water

PhD
Professor
Rheumatology, Allergy & Clinical Immunology
The MIND Institute
javandewater@ucdavis.edu

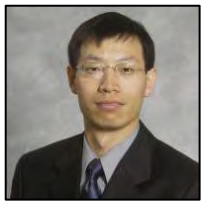
Keywords: neuroimmunology, autoimmunity, autism, immune dysregulation

Research Interests: Understanding the immunobiology of autism spectrum disorder and schizophrenia. Using animal models to determine the pathologic consequences of maternal autoantibodies to proteins in the developing brain and maternal immune activation on neurodevelopmental outcome and behavior.

Sebastian Winter

PhD
Associate Professor
Division of Infectious Diseases & Internal Medicine
sebwinter@ucdavis.edu

Keywords: enteric pathogens, metabolic interactions, intestinal inflammation
Research Interests: The Winter lab seeks to better understand the chemical biology of host-microbe interactions. We are particularly interested in the metabolic interactions between the host and its microbiome in settings of intestinal inflammation, and the metabolism of enteric pathogens during infection.



Huaijun Zhou

PhD
Professor
Chancellor's Fellow
Animal Science
hzhou@ucdavis.edu

Keywords: epigenomics, innate immunity, regulatory elements, viral infection

Research Interests: Dissection of regulatory mechanism of host response to viral and bacterial infection using high-throughput CRISPRa and CRISPRi system.

Our core facilities

UC Davis is in the enviable position of having a large number of talented labs across the biological spectrum. In support of scientific endeavors, UC Davis hosts more than 20 state-of-the-art shared research facilities that are housed by individual departments, centers, and institutes at both our Davis and Sacramento campuses. We encourage you to explore these at the website https://research.ucdavis.edu/research/core-facilities-services/uc-davis-core-facilities/


Bioinformatics Core

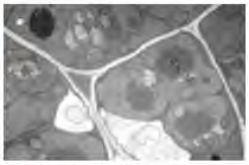

Campus Mass Spectrometry Facility


Center for Molecular and Genomic Imaging


College of Biological Sciences DNA Sequencing Facility


Controlled Environment Facility


DNA Technologies and Expression Analysis Cores


Biological Electron Microscopy Facility


Flow Cytometry Shared Resource Laboratory

Health Sciences District Advanced Imaging Facility


High Performance Computing for Research


Imaging Research Center


Interdisciplinary Center for Inductively-Coupled Plasma Mass Spectrometry

Keck Spectral Imaging Facility

Light Microscopy Imaging Facility, Department of Molecular and Cellular Biology

Mouse Biology Program


Nuclear Magnetic Resonance Facility

Set up your future success

How do you plan to use your PhD?

No matter where you want to go or what you want to do, UC Davis has you covered with a plethora of programs to prepare for your post-PhD career!

Mike & Renee Child Institute for Innovation and Entrepreneurship

The Child Family Institute for Innovation and Entrepreneurship integrates science and business for social benefit. They bring together researchers in science and engineering with faculty, MBA students, UC Davis undergraduates, experienced entrepreneurs, investors and corporate leaders to support technology transfer and commercialization activities through entrepreneurship academies and workshop opportunities.
http://gsm.ucdavis.edu/entrepreneurship

Designated Emphasis in Biotechnology (DEB Program)

An inter-graduate group program that promotes interdisciplinary research environments and provides well-coordinated, cross-disciplinary training with the mission of preparing well-educated graduate students to become research leaders, visionaries, entrepreneurs, researchers, and teachers in the broad area of in the critical area of biomolecular technology.
http://www.deb.ucdavis.edu

Center for Educational Effectiveness (CEE)

CEE provides leadership and support for instructional improvement and effective learning for all UC Davis students. This involves workshops on teaching and learning in hybrid and e-learning classrooms, a Graduate Teaching Community (GTC) for graduate students to meet and explore effective teaching techniques, and courses on teaching.
http://cee.ucdavis.edu

Professors for the Future (PFTF)

Professors for the Future is designed to prepare UC Davis doctoral students and postdoctoral scholars for an increasingly competitive marketplace and a rapidly changing university environment. Professors for the Future (PFTF) is a year-long competitive fellowship program designed to recognize and develop the leadership skills of outstanding graduate students and postdoctoral scholars who have demonstrated their commitment to professionalism, integrity, and academic service.
https://gradpathways.ucdavis.edu/pftf

Leaders for the Future

Leaders for the Future is a collaborative program between the Internship and Career Center, GradPathways, and the Mike and Renee Child Institute for Innovation and Entrepreneurship. The program engages graduate students and postdoctoral scholars in immersive professional opportunities with a focus on developing business and professional skills.
https://innovate.ucdavis.edu/leaders-future

GradPathways

GradPathways is a premier professional development program designed to help graduate students and postdoctoral scholars succeed both at UC Davis and in their chosen career paths through a wide variety of workshops and consultation opportunities.
https://gradpathways.ucdavis.edu/

UC Davis Internship and Career Center

The ICC provides comprehensive career services for UC Davis Master's and Ph.D. students. Career advisors can assist with all aspects of finding a career within or beyond academia. Services include confidential one-to-one advising, individualized C.V., resume, and cover letter review, and a variety of workshops and career treks.
https://icc.ucdavis.edu/

Enjoy the good life in Cowtown, USA!

Life in Northern California

We are excited that you are considering UC Davis for graduate school. While the main campus is located in the heart of Davis, UCD's School of Medicine is located in Sacramento and houses the nursing school, teaching hospital, and many cutting edge research labs and centers. As you consider making the move to our area, we hope that you consider all that Davis and Sacramento have to offer!

Both Sacramento and Davis are conveniently located central to several exciting and popular northern California destinations: the exciting and culturally rich city of San Francisco, the beautiful wine country of Napa Valley and the stunningly picturesque Lake Tahoe area, which offers a variety of activities for every season of the year. Winter activities in northern California include snowboarding, skiing, and snowshoeing, while spring and summer activities include hiking and camping, as well as water sports such as kayaking and paddle boarding at various nearby lakes and national parks.

Lake Tahoe

Napa Valley

San Francisco

Sacramento

Davis

Life in Davis

Davis is a university-oriented city within Yolo County that is well known for its small town atmosphere, high quality educational institutions, energy conservation, red double-decker buses and being a bike-friendly town. Though it has a small town feel, it is not small in the events, activities, nearby nightlife, and national parks that Davis offers for an active and healthy lifestyle. Campsites, hiking, and biking trails are all central in Yolo County. Some of these include the Yolo Bypass Wildlife Area, Pierce Canyon Falls Trail, The Greenbelt and UC Davis's very own Arboretum.

One of the best things about being a Davis resident is the convenience of being very close to campus and the student-friendly eateries which have various happy

The Arboretum stretches along Putah creek, offering ample space to stroll, lounge, and enjoy the outdoors. Similar pathways called greenbelts stretch all across Davis—making it a runner's and biker's paradise.

hour specials every day of the week! There are also special happy hours and weekly specials, and trivia almost every day of the week at bars such as University of Beer, Sophia's, and Three Mile Brewing Co.

Art installations scatter downtown, bringing even more charm to the walkable neighborhood full of shops, restaurants, and entertainment.

Furthermore, Davis promotes a healthy lifestyle and is well known for its Farmer's Market held every Wednesday evening and Saturday morning, with live entertainment from local bands and artists. Other fun activities within Davis include $7 movie night on Tuesdays and various pet- and kid-friendly weekend activities both on and off campus throughout the week. For those interested in the performing arts, the Mondavi Center has a wide variety of programs throughout the year that include symphony orchestras, dance programs and jazz just to name a few!

Life in Sacramento

As one of the most historic cities in California, Sacramento boasts an impressive array of landmarks, parks, amenities and other must-see points of interest. Sacramento is home to our state capital, a bustling downtown and midtown area and a quaint historical old town. The proximity of Sacramento to neighboring counties and cities–such as Lake Tahoe, San Francisco, Napa Valley, and Reno Nevada –allow for a variety of outdoor activities, social events and day trips to participate in throughout the year. Additional benefits of living in Sacramento include its proximity to the main campus in Davis, affordable housing options ranging from studio apartments to single family homes, plenty of social events, and hip new restaurants/bars.

Sacramento is home to the UC Davis Health System (UCDHS) that houses our medical school and many research laboratories. This provides a unique opportunity for our graduate students who wish to live in Sacramento to also conduct research close to their homes, while maintaining only a short drive to the Davis main campus. Life in Sacramento is centered within the midtown, also known as the central grid, and east Sacramento areas. The central grid serves as a one-stop-

Visit the Capitol building and stand under the beautiful rotunda or wander the sculpture garden. Sacramento offers a lively downtown scene, including indoor mini golf, live music, and even a speakeasy.

shop for eateries, art and culture, parks, coffee/bakeries, spas, fashionable shops, and many additional services. On the 2nd Saturday of every month, Midtown Sacramento galleries and local businesses host an open house evening where attendees can enjoy the art exhibits, local artists, food and wine, live music, street fairs and special events. Sacramento is also home to many Farmer's markets that are available throughout the week, year-round, in various locations, including the weekly Wednesday afternoon Farmer's market held at the UCDHS from May to October. A handful of our most iconic features to the city include the California State Capitol, Old Sacramento, Sutter's Fort, and the Golden 1 Center, home to the Sacramento Kings.

The Golden 1 center in Sacramento hosts more than just basketball games. The surrounding neighborhood is full of shops and restaurants all within walking distance. (Photo from Stephen Leonardi on Un-Splash.)

This could be you! Some of our students enjoy the sunrise views over Lake Tahoe after attending the annual Granlibakken meeting. GGI is proud to be able to send all 1 years to this conference held in Tahoe City every October.

For active lifestyles, the American River Parkway runs from Folsom Lake down to the Sacramento River and offers both paved and non-paved trails along the American River. This is a great place to ride your bike, run, walk or find a nice place to hang out and relax. Picnic tables, rope swings and parks are located all along the parkway and river. Folsom Lake is also a haven of recreational activities ranging from hiking, picnicking to swimming and an array of water sports. Many of our graduate students choose to live in Sacramento not only because of its affordable living and proximity to the Sacramento campus but also for the numerous activities this historic city has to offer!

THE SIERRAS: JUST A HOP, SKIP, AND A JUMP AWAY

Lake Tahoe is about a two-hour drive from Davis and offers an exorbitant number of activities: from skiing and snowboarding in the winter to hiking and wildflower searching in the summer. The sierras are full of state parks and the Tahoe National Forest. Whether you're looking for a day trip or a weekend getaway, Tahoe is within easy reach for Davis and Sacramento residents.

Finding your new home

Finding housing can be daunting, luckily there are plenty of resources to help

On-Campus Housing

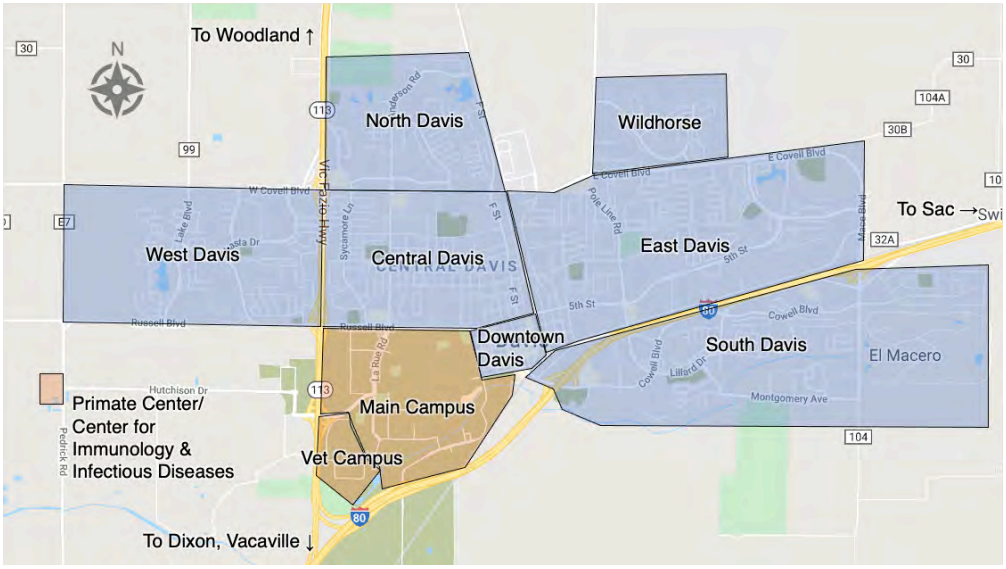
UC Davis has limited on-campus housing. Several of these housing options may provide daycare services and afterschool programs. Availability and applications dates can change quickly. Check websites for the most up to date information. Learn more about both types of housing at https://housing.ucdavis.edu/graduate-and-professional-housing/

Apartments	Cooperative Housing
Solano Park Apartments	The Baggins End Domes
8th & Wake	Tri-Cooperatives
Sol at West Village	
Russell Park	
The Atriums at La Rue	
The Colleges at La Rue	
Primero Grove	
Orchard Park	

Off Campus Housing

Most of our students live on non-campus affiliated properties in a mix of apartment complexes, duplexes, and stand-alone houses. Local resources for finding housing include the newspapers *The California Aggie* and *The Davis Enterprise.* Lyon Realty and King Properties also have listings on their sites. Rental availabilities can also be found on the usual popular sites like Zillow, Apartments.com, and even Davis-based Facebook groups. Our best recommendation is to talk to current students who have gone through the process. Typically, rent in Woodland and Sacramento are cheaper, but they do come with a longer commute.

As of February 2023, the average rent for a one-bedroom apartment in Davis is $1,923 with a range of $1,705 to $2,030 (apartmenthomeliving.com).



Davis is comprised of several neighborhoods, as shown above. Each is composed of a mix of detached housing and apartment complexes. Sections marked in orange are campus areas. Most classes are located within the vet campus. Sacramento is due east on the I-80.

Student Poster Abstracts

Abstract Index

III. Immune Regulation

IV. Neuroimmunology

I. Allergy and Autoimmunity

1. Augmentation of Oral Immunotherapy with Tolerance-inducing Nanoparticles

Rian Harriman[1], Nicolas Radoc[2], Jamal S. Lewis[1,2]

[1]Graduate Group in Immunology, [2]Department of Biomedical Engineering, University of California, Davis

Roughly 15 million Americans suffer from food allergies which, in severe cases, can be life threatening. Allergic individuals typically manage their conditions through strict food avoidance and/or the adminstration of antihistamine upon accidental exposure. Presently, oral immunotherapy (OIT) is the most efficacious option to achieve sustained unresponsiveness (SU) in allergic patients but is limited by the risk of triggering anaphylaxis and requiring intensive medical supervision. Moreover, SU is only established in 13-36% of paitents undergoing the therapy. Several clinical studies indicate that SU after OIT is correlated with increased T regulatory cell populations, which suggests the supplementation of OIT with tolerogenic immunomodulatory factors will increase its efficacy. Polysaccharide A (PSA), a commensal molecule produced by the gut-symbiont *Bacteroides fragilis,* has been shown to have Treg-inducing capabilities within the gut. The tolerance-inducing capacity in combination with its polymeric structure makes PSA an intriguing biomaterial for the formulation of tolerogenic nanoparticles. We hypothesize that the encapsulation of allergen within PSA nanoparticles (NPs) will show significant improvements in efficacy and safety over traditional allergen-only oral immunotherapy due to PSA NPs ability to (i) induce Treg differentiation and deliver allergen simultaneously, and (ii) to shield the allergen from IgE receptor-mediated mast cell activation until internalization by intestinal dendritic cells. W show that PSA NPs can be readily fabricated using water/oil emulsification with glutaraldehyde crosslinking and maintain immunoregulatory capability, including TLR2 stimulation and $CD4^{+}IL\text{-}10^{+}$ T cell differentiation. PSA NPs have the potential to become a “plug-in-play” system to induce specific tolerance to any encapsulated allergen. (Funding: NIAID 5R03AI138191-02)

2. Mechanistic and Therapeutic Role of the TLR4 Signaling Pathway in T1D

Nicolle K Martin[1], Luke S Heuer[2], William M Ridgway[2]

[1] Graduate Group in Immunology, [2]Division of Rheumatology, Allergy and Clinical Immunology, University of California, Davis

Type 1 Diabetes (T1D) is a chronic disease caused by the autoimmune destruction of insulin-producing pancreatic beta cells, and there is currently no treatment that reverses the disease. Most T1D reversal approaches have failed in clinical trials and thus an ongoing need exists for novel therapies targeting new immune pathways. We have exciting data showing that a TLR4/MD2 agonistic antibody (TLR4-Ab) permanently reversed T1D in 71%, and induced a significant clinical effect in 90%, of acutely diabetic non-obese diabetic (NOD) mice. Recently, we showed that TLR4-Ab can mobilize and activate myeloid-derived suppressor cells (MDSCs) that suppress T cells and reverse T1D. We showed that TLR4-Ab remains sequestered in endosomes, unlike the TLR4 agonist LPS (which cannot reverse T1D). However, the mechanism by which TLR4-Ab induces MDSCs and reverses T1D remains unclear. TLR4-Ab is an IgG3 isotype with the longest hinge region, increased glycosylation sites, and can form cryoglobulins, impacting avidity and internalization. We hypothesize that TLR4-Ab endosomal sequestration causes sustained TRIF-driven endosomal signaling and that the IgG3 Fc portion of the TLR4-Ab is critical for these effects. We show that immobilization of intact TLR4-Ab eliminated NFκB signaling, strongly supporting the hypothesis that internalization and endosomal sequestration is necessary for TLR4-Ab effects. We also demonstrate that TLR4-Ab treatment of bone marrow cells induces the production of IFNβ and IL10, both downstream products of TLR4 endosomal signaling via TRIF/TRAM which is important for immunomodulation. In addition, TLR4-Ab F(ab) and F(ab)2 fragments do not elicit full NFκB signaling compared to intact TLR4-Ab, implicating a critical role for Fc structure in TLR4-Ab function. Lastly, TLR4-Ab F(ab)2 fragments do not trigger TLR4 internalization in RAW cells analyzed by imaging flow cytometry. These studies are important in order to characterize the mechanisms by which TLR4-Ab reverses acute T1D for translation to human applications. (Funding: NIH 1R21AI120084-01A1)

3. Environmental factors underlying divergent AhR-mediated CD4+ T cell differentiation

Clarisa Martinez[1], Allison K Ehrlich[2]

[1]Graduate Group in Immunology, [2]Department of Environmental Toxicology, University of California, Davis

Type 1 diabetes (T1D) is an incurable autoimmune disease caused by T cell-mediated destruction of insulin-producing beta cells. In addition to a genetic predisposition, susceptibility to T1D is influenced by environmental factors including chemical contaminants, dietary phytochemicals and microbial dysbiosis. Connecting these genetic and environmental interactions is the aryl hydrocarbon receptor (AhR), a ligand activated transcription factor. AhR ligands include 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD), an environmental pollutant, diet derived metabolites in cruciferous vegetables (e.g. indole-3-carbinol), and microbiota-derived tryptophan metabolites. Our laboratory previously found that systemic activation of AhR by TCDD increases immunosuppressive CD4+ T regulatory cells and prevents the development of T1D in nonobese diabetic (NOD) mice. In contrast, dietary indole-3-carbinol activates AhR in the intestine, increases a subset of proinflammatory CD4+ T-helper 17 cells, shifts the gut microbiome, and promotes T1D in NOD mice. These contradictory data led us to the question: how does activation of the same receptor promote divergent CD4+ T cell subsets and T1D phenotypes? Our central hypothesis is that AhR-microbiome interactions influence the outcome of CD4+ T cell differentiation. To test this hypothesis, we will analyze CD4+ T cell differentiation following TCDD and indole-3-carbinol exposures in three different NOD mouse models: 1) transgenic mice with islet antigen-specific CD4+ T cells, 2) AhR knockout mice, and 3) gnotobiotic mice. Ultimately, the data will help elucidate how activation of AhR influences CD4+ T cell differentiation, identify how environmental factors contribute to T1D susceptibility, and uncover how AhR can be targeted for T1D prevention. (Funding: K99DK117509-01, R00 DK117509-03).

4. Re-engineering REGvac for Rheumatoid Arthritis Immunotherapy

Allen B. Tu[1,2], Natalia Vapniarsky-Arzi[3], Jamal S. Lewis[4]

[1]Graduate Group in Immunology, [2]Department of Biomedical Engineering, [3]Department of Pathology, Microbiology & Immunology, School of Veterinary Medicine, University of California, Davis, [4]J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida

Rheumatoid Arthritis (RA) is a debilitating autoimmune disease affecting ~1% of the population. It is characterized by inflammation of the joint synovium leading to bone and cartilage destruction. There is currently no cure and treatment options require lifelong management of immunosuppressive drugs. However, these drugs are accompanied by many adverse effects such as increased risk of infection and acute and chronic toxicities. The ongoing COVID-19 pandemic has underscored a critical need for new therapies that do not immunocompromise the patient. In this study, we have rationally designed a novel poly (lactic-co-glycolic) acid (PLGA)-based microparticle system, termed REGvac, that upon subcutaneous delivery facilitates generation of tolerogenic dendritic cells (tDC) to mediate antigen-specific tolerance towards rheumatic antigens. This is achieved through delivery of REGvac which is comprised of (1) a non-phagocytosable 30 um PLGA microparticle encapsulating transforming growth factor β1 (TGF-β1) and granulocyte-macrophage colony-stimulating factor (GM-CSF), and (2) a phagocytosable 1 um PLGA microparticle encapsulating vitamin D3 (a potent tolerogenic factor) and the rheumatic antigens type II collagen (col II) and citrullinated fibrinogen. RA is induced in DBA/1J mice via immunization with type II collagen and citrullinated fibrinogen. Onset of severe RA (clinical score of 6) initiates therapy with either REGvac, or methotrexate, thrice for the first week, followed by once weekly for seven weeks. 8 weeks post-treatment, spleen, inguinal LNs, and popliteal LN are assessed for immune cell composition via flow cytometry. We found that REGvac treatment impaired bone marrow-derived dendritic cell maturation and promotes regulatory T cell generation *in vitro*, and ameliorated RA symptoms and halted disease progression *in vivo*. (Funding NIH R01AI139399-02, NIGMS T32GM099608)

II. Host-Pathogen Interactions

5. Developing a genetic screening method to study phenotypic antibiotic tolerance in *Mycobacteria*

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To be effective, antibiotic therapy must navigate numerous biological hurdles. Among these is that a bacterium may exist in one of several, potentially diverse, phenotypic states at any given time. One factor that influences the phenotype of a bacterium is the environment that surrounds it. For a pathogen like *M. tuberculosis*, *in vivo* conditions notably include stressors such as nutrient starvation, hypoxia, low pH, and reactive nitrogen species, which are associated with host immunity in macrophage phagosomes and granulomas. Thus, antibiotics which are tested under standard *in vitro* growth conditions may not display the same activity *in vivo*. To better understand this phenomenon, we searched for examples where host relevant stressors alter the effectiveness of clinically relevant antibiotics used to treat *M. tuberculosis*. As a proof of concept, we began study in the fast-growing organisms *M. smegmatis*, a commonly used model organism, and *M. abscessus*, a highly antibiotic resistant emerging pathogen. In *M. smegmatis*, we have observed inducible multi-drug tolerance in response to numerous stress conditions, including nutrient starvation, hypoxia, and combined acid/reactive nitrogen species treatment. However, in *M. abscessus*, we have only observed inducible multi-drug tolerance in response to nutrient starvation. In the future, we plan to expand these studies into *M. tuberculosis*, and to conduct loss of function genetic screens using transposon insertion sequencing to identify the genes and pathways required for stress induced antibiotic tolerance. (Funding: Pew Biomedical Scholar Grant to BHP)

6. TRPV1 is a critical determinant of Host immune responses to the enteric bacterial pathogen *Citrobacter rodentium*

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The gastrointestinal (GI) tract is densely innervated by a variety of neuronal types that function to maintain homeostasis by regulating physiology and coordinating immunological responses. These include specialized sensory neurons that detect noxious stimuli due to expression of the ion channel transient receptor potential vanilloid receptor 1 (TRPV1) channel. Activation of TRPV1+ neurons in the intestine can cause the release of neuropeptides that stimulate neurogenic inflammation in the surrounding tissue, increasing blood vessel permeability and immune cell recruitment. Enteric bacterial infections remain a significant health problem, and Citrobacter rodentium is an excellent model of attaching and effacing pathogens in vivo. Here we have used C. rodentium infection to assess the role of TRPV1 in the immunological response. Mice lacking TRPV1 (TRPV1-/-) had significantly higher C. rodentium bacterial burden in the distal colon and fecal pellets compared to wildtype (WT) mice. This correlated with an increase in colonic crypt hyperplasia and proliferating Ki67+ cells in TRPV1-/-mice compared to WT mice. Despite the increase in bacterial burden and inflammation, there was no difference in T cells recruited to the colon or their production in IFNy, IL-17, or IL-22. However, there was a significant decrease in colonic neutrophils in infected TRPV1-/- mice compared to WT mice. There appeared to be no deficiency in the maturation of neutrophils in the bone marrow, suggesting that there was a regulation of the neutrophil entry into the colon from blood vessels. Indeed, there was a significant decrease in the neutrophil-specific chemokines and the adhesion molecule ICAM-1 in the distal colon of TRPV1-/- mice compared to WT mice determined by qPCR. Our study shows that TRPV1 is important in regulating the host immune response to C. rodentium, modulating the surrounding tissue to express crucial proteins that recruit neutrophils during enteric infection. (Research funding provided by R01AI150647, R21AI148188).

7. Optimal formation of Hepatic Tissue Resident Memory CD4 T cells Requires T-bet Regulation of LFA-1

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Tissue resident memory (TRM) CD4 T cells contribute to robust protection of barrier surfaces against wide range of pathogens. Here, we investigated the role of T-bet in the formation of *Salmonella*-specific CD4 TRM in the liver. Activated T-bet-deficient CD4 T cells did not efficiently populate the liver or transition to TRM compared with wildtype CD4 T cells. Ectopic expression of T-bet enhanced the formation of liver CD4 TRM, but only when competing with wild-type CD4 T cells. Hepatic TRM typically expressed higher levels of LFA-1, and depended on T-bet expression. Competitive advantages of seeding liver niches were blocked by antibody neutralization of LFA-1. Together, activated CD4 T cells compete for entry in liver niches via T-bet-induced expression of LFA-1, allowing TRM precursors to access subsequent hepatic maturation signals. These findings uncover an essential role for T-bet in liver TRM CD4 formation and suggest enhancement of this circuit could increase the efficacy of vaccines that require hepatic TRMs. (R01AI139047, R01AI139402, T32 AI060555)

8. Collaborative Cross Mice as a New Model for Diverse Human Outcomes of St. Louis Encephalitis Virus Disease

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St. Louis encephalitis virus (SLEV) is a mosquito-borne flavivirus that causes a range of disease manifestations in humans, spanning asymptomatic infection to encephalitis and death. SLEV is detected annually in California and in the Western United States. Current SLEV mouse models are limited since they rely on use of immunodeficient mice or inoculation routes which artificially bias towards increased neurovirulence to model only severe SLEV. To circumvent limitations of existing SLEV mouse models, the goal of this project is to develop an immunocompetent SLEV mouse model using Collaborative Cross (CC) mice. Recombinant CC mice have been generated from 8 common inbred lab strains and, unlike immunodeficient mice, model diverse human outcomes to many viral infections, including the flaviviruses Powassan, Zika, and West Nile viruses. We hypothesize that CC mice model human SLEV disease by producing clinical disease, viral tropism, and viral kinetics that parallel human SLEV disease outcomes and that protection from central nervous system (CNS) disease is mediated by a robust innate immune response. This hypothesis will be tested by experimentally inoculating CC mice with SLEV subcutaneously to mimic mosquito transmission and then assessing clinical disease, survival, and virus infection kinetics in blood and tissues in mice sacrificed at different times after inoculation. We will also determine whether elevated innate immune responses associate with absence of SLEV CNS disease. The circulating effector response (serum, spleen), tissue immune response (kidney), and CNS (brain) innate response will be defined by measuring the antiviral sensor RIG-I and interferon gene expression and cytokine levels, and correlated with clinical disease, virus levels in blood and target tissues, neuroinvasion, and neuropathology. This novel model is aimed at recapitulating the spectrum of human SLEV outcomes and can be used to further study pathogenesis, immune responses, virus-host interactions, viral and host genetic determinants of severe disease.

9. Identifying the mechanism of *Chlamydia muridarum* clearance by circulating CD4 T cell memory

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Tissue resident memory (TRM) cells are thought to be essential for secondary clearance of *Chlamydia* from the female reproductive tract (FRT), but recent parabiosis studies show that circulating memory can be sufficient. Here, we further examine the mechanism of robust protective immunity in the FRT mediated by distally generated CD4 T cells after intranasal (INAS) immunization. Using a TCR transgenic adoptive transfer system with *Chlamydia*-specific CD4 T (TP1) cells, INAS immunization established an elevated and stable circulating CD4 memory TP1 population, while minimally seeding the FRT. This circulating CD4 memory response allowed INAS-primed mice to resist FRT infection for up to six months post-immunization. Accelerated recruitment of circulating *Chlamydia*-specific memory cells to the FRT was documented following cervicovaginal infection. Furthermore, clearance of *Chlamydia* from the FRT did not depend on T-bet or IFN-γR expression by bone marrow-derived cells. Thus, the establishment of a strong circulating memory response allows robust FRT protection by atypical memory CD4 Th1 cells. Current studies are examining the mechanism of CD4 recruitment and non-IFN-γ-dependent bacterial clearance within the FRT. Greater knowledge of the mechanism of circulating CD4 protection of the FRT may allow the development of new parenteral vaccines for *Chlamydia*.

10. The phenotype of Long-Lived Controller Memory T Cells Expressing T Cell Factor 1 and Eomesodermin in SIV Infection

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Vaccination aims to produce a long-lasting adaptive immune response that enables an anamnestic response immediately upon pathogen encounter, however, long-lasting immunity and protection are not always achieved. The mechanisms by which long-lived memory T cells are generated are incompletely understood. Other studies demonstrate that T cell factor 1 (TCF-1) and Eomesodermin (EOMES) have been linked to a more effector phenotype in cancer, with reduced T cell exhaustion and increased clearance of cancer. We propose that the establishment of durable memory T cell responses in some vaccinees reflects the predominance of TCF-1 and EOMES, favoring the generation of T stem cell-like memory cells (T_{SCM}). We took peripheral blood mononuclear cells from rhesus macaques vaccinated against SIV by adenoviral vectors that later go on to stringently control SIV infection. After SIV challenge, PBMCs were stained for memory T cells by fluorescent-antibody cell sorting (FACS). Plasma was taken from macaques weekly to monitor levels of viral loads; animals under 10^3 are considered controllers while non-controller macaques have plasma viral loads above 10^4. We found in $CD8^+$ memory T cells, a population of T_{SCM} and central memory T cells expressing higher levels of TCF1, EOMES, and Ki67 (p-value <= 0.05). Additionally, we saw less interferon-gamma (IFN-γ) expression in $CD8^+$ memory T cells in controller macaques compared to non-controller macaques. The data we collected suggests that stringent control of SIV infection may come from a memory T cell population that expresses high levels of TCF-1, EOMES, and Ki67, while having a low expression of IFN-γ. These results are important for determining a memory T cell phenotype that is long-lived and can control infection for producing more durable vaccines.
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11. Determining how the detection of *Toxoplasma gondii* by human immune cells leads to the production of interferon gamma

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Toxoplasma gondii is considered as a leading cause of death from foodborne illness with ~ 30% of the population being infected. The cytokine IFN**γ** controls *Toxoplasma* infection by upregulating a variety of antimicrobial mechanisms. In mice, Toll like Receptor (TLR) 11/12 activation by *Toxoplasma* profilin triggers Dendritic Cells to secrete IL-12 which activates Natural Killer and T cells to secrete IFN**γ**. In mice, IFN**γ** upregulated Immunity Related Guanosine Triphosphatases (IRGs) that can destroy the vacuole in which the parasite resides. However, humans do not have TLR11/12 or IRGs and the *Toxoplasma* Rhoptry (ROP) and dense granule (GRA) secreted effector proteins that determine virulence in rodents play no role in human cells. Our previous work discovered that parasite effectors GRA15 and GRA24, which activate cell NFkB and P38 MAPK, induce the production of IL-18, IL-1**β** and IL-12 by monocytes which stimulate IFN**γ** production likely by NK and T cells. Human peripheral blood mononuclear cells (hPBMCs) infected with GRA15/24 double knockout parasites still produce IFN**γ** albeit less than wildtype. Here we aim to determine which immune cells are mounting a response to wild-type parasites or parasites lacking GRA15/24. V**γ**9Vδ2 T cells recognize phosphoantigens such as €-4-hydroxy-3-methyl-but-2-enyl pyrophosphate (HMBPP) leading to robust expansion and IFN**γ** secretion. *Toxoplasma* utilizes the 1-deoxy-d-xylulose-5-phosphate (DOXP) pathway to synthesize isoprenoid precursors which results in the synthesis of HMBPP. We hypothesize during WT infection IFN**γ** is produced by T, NK, and V**γ**9Vδ2 T cells while in GRA15/24 knockout parasites V**γ**9Vδ2 T cells are the main producers of IFN**γ**. (Funding: NIHR21AI149071)

12. RhCMV: a Catalyst for Heightened Inflammation in SARS-CoV-2

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SARS-CoV-2 infection results in a spectrum of disease severity attributable to the magnitude of the underlying inflammatory response. Aged individuals with co-morbidities are most vulnerable and severely affected, but the mechanisms driving aberrant immune responses fueling SARS-CoV-2 immunopathology in this high-risk population are not fully elucidated. Given that reactivation of cytomegalovirus (CMV), a highly prevalent beta herpesvirus, underlies inflamm-aging and drives hyperinflammation in critically ill patients, we hypothesized that CMV reactivation following SARS-CoV-2 underlies immunopathology. To test this hypothesis, we utilized the rhesus macaque model of natural rhesus (Rh)CMV infection to investigate the extent of CMV reactivation following experimental SARS-CoV-2 infection. In order to assess CMV reactivation, eight aged, type 2 diabetic RhCMV-seropositive rhesus macaques (sera anti-CMV IgG: 300-1400 ng/ml) were infected with high-dose SARS-CoV-2 ($2.5x10^6$ PFU) and monitored for 7 days prior to euthanasia. Samples from the respiratory tract, intestinal tract, and blood were collected to assess viral and inflammatory dynamics in distinct tissue compartments. Following infection, SARS-CoV-2 replication was observed throughout the respiratory tract, which was associated with local and systemic inflammation and immune activation. Lung histopathological assessments revealed development of interstitial pneumonia with colocalization of SARS nucleocapsid protein within pneumocytes. RT-qPCR assays targeting RhCMV gB showed CMV DNA within the caudal lung lobe (up to 10^3 CMV DNA copies/mg of tissue). Additionally, increased RhCMV viral loads correlated with worsened clinical scoring. Strikingly, there was an increase in effector memory T-cell populations at day 3 that dissipated prior to SARS-CoV-2 viral clearance, suggesting a memory response to a preexisting pathogen such as RhCMV. Additionally, we found RhCMV reactivation in the ileum, where high levels of ACE2 have been previously reported. These data suggest CMV reactivation in secondary SARS-CoV-2 target sites and require further investigation. However, absence of RhCMV in tissues such as the heart suggests SARS-CoV-2 cardiac events are independent of CMV. Our findings led us to hypothesize that reactivation of CMV in the lungs and other sites contributes to SARS-CoV-2 disease severity in high-risk individuals. Delineating how CMV reactivation drives immune activation following SARS-CoV-2 infection may provide deeper insights into mechanisms underlying COVID severity in populations most vulnerable to the hyperinflammatory manifestations of SARS-CoV-2.

13. Identification of novel genes that regulate B-1 cells

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IgM is the first antibody produced in ontogeny and in response to an initial antigen exposure. It plays an important role in effective immune protection, and is required for maximal antigen-specific IgG responses. In mice, most circulating serum IgM is generated by fetal-derived B-1 cells in spleen and bone marrow. How B-1 cells preferentially develop into natural IgM secreting cells is incompletely understood. To identify candidate genes critical for B-1 cells development and/or maintenance we generated parts of a larger immunophenotyping database Knock Out Mouse Project (KOMP) providing results of the flow cytometric evaluation of spleen cells from 641 mouse strains, each containing a single-gene deletion as well as 200 individual congenic control mice, identifying 58 distinct leukocyte subsets for each spleen. We generated and curated a complete list of each gene found to be associated with B-1 cell changes. Seven genes were identified that significantly reduced frequencies of CD5+ B-1 cells in males and/or females, of which three were uniquely altering the B-1 cell subset. None of these genes have been associated with B-1 cell regulation previously. Using qRT-PCR we found that 4 showed B-1 cell intrinsic gene expression. Ongoing work is to determine the impact of each gene on serum antibody levels and immune protection to influenza virus challenge. This work was supported by NIH UM1 OD023221 (KCKL), R0AI148652 (NB), and the Graduate Student Support Program UC Davis (SR).

14. Antibiotic Treatment During Infancy Alters the Gut Microbiome and Metabolites in Conjunction with The Lung Transcriptome

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Antibiotics are frequently used to treat infants for respiratory infections but may be problematic long-term due to effects on the microbiome. To interrogate the impact of early-life antibiotics on the gut-lung axis in infant monkeys, we hypothesized that the metabolism of the gut microbiome is linked to the transcriptome of the developing lung. Newborns received a daily dose of a broad-spectrum antibiotic cocktail consisting of ampicillin, gentamicin, and vancomycin (targeting gram-positive and negative bacteria) for 7 days during the first week of life; control animals received saline. Microbial DNA was extracted from rectal swabs collected at 6 months of age. 16S rRNA sequencing was conducted on V3-V4 amplicons. Reads were analyzed using Picrust2 and untargeted metabolomics. The lung transcriptome was evaluated via bulk RNAseq on right cranial lobes collected during necropsy at 6 months of age. Gut microbiome analysis using Picrust2 showed antibiotic-treated animals had significantly increased numbers of pathways that convert pyruvate to propionate and butyrate intermediates propanoate and butanoate. In contrast, control animals showed an increase in the Pyruvate Fermentation to Acetate pathway. When considering sex, we found that antibiotic-treated males had a reduction in the Mixed Acid Fermentation pathway relative to antibiotic-treated females. 15 of the 86 GPRs detected by RNA-seq analysis of the lung had known ligands present in the gut microbiome. In addition, antibiotic-treated males showed dysregulation of lung GPR expression for P2RY14, SUCNR1, GPR174, and LPAR5 relative to controls. Preliminary metabolomics analysis revealed a trend toward reduced abundance of medium-chained fatty acids in antibiotic-treated males. Antibiotic-treated infant monkeys showed significant differences in pathways known to produce short-chain fatty acids. The presence of GPRs in the lung that can respond to microbial metabolites suggests a potential mechanism by which alterations in the gut microbiome following early-life antibiotic treatment may influence normal lung development. (Funding: NIH R01AI138553, NIH P51OD011107)

15. Investigating the mechanism by which CBL restricts antiviral responses

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Mycobacterium tuberculosis (*Mtb*) is a facultative intracellular bacterium that enters the host through inhalation and is taken up by macrophages through phagocytosis. After phagocytosis, *Mtb* inhibits phagosome maturation and permeabilizes the vacuole introducing secreted factors and nucleic acids to the cytoplasm of the host to modulate immune functions. Recently published work from our lab demonstrated LpqN as a novel virulence factor whose absence resulted in an attenuated *Mtb* mutant strain that failed to successfully replicate *in vivo* and *ex vivo*. By examining the host factors that interacted with LpqN, we determined that the growth of the attenuated Δ*lpqN* mutant was rescued in the absence of the host E3 ubiquitin ligase, CBL, signifying the potential importance of CBL for antibacterial responses. Moreover, our lab discovered that Cbl-/- BMDMs infect with Mtb displayed a hyperactive antiviral phenotype as indicated by increased antiviral mediators. Thus, while macrophages that lacked CBL were more permissive for *Mtb* growth, paradoxically they were more resistant to viral infections. This suggested that CBL acts as a negative regulator of antiviral responses. To further elucidate CBL's role in antiviral response we generated CBL knockdown in human monocyte cell lines, THP-1, and HL60, using short hairpin RNA. These knockdown cell lines were stimulated with either viral mimetics or *Mtb*. Antiviral response was quantified by measuring mRNA levels of IFNβ and IFIT1 through qRT-PCR. A two/three-fold increase in IFNβ/IFIT-1 was detected in the CBL deficient macrophages compared to wildtype, suggesting CBL restricts antiviral response in human macrophages as well. Additionally, we infected CBL-deficient human macrophages with Δ*lpqN* strain expressing a Lux operon, allowing us to measure *Mtb* replication through bioluminescence. Our assay demonstrated a significant increase in bacteria growth in CBL deficient macrophages compared to wildtype, suggesting an important role for CBL in inhibiting *Mtb* replication. Finally, to determine the mechanism CBL utilizes to repress antiviral response, we generated catalytically inactive CBL-deficient THP-1 cells to address the necessity of ubiquitination in our model and determined that ligase function is necessary to restrict *Mtb* growth. (NIAID 5R01AI144149-04).

16. Sex-Dependent Effects of Neonatal Antibiotic Treatment on Pulmonary Immunity-Related Gene Expression

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Antibiotics are commonly administered to infants to treat respiratory tract infections but can disrupt the developing microbiota. Since the microbiota can influence pulmonary immune responses, we hypothesized that antibiotic treatment during infancy can alter immune-related pulmonary gene expression. To test our hypothesis, we conducted bulk RNA-seq on lung tissue from infant rhesus macaques to determine antibiotic treatment-associated changes in the lung transcriptome. Indoor-housed infants received a daily administration of an antibiotic cocktail consisting of ampicillin, gentamicin, and vancomycin during the first week of life, while controls received saline. Animals were sacrificed for tissue collection at 6 months of age. Bulk RNA-seq assessed differential gene expression in lung tissue (n=4 per group, 2 males and 2 females each), and KEGG pathway and Gene Ontology (GO) analysis determined pathway enrichment. qRT-PCR confirmed differential gene expression. The lung transcriptome of antibiotic-treated and control animals showed differences in immune-related pathways, including increased enrichment for GO pathways B cell differentiation (2.11-fold-enrichment (FE)) and activation (1.84 FE) in antibiotic-treated animals compared to controls. When stratified by the sex, GO analysis showed that control females had higher enrichment for immune-related processes such as antigen processing and presentation (2.37 FE) and negative regulation of viral process (2.16 FE) compared to antibiotic-treated females. Compared to control males, antibiotic-treated males had greater enrichment for regulation of interferon-beta production (2.4 FE) and regulation of viral genome replication (2.14 FE). Via qRT-PCR, *ADAMDEC1*, a metalloproteinase predominantly expressed by macrophages, was significantly more highly expressed in control males compared to antibiotic-treated males, with no difference between female groups. In summary, we found sex-dependent enrichment of immune-related pathways in the lungs of antibiotic-treated and control animals. This demonstrates that while dysbiosis can affect the pulmonary immune responses, it is crucial to consider that sex may influence the effects of the microbiota on immunity. (Funding**:** T32 HL007013, NIH R01AI138553, NIH P51OD011107).

III. Immune Regulation

17. Revisiting the Network Hypothesis: Development of anti-idiotype antibodies to ACE2 following SARS-CoV-2 mRNA vaccination in mice

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The SARS-CoV-2 pandemic necessitated expedited development of vaccines, which were given to the general population after clinical trials. Preclinical modeling of these novel mRNA vaccines has lagged behind, which has been detrimental in assessing adverse reactions. One aspect of antibody formation and regulation involves generating anti-idiotypic antibodies, as originally postulated by Neils Jerne in the "Network Hypothesis." VDJ rearrangement produces new proteins that can be potentially immunogeneic, generating antibody responses directed toward the paratopes. These anti-idiotype antibodies can then bind the original antibodies and facilitate their clearance. Some of these anti-idiotype antibodies, by virtue of binding the paratope region, could act as a "mirror" capable of binding the original antigen's target. The antigen used in CoV2 vaccines is capable of binding ACE2, and some of the paratopes of antibodies induced to the Spike protein could potentially target ACE2. As vaccinations trigger more robust immune responses with each boost, it is possible that these anti-idiotype antibodies could also be amplified. We therefore wanted to determine if anti-idiotype responses capable of binding ACE2 could result after repeat vaccination. Using wild type and K18 human ACE2 transgenic mice, we demonstrated that repeated Moderna vaccination, which followed the vaccination schedule of humans, produced a stronger anti-spike antibody response with each boost. This also coincided with the presence of anti-idiotype antibodies capable of binding ACE2, which were similarly elevated with each boost. Strikingly, K18 mice that were repeatedly vaccinated had an observable defect in clot time when blood was drawn, which did not occur in wild type mice, indicating the presence of human ACE2 could be a catalyst for thrombocytopenic events with repeated vaccination. This is particularly pertinent given the thrombolytic defects observed in some CoV2 infections. These results indicate that preclinical assessment of the immune pathways involved in CoV2 infection and vaccination are warranted. (Funding: R01 HL140921).

18. Identifying regulators of antibody secretion

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Alternative polyadenylation (APA) is a type of post-transcriptional regulation that occurs throughout development and cellular differentiation to create multiple isoforms from one gene. Over 70% of mammalian genes are regulated by APA, but the regulatory mechanisms and relevance in different cellular contexts is not fully understood. An attractive model system to gain insight into this process is immunoglobulin (Ig) expression. B cells can synthesize either a secretory or membrane Ig heavy chain (IgH) from the same transcript through competing alternative splicing and APA. B cells predominantly produce the isoform encoding membrane IgH, but during plasma cell (PC) differentiation switch to utilizing the proximal poly (A) site of the primary IgH transcript. This generates a shorter isoform encoding secretory IgH, also known as antibody. Although the differential expression of these isoforms has been known for over 40 years, the exact molecular switch that directs cell stage-specific APA of the IgH transcript in PCs remains enigmatic. To identify regulators of this process, we will perform a genome-wide knock-out CRISPR library screen in Cas9-expressinging primary B cells. Utilizing a novel, fluorescently labeled probe that hybridizes to the secretory IgM transcript as our readout, we will identify "hits" that positively or negatively impact APA at the IgH locus. After validation, screen "hits" will be further investigated for potential regulation of global APA in PCs through 3'-end RNA-sequencing. Through this screen we hope to better understand the mechanisms regulating antibody secretion in PCs, a process critical for neutralizing pathogens yet detrimental in autoimmune diseases, and gain insight into the global regulation of APA. (Funding: NIAID R01AI170840-01)

19. Osteosarcoma tumorigenesis is affected by microenvironmental and immune factors in 3D engineered bone marrow model

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Osteosarcoma (OS) is the most common primary malignant bone cancer in children and adolescents, yet treatment has remained unchanged for 4 decades and offers less than a 25% 5-year survival rate for those with metastatic disease. This underscores a critical lack of understanding of OS progression and necessitates the study of this disease in a novel system. Here, we adapt a previously described engineered bone marrow (eBM) construct for use as an *in vitro* model and describe OS loading studies to demonstrate that these constructs provide a novel platform to study the microenvironmental and immune factors in tumor progression. eBM is formed by implanting acellular bone-inducing constructs in C57BL/6 mice. After 8 weeks, constructs are harvested and used *in vitro*. Homotypic cultures of highly metastatic K7M2 and less metastatic K12 OS cell lines, as well as pre-osteoblastic MC3T3 cells as a control, were loaded into the eBM. eBM was also loaded with heterotypic cultures comprised of each cell line and IC-21 macrophages at an 85:15 ratio and cultured under 21% and 5% O_2. Flow cytometry for OS cell number and macrophage polarization revealed that both K7M2s and K12s under heterotypic culture exhibited significantly decreased cell number only under 21% O_2. However, M1 and M2 macrophage behavior were not consistent between K7M2s and K12s despite total macrophage numbers remaining constant, suggesting that the inflammatory status of the immune microenvironment does not dictate OS behavior as previous studies often conclude. The eBM in this project mimics the complex environment in which OS arises, thereby surpassing other *in vitro* models that fail to account for these key parameters. The effective use of this model will advance the treatment of patients afflicted by OS.
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20. Tet1 Regulates Diesel Exhaust Particle (DEP)- Induced Th17 Immune Response

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Environmental exposures, including air pollution, are known to increase the risk of asthma susceptibility and severity via epigenetic regulation. However, the molecular mechanism(s) directly involved in air pollution-induced asthma is not fully understood. Previous studies have shown that exposure to diesel exhaust particles (DEP), a major component in traffic-related air pollution, can promote airway inflammation and oxidative stress, as well as exacerbate lung function impairment and disease severity in both asthma patients and asthmatic animal models. In particular, a Th17 immune response resulting from DEP exposure increases the risk of severe and persistent asthma. We have previously shown that Tet1 (Tet Methylcytosine Dioxygenase 1) protected against house dust mite (HDM)-induced lung inflammation, possibly through upregulation of detoxication enzymes and downregulation of proinflammatory cytokines. Therefore, we sought to examine the role of Tet1 in DEP-induced lung inflammation in mice. In this study, we used $Tet1^{+/-}$ mice (HET) and their wildtype littermates ($Tet1^{+/+}$, WT) in a DEP-induced lung inflammation model, in which the mice were intratracheally challenged with saline or DEP (150μg×9 times) over a period of 3 weeks. We found that Tet1 deficiency increased airway hyperresponsiveness (AHR) and demonstrated a trend of increased total immune cell counts, including neutrophils, in bronchial alveolar lavage fluid (BALF). Consistently, an increase in chemokines associated with neutrophil infiltration, CXCL5 and CXCL15, was observed in the BALF of HET mice compared to WT when exposed to DEP. The mRNA expression levels of *Il17a* and *Il17f* in the lungs were also significantly increased, suggesting an increased Th17 response. Altogether, our findings indicate that Tet1 deficiency significantly enhances DEP-induced lung inflammation in mice, which may be due to the upregulation of a Th17 response. Further studies will be performed to explore the underlying mechanisms involved in this protective role of Tet1 against DEP-induced lung inflammation.
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21. The impact of mesenchymal transition and macrophage phenotype switching in immunotherapy-resistant melanoma

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Anti-PD-1 refractory melanoma remains a devastating clinical challenge. We have previously defined AXL tyrosine kinase is an emerging target of interest implicated in epithelial to mesenchymal type transition (EMT), tumor associated macrophage behavior, and immunotherapeutic resistance. Here, we aim to define the mechanisms by which AXL mediates tumor-immune crosstalk and the role of AXL inhibition strategies in mitigating resistance to modern immunotherapy. For preclinical studies, YUMM1.7 (anti-PD-1 resistant) melanoma cells were used for in vitro proliferative and migratory assays. RAW macrophages were treated with GAS6 stimulation, GM-CSF stimulation, GAS6 inhibitor: warfarin, or AXL TK small molecule inhibitor bemcetinib. In vivo, subcutaneous tumors were treated with multiple AXL inhibition strategies as single agent or in combination with Invivomab (Anti-PD-1). For clinical studies, blood obtained from melanoma patients and evaluated for serum levels of sAXL by ELISA and TCGA-SKCM melanoma tumor mRNA expression and clinical data for metastatic melanoma patients were downloaded from the GDC legacy archive (https://portal.gdc.cancer.gov/legacy-archive) (n = 471). Differences in Kaplan-Meier survival curves based on level of expression were tested using G-rho family tests. Strength of relationships between biomarkers were measured using Pearson's correlation. All statistical analysis were performed using R package "survival".g. Serum detectable sAXL significantly increased by stage with highest levels noted in stage IV patients ($p=0.03$). AXL high expression was associated with PD-1 nonresponse in Stage IV patients ($p<0.01$). AXL expression diverged from T-cell related signatures but was associated with increase in immunosuppressive myeloid signatures ($p<0.001$). In vitro, Melanoma cell migration was significantly increased with exogenous Gas6 exposure and this effect was inhibited by warfarin ($P<0.05$). GAS6 sand GM-CSF stimulation increased macrophage proliferation however only GAS6 increased M2 expression markers of AXL and Arginase ($p<0.05$). Low dose warfarin or bemcitinib reduced Arginase expression in RAW macrophages, shifting toward anti-tumor M1 phenotype ($p<0.05$). In vivo, YUMM1.7 tumor growth was significantly inhibited by single agent warfarin, bemcetinib, or cabozantinib (RET/VEGFR2/cMET/AXL inhibitor). Tumor size was not significantly inhibited by single agent Invivomab, in line with known immunotherapeutic resistance. Combination with either warfarin, bemcetinib, or Cabozantanib significantly reduced tumor growth ($p<0.02$). Our data indicate myeloid specific immunosuppressive effects of AXL activity in the tumor microenvironment are a viable target in PD-1 refractory melanoma. Analysis is ongoing to elucidate impact of AXL driven EMT on macrophage function in multiple preclinical models of melanoma. Investigation of specific mechanisms by which AXL directed therapy may improve immunotherapeutic response is warranted. (Funding: 5K12-CA138464)

22. Inhibitory Receptor TIGIT is a critical regulator of Natural Killer Cell Maturation and Survival Following Bone Marrow Transplantation

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TIGIT has emerged as a critical regulator of phenotype and function in mouse and human NK cells with key studies showing TIGIT upregulation suppresses NK anti-tumor responses. However, the role of TIGIT in NK cell reconstitution and maturation following bone marrow transplantation (BMT) has not yet been elucidated. BMT is an important procedure whereby donor hematopoietic stem cells are transferred to a patient, after chemotherapy, to treat genetic diseases and malignancy, and NK cells have been shown to be critical mediators of immune reconstitution following BMT. We hypothesize that TIGIT regulates NK reconstitution following BMT, balancing decreased NK activation with enhanced survival and allows TIGIT expressing NK cells to reconstitute following BMT more quickly than NK cells lacking TIGIT. We therefore performed syngeneic BMT in B6 mice using donor bone marrow from wild type (WT) and TIGIT knockout (TKO) mice. NK cell numbers on days 7, 14 and 21 post BMT were similar between WT and TKO mice in the spleen and bone marrow (BM). However, the NK cells from WT mice expressed significantly more KLRG1 and Ly49G2, markers that correlate with more NK maturation, on days 14 and 21, indicating that NK cells expressing TIGIT could mature more rapidly. Furthermore, on day 14, splenocytes from TKOs demonstrated significantly lower cytotoxicity against YAC-1 targets, a mouse lymphoma cell line, than their WT counterparts, although these differences normalized by day 21. Reconstituting NK cells from TKO mice also displayed significantly greater apoptosis on days 14 and 21 when compared to WT controls. Overall, our results indicate that TIGIT appears to play an important role in regulating NK cell responses following BMT, suggesting that TIGIT blocking strategies immediately following BMT could increase NK apoptosis and delay the maturation of NK cells with potential adverse effects on anti-tumor responses. (Funding: T2021-016).

23. N-Glycans and Immunomodulation of Recombinant Bovine Lactoferrin

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Bovine lactoferrin (Lf), an immunomodulatory milk glycoprotein, has been approved for infant formula supplementation to confer functions that are critical for immune development: antimicrobial and anti-inflammatory activity, iron regulation, microbiome development, and barrier defense. About 55% of infants in the US rely on infant formula to supplement nutrition in the first 3 months of life (CDC National Immunization Survey 2020-2021). Yet, most infant formulas are not supplemented with lactoferrin, in part because isolation from cow's milk has significant drawbacks for production scaling. Precision fermentation offers a way to generate recombinant bovine lactoferrin from microbial hosts without the use of cows. A major challenge of precision fermentation is replicating the native glycan profile of mammalian proteins in microbial hosts which may have functional consequences on immune signaling through lectin and toll-like receptors. We hypothesized that recombinant bovine lactoferrin (rbLf) generated via precision fermentation would have a different N-glycan profile compared to cow milk-derived lactoferrin (cMDLf). In collaboration with Lebrilla Lab at UC Davis, we confirmed rbLf has a different N-glycan profile characterized by increased abundance of high-mannose type glycans. There is limited knowledge on the precise role of N-glycans in lactoferrin functionality and immunomodulation, leaving a gap in knowledge on how non-native N-glycans will impact rbLf antimicrobial activity and immune regulation. To compare rbLf and cMDLf function, we performed an *in vitro* assessment of Lf:LPS binding followed by an *ex vivo* activation assay utilizing alveolar macrophages co-cultured with bLf and LPS. Preliminary data provides evidence that rbLf and cMDLf interact with LPS at similar binding efficiencies. Although macrophages contain high-mannose receptors (CD209, CD206) that can be engaged by high-mannose glycans, neither rbLf nor cMDLf induced inflammatory activation after 24 hours co-culture with PAMs. In the future, we aim to expand immunological readouts to characterize microbiome development and intestinal barrier defense. (Funding: TurtleTree, Ji Lab: Hatch/Mutltistate CA-D-NTR-2428-RR)

24. Pre-clinical evaluation and first-in-dog clinical trial of intravenous infusion of PBMC-expanded adoptive NK cell therapy in dogs with cancer

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Natural killer (NK) cells are cytotoxic immune cells capable of recognizing heterogeneous cancer targets without prior sensitization, making them promising prospects for use in cellular immunotherapy. Previously, CD5 depletion of peripheral blood mononuclear cells (PBMCs) has been used in dogs to isolate and expand a $CD5^{dim}$-expressing NK subset prior to co-culture with an irradiated feeder line, but this can limit the yield of the final NK product. This study aimed to assess NK activation, expansion, and preliminary clinical activity in a first-in-dog clinical trial using unmanipulated PBMCs without CD5 depletion to generate our NK cell product. Starting populations of CD5-depleted cells and PBMCs were co-cultured with irradiated K562-C9-mIL21 cells and 100IU/mL rhIL-2 for 14 days. Phenotype and cytokine secretion were measured, and samples were sequenced using the 3'-Tag-RNA-Seq protocol for gene profiling. In addition, a first-in-dog feasibility clinical trial was performed in dogs with melanoma (N=5) using allogeneic NK cells, expanded from unmanipulated PBMCs. Flow analysis showed similar upregulation of NKp46 in both groups post-expansion. Median production of canonical NK cytokines, IFN-y and GM-CSF, at day 14 was over 5-fold greater in PBMC-expanded compared to CD5-depleted NK cells. Sequencing data showed principal component sample variance based on dog donor and upregulation of NK pathways related to activation and function in both groups. PBMC-expanded allogeneic NK cells led to no serious adverse events and demonstrated preliminary data for efficacy, with one dog surviving 445 days post-treatment. Peripheral blood gene expression significantly changed from pre-treatment and post-transfer across all patients. Overall, the use of unmanipulated PBMCs appears safe and potentially effective for canine NK immunotherapy with equivalent or superior results to CD5 depletion in NK expansion, activation, and cytotoxicity. Our pre-clinical and clinical data support further evaluation of this technique as a novel platform for optimizing NK immunotherapy in dogs. (Funding: National Institutes of Health/National Cancer Institute grant U01 CA224166-01, the 3U01CA224166-02S1 and 5R03CA252793-02 grants, and the V Foundation Victory over Cancer through the Canter Laboratory. Student support was provided by the AVMA/AVMF 2nd Opportunity Summer Research Scholarship.)

25. Understanding B cell subpopulations in Tumor microenvironment

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B cells are multifunctional lymphocytes that play important roles in immune defense. There is increasing evidence showing correlation of B cell infiltration and favorable prognosis in certain tumor indications. Yet, knowledge about B cell subpopulations and their functions associated with the survival significance is still incomplete. In this study, we aim to investigate the phenotypic profile of B cells in lung adenocarcinoma (LUAD) where high B cell infiltration correlates with favorable survival significance. We identify a subset of memory B cells that are specifically enriched in the tumor and not in normal adjacent tissues or peripheral blood. This tumor infiltrating memory B cell subset readily differentiates into plasma blasts/plasma cells upon receiving BCR stimuli with CD40 stimulation. Functional significance of this Tbet hi memory B cell subset in anti-tumor immunity will be investigated in future studies. (Bristol Myers Squibb)

26. Variability of vaccine response during wildfire smoke exposure is associated with altered Natural Killer (NK) cell activation and Surfactant Protein D release

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The effects of environmental exposures such as wildfire smoke, on the role of innate immune cells during a vaccine response are poorly understood. Natural Killer (NK) cells are critical in early stages of the immune response, and can produce large amounts of proinflammatory cytokines in response to environmental exposures. We hypothesized that NK cell phenotype changes in response to wildfire smoke inhalation and that such changes have a predictive value to determine long term vaccine response to SARS-COV-2. We investigated how BNT162b2 vaccination during wildfire smoke exposure affects innate immune populations in the blood, and whether this impacts subsequent production of protective antibodies against SARS-CoV-2. 52 age- and sex-matched healthy subjects (26-82 years old) recruited from the Sacramento region were divided into vaccine (n=28) and placebo (n=24) groups. Subjects in the vaccine group received BNT162b2 during heavy wildfire exposures while placebo subjects received the same vaccination later during clean air conditions. Peripheral blood was collected before, and over multiple timepoints post vaccination. Cells were stained using a focused flow cytometry panel and multicolor assessment was performed by FACS data analyzed on FlowJo. Antibodies against spike (S) and Nucleocapsid (N) proteins of SARS-CoV-2 were also measured using a quantitative multiplex test. At 6 months after vaccination during clean air conditions, we found increased CD56bright/CD56dim NK cell ratio ($p=0.02$), and IL-13+ CD56bright NK cell numbers in circulation ($p=0.0002$) unlike the wildfire smoke exposed group where we observed decreased IL-13+ CD56bright NK cells and significant leakage of Surfactant Protein D concentrations from the lung into the circulation ($p<0.001$). At 6 months post- vaccination, production of anti-SARS-CoV-2 antibody declined for all subjects irrespective of smoke exposure, with a high degree of variability we do not understand. We propose that wildfire smoke inhalation sequesters activated, pro-inflammatory NK cells to the lung, interfering with vaccine response. (Funding: NIEHS T32 ES007059)

27. Asymmetrical Expression of the Inhibitory Receptor PD1 and the Activation Receptor CD25 in T-cells Post-Activation

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After TCR engagement, T cells induce expression of both CD25, which forms the IL2 high affinity receptor complex promoting activation and proliferation, and PD1, which can down-regulate activation. Cessation of TCR stimulation leads to eventual contraction of T cell responses. Chimeric antigen receptor (CAR) T cell therapy has seen increased use in the past decade. CAR T-cells are activated and transduced *ex vivo* and expanded with low amounts of cytokines prior to administration. The expression of CD25 and PD1 on CAR T cells at different stages of the process has been incompletely characterized. Purified T cells were activated *in vitro* for 3 days followed by expansion using low dose IL2. We demonstrate that both CD25 and PD-1 are strongly upregulated during initial activation, but by day 8, under expansion conditions, PD1 is downregulated to negligible levels. Despite the absence of TCR signaling, CD25 expression remains moderate-to-high explaining the ability to maintain proliferation. This discrepancy was higher in transduced CAR T-cells compared to activated non-transduced (NT) T cells indicating the possibility of tonic signaling via CAR. Furthermore, restimulation of both NT and CAR-T cells after this expansion phase resulted in further increased CD25 expression whereas PD-1 expression remained low. Our studies suggest that during initial activation, TCR engagement is necessary to maintain PD-1, but not CD25 expression. However, upon restimulation, TCR engagement is capable of further upregulating CD25, but not PD-1 expression. These results indicate that TCR signaling induces asymmetrical expression of PD-1 and CD25, a dynamic interplay that may regulate T-cell function and memory response, and that PD1 may not be a limiting factor in the process.

28. Investigating Unknown Plasma Cell Differentiation Checkpoints Using A Novel IRF4 Haploinsufficient Mouse Model

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High expression of the IRF4 transcription factor (TF) is required for upregulation of the Blimp-1 TF to commit an activated B cell toward the plasma cell (PC) fate. Our lab has shown in B cell-specific IRF4 haploinsufficient mice, not only is PC quantity expectedly diminished, but surprisingly, PC *quality* was impaired as well. Preliminary data has shown that $IRF4^{+/-}$ PCs display only partial repression of B cell lineage markers (B220, CD22, CD19), reduced upregulation of a set of PC markers (Ly6c, CXCR4), and importantly, reduced antibody secretion, suggesting both phenotypic and functional impairment. These cells do not exhibit ectopic expression of known negative regulators of PC differentiation. Although these cells display the hallmarks of a functional PC, they fail to develop into functionally complete PCs, suggesting there exists unknown genetic barriers to full PC development. We propose to use the IRF4 haploinsufficient model as a novel tool to investigate unknown genetic PC checkpoints. *We hypothesize that dynamic accumulation of IRF4 fine-tunes the expression of agonistic and antagonistic PC regulators to dictate full PC differentiation and activity*. We will collect genome-wide measurements of gene expression pattern, chromatin accessibilities, and IRF4 binding of wildtype and $IRF4^{+/-}$ PCs using RNA-sequencing, ATAC-sequencing, and ChIP-sequencing technologies. We will then integrate these datasets to establish a whole genome landscape of IRF4 activity and investigate differential patterns identified between wildtype and $IRF4^{+/-}$ PCs. Integration of these datasets will allow us to investigate direct and indirect IRF4 regulation, and possibly identify yet-unknown PC regulators. The goal of this study is to illuminate a more extensive gene regulatory network of PC differentiation and to identify yet-unknown checkpoint barriers to PC differentiation. (NIAID R01AI170840-01).

IV. Neuroimmunology

29. a4 integrin+ CCR5+ CD4 T cells mediate acute SIV CNS seeding in Rhesus Macaques

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CCR5+ CD4 T cells survey the CNS during homeostasis and the majority of their counterparts in circulation express the integrin α4 receptor, important for CNS entry. These data implicate CCR5+ α4+ cells in CNS viral seeding during HIV infection. To determine whether blocking α4 reduces early CNS viral seeding, we treated rhesus macaques with anti-Rh-α4 (25mg/kg, n=4) or IgG (n=4) before and during SIV infection. Rh-α4 resulted in complete receptor coverage leading to profound lymphocytosis prior to and during acute SIVmac251 infection (3-fold; $p<0.05$). Within the CSF, a trend for elevated lymphocyte counts was noted with a surprising increase in frequencies of CCR5+ CD4 T cells prior to infection. Following infection, CSF CD4+ CCR5 frequencies increased in all Rh-α4-treated animals, while only two IgG treated animals displayed a similar trend. Based on a negative correlation between CSF vRNA and CCR5+ CD4 T cells in a previous study ($r = 0.5$, $p< 0.01$), we predicted that increased CCR5+ CD4 T cells at week 1 post SIV was consequent to decreased CNS viral seeding in Rh-α4 treated animals. Consistently, Rh-α4 resulted in significantly lower CSF viral loads at week 1 (median vRNA (copies/ml CSF): Rh-α4, 305; IgG, 12,650). Thus, CCR5+ α4+ CD4 T cells mediate early viral seeding within the CNS. Ongoing studies assessing whether Rh-α4 treatment decreases viral seeding and attenuates SIV induced microglial and T cell activation within the brain parenchyma will provide insights into the role of CD4 T cells in acute CNS viral seeding and subsequent neuroinflammation. [Funding: K01OD023034, R03AI138792 (SSI), RF1 RF1AG061001, P51OD011107-57S1 (SSI, JHM), AMID T32 (SE)]

30. Neuroinflammatory transcriptional programs induced in rhesus macaque brain tissues during acute SIV infection.

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Immunosurveillance of the central nervous system (CNS) is vital to resolve infection and injury. However, immune activation within the CNS in the setting of chronic viral infections, such as HIV-1, is strongly linked to progressive neurodegeneration and cognitive decline. Early establishment of HIV-1 in the CNS following infection underscores the need to delineate features of acute CNS immune activation as these early inflammatory events may mediate neurodegenerative processes. Here, we focused on elucidating molecular programs of neuroinflammation in brain regions commonly implicated in HIV CNS disease. To this end, we assessed transcriptional profiles within the subcortical white matter of the pre-frontal cortex (PFCw), as well as synapse dense regions of the hippocampus, superior temporal sulcus (STS), and caudate nucleus in rhesus macaques during acute SIV infection using both bulk tissue and single cell (sc) RNA sequencing (RNA-seq) methods. Bulk tissue RNA-seq showed that SIV-induced transcriptional alterations were concentrated to the PFCw (871 differentially expressed genes [DEGs]) and STS (884 DEGs) ($p<0.01$) with upregulation of gene expression pathways controlling innate and T cell inflammatory responses at 28 days post-infection. Furthermore, enrichment of pathways regulating mitochondrial respiratory capacity, synapse assembly, and oxidative and endoplasmic reticulum stress were observed. In corroboration of observed T cell inflammatory signatures, scRNA-seq analysis of $CD45^+$ cells isolated from rhesus brain tissues identified T cell transcriptional signatures (CD3D, CD3E, and CD3G) at 21 days post-SIV infection. These acute neuroinflammatory features were substantiated by increased influx of activated T cells into the CNS based on flow cytometric analyses. Overall, our data show perturbations of important immune, neuronal, and synaptic pathways within key anatomic regions controlling cognition and motor function during acute SIV infection and provide a valuable framework to understand early molecular features of HIV associated neurodegeneration. [Funding: K01OD023034, R03AI138792 (SSI), RF1 RF1AG061001, P51OD011107-57S1 (SSI, JHM), AMID T32AI060555 (SRE), Floyd and Mary Schwall Medical Research Fellowship (CH)]

31. Maternal Immune Activation during Gestation Leads to Immune System Imprinting in Offspring

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Activation of the maternal immune system during pregnancy is an environmental risk factor for a plethora of neurodevelopmental disorders such as autism spectrum disorder and schizophrenia. To date, studies have found that maternal immune activation (MIA) induces neuropathological and behavioral abnormalities in adult offspring. Little is known about the impact MIA has on the development and function of the offspring's immune system. To assess the impact of maternal immune perturbation on offspring immune function and response, we performed a longitudinal study of MIA in the nonhuman primate model via polyinosinic:polycytidilic acid (PolyICLC). Specifically, twenty-four pregnant rhesus macaques were given three injections of PolyICLC (a viral mimic) or saline between gestational days 43-46. To confirm MIA, cytokine and chemokine levels in plasma isolated from dam peripheral blood obtained 6-hours post final PolyICLC injection were measure by Luminex. The offspring were then surveyed from birth with blood collected at postnatal day (PND) 30, PND 90, PND 180, 1yr, 2yr, 2,5yr, 3yr, 3.5yr, and 4yr. Similarly, plasma from these timepoints was used to measure cytokine and chemokine expression. Moreover, offspring cognition and behavior was investigated for future correlation analyses. PolyICLC injection during early gestation altered maternal cytokine profiles with increased expression of antiviral cytokines such as IFN-γ, IL-12/23, IL-15, and IL-18 as well as cytokines associated with anti-inflammatory , T cell and T_H2 responses in the MIA dams compared to saline controls. Further, longitudinal analysis of MIA offspring profiles revealed persistent changes in the expression of various cytokines and chemokines associated with innate and adaptive immune responses as compared to saline offspring. Taken together, our data show MIA during early gestation not only alters dam immune profiles but has a long-term impact on the offspring's immune profile and subsequent responses, further substantiating the presence of a direct link between maternal immune perturbation during gestation and immune system imprinting in offspring. (Funding: P50MH106438)

32. Sex-specific neonatal immune signatures in neurodevelopmental disorders

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Immune dysregulation, including aberrant peripheral cytokine/chemokine levels, is implicated in neurodevelopmental disorders (NDD) such as autism spectrum disorder (ASD). While the diagnosis of ASD is more common in males compared to females, sex effects in immune dysregulation related to neurodevelopment remain understudied. The aim of this exploratory study was to determine whether there are sex-specific effects in neonatal immune dysregulation with respect to an ASD or delayed development (DD) diagnosis. We utilized the data from the Early Markers for Autism study, a population-based case-control study of prenatal and neonatal biomarkers of ASD. The immune profile of newborns later diagnosed with ASD (n= 482, 91 girls), DD (n= 140, 61 girls) and sex-matched general population controls (GP; n= 378, 67 girls) were analyzed using neonatal bloodspots (NBS) via 42-plex multiplex assay. Multiple linear regression analysis was performed to identify whether sex was associated with differences in cytokine/chemokine levels of children with ASD, DD, and GP. A sex by diagnosis interaction effect was observed only for the chemokine macrophage migration inhibitory factor (MIF), with males displaying higher levels of NBS MIF than females in the GP control group ($p= 0.02$), but not in ASD ($p= 0.52$) or DD ($p= 0.29$) groups. We found that regardless of child diagnosis, newborn blood spot eluates from females had a significantly higher concentration of granulocyte chemotactic protein 2 (GCP-2; $p< 0.0001$), macrophage inflammatory protein 2-alpha (GROβ; $p= 0.002$), interferon-inducible t-cell alpha chemoattractant (I-TAC; $p< 0.0001$), stromal cell-derived factor 1 alpha and beta (SDF-1α-β; $p= 0.03$), interferon-gamma induced protein 10 (IP-10; $p= 0.02$), macrophage inflammatory protein 1-alpha (MIP-1α; $p= 0.02$), , and interleukin-12 active heterodimer (IL-12p70; $p= 0.002$) than males with the same diagnosis. In contrast, males had a higher concentration of secondary lymphoid-tissue chemokine (6CKINE; $p= 0.02$), monocyte chemotactic protein 1 (MCP-1; $p= 0.005$) and myeloid progenitor inhibitory factor 1 (MPIF-1; $p= 0.03$) than females. Similar sex effects were observed when analyses were restricted to NBS from ASD and DD goups, and diagnosis was further classified as ASD with intellectual disability (ID), ASD without ID, and DD (GCP-2, $p= 0.007$; I-TAC, $p= 0.001$; IP-10, $p= 0.005$; IL-12p70, $p= 0.03$ higher in females, MPIF-1, $p= 0.03$ higher in male). This study is the first to examine sex differences in cytokine/chemokine concentrations and whether these differences are associated with neurodevelopmental outcomes while highlighting the importance of considering sex as a critical factor in understanding the biology associated with development of an NDD. (Funding: National Institutes of Health through awards R01ES016669, P50HD103526, and P50MH106438)

33. Effects of Gestational Autoantibody Exposure on Early Postnatal Cytokines and Chemokines

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Maternal immune dysregulation during pregnancy can negatively impact offspring neurodevelopment and immune function. Immune signaling molecules, such as cytokines and chemokines, are essential for cell regulation, growth, and differentiation in the fetal and postnatal brain. In the maternal autoantibody related (MAR) subtype of autism spectrum disorder (ASD), mothers produce antibodies reactive to self-proteins found in the developing fetal brain, such as collapsin response mediator proteins 1 and 2 (CRMP1/2), stress-induced phosphoprotein 1 (STIP1), and lactate dehydrogenase A and B (LDHA/B). To address the effects of autoantibody exposure on offspring neuroimmune signaling molecules, we used our preclinical rat model in which dams were immunized with a mixture of adjuvant and LDHA/B+CRMP1+STIP1 or adjuvant only to induce endogenously produced specific autoantibodies in the absence of inflammation. Male and female pups from treated (n=15/sex) and control (n=15/sex) dams were euthanized at postnatal day two (PND2), and brains and sera samples were collected. A multiplex assay was used assess neonatal cytokine/chemokine levels in the brain and the periphery. Multiple regression analyses were performed to compare between pups from immunized dams and controls. Several proinflammatory cytokines, including interleukin (IL) 6 (IL-6, p=0.0004), interferon-gamma (IFN-γ, p=0.0193), IL-10 (p=0.0004) and IL-18 (p=0.0004) were significantly decreased in the brains of pups from treated dams compared to controls. Leptin (p=0.0006), tumor necrosis factor-α (TNFα, p=0.0137), and vascular endothelial growth factor (VEGF, p=0.001) were significantly decreased in the sera, while IL-1α (p=0.0206) was significantly increased in the sera of pups from treated dams versus controls. In both the sera and brain, RANTES (CCL5; brain, p=0.0004; sera, p=0.0154) was significantly decreased and epidermal growth factor (EGF; brain, p=0.0004; sera, p=0.0011) was significantly increased in pups from treated dams compared to pups from controls. These data suggest that persistent gestational exposure to specific maternal antibodies alters the levels of neonatal cytokines/chemokines in both brain and the periphery, which may play a role in ASD-like behaviors in offspring. (Funding: NICHD IDDRC P50HD103526)

34. Regulatory T cell Phenotypes in Autism Spectrum Disorder and Associations with Aberrant Behaviors

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder diagnosed in infancy and is characterized by social and communicative deficits and restrictive and repetitive behaviors. Immune abnormalities are frequently cited in children and adults with ASD, suggesting an issue with immune regulation. Regulatory T cells (Tregs) are essential for immune regulation and function by directly suppressing the activity of immune cells or aiding in the secretion or activation of immune cytokines. Our group has previously found that children with ASD have lower Treg frequencies and their related immunoregulatory cytokines (e.g., transforming growth factor-β1) than typically developing (TD) counterparts. However, little is known about Treg phenotypes in ASD. Our study sought to understand how the Treg phenotype and their expression of regulatory markers differ in ASD and TD children recruited from the Childhood Autism Risk from Genetics and Environment (CHARGE) study. Peripheral blood was collected during study visits and processed using density gradient separation to isolate peripheral blood mononuclear cells (PBMCs). PBMCs were activated with anti-CD2/CD3/CD28 beads for 24 hours. Following activation, PBMCs were stained for CD3, CD4, CD25, Foxp3, CD127, α4β7, Cytotoxic T-Lymphocyte Antigen 4 (CTLA-4), glucocorticoid-induced TNFR-related protein (GITR), glycoprotein A repetitions predominant (GARP, latent TGF-β1 receptor), and latency-associated peptide(LAP) for flow cytometry analysis. Our ASD group(n=28) had significantly fewer LAP+, GARP+LAP+ and GITR+ Tregs than our TD group (n = 12). Moreover, α4β7+LAP+ Tregs was associated with improved scores on the aberrant behavior checklist (ABC) assessment. This data suggests that Tregs from children with ASD are less capable of binding and activating the immunoregulatory cytokine TGF-β1. Improving Treg-mediated activation of immunoregulatory cytokines may be a therapeutic target, as LAP+ Tregs that express the gut-homing integrin α4β7 are correlated with improved behavioral outcomes. Future studies should investigate causative factors for Treg mediated immune dysregulation in ASD (Funding: NICHD 5RO1HD090214-05)

35. Unraveling neuroimmune circuits that control inflammation and macrophage function in the pleural cavity

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While lung inflammation is an essential component in the host response and clearance of infiltrating pathogens, excessive inflammation can result in further tissue damage. Therefore, finely tuned immune responses are required for host protection and a return to homeostasis. Macrophages, a heterogenous subset of innate immune cells, are known regulators of inflammation via the release of cytokines and chemokines and phagocytosis of bacteria and debris. A specialized subset of macrophages in the peritoneal and pleural cavities can also form protective aggregates during systemic bacterial infection in a phenomenon known as macrophage disappearance reaction (MDR). In the peritoneum these macrophages are induced to adhere to the mesothelial lining in aggregates, trapping bacterial pathogens to prevent further dissemination. Recently B-cells, which are abundant in the peritoneal and pleural cavities, have been described that express the enzyme Choline Acetyltransferase (ChAT) and produce the neurotransmitter acetylcholine (ACh). In preliminary studies, mice lacking ChAT in B-cells (MB1.Cre+ $ChAT^{f/f}$) had significantly increased MDR compared to WT controls. Adherence of macrophages to the mesothelial cells of these cavities is particularly evident on the diaphragm. Although it is well appreciated that Ach release from ChAT+ B-cells is induced by neurotransmitters, the signals and neuronal structures in the pleural cavity that regulate this process are unknown. Innervation of the diaphragm consists of motor and sensory fibers from the phrenic nerve. Preliminary studies indicate that regions with phrenic nerve innervation are located in close proximity to macrophage aggregates on the diaphragm during homeostasis and acute inflammatory stimuli. With this in mind, our general hypothesis is that specific neuronal subtypes within the phrenic nerve are part of a host-protective neuro-immune circuit that serves to regulate inflammation. (Funding: CZI 2020-217656)

36. CSF1R signaling modulates myeloid subsets and dictates CNS lesion localization in experimental autoimmune encephalomyelitis

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Colony stimulating factor 1 receptor (CSF1R) signaling promotes the development, survival, proliferation, migration, and differentiation of tissue macrophages, dendritic cell subsets, monocytes, and osteoclasts. Many groups previously showed that CSF1R antagonism mitigates clinical severity in experimental autoimmune encephalomyelitis (EAE) and this was initially attributed to microglia depletion. However, due to its broad expression, it is unlikely that the contribution of CSF1R to neuroinflammation is limited to microglia depletion. Using a CSF1R antagonist PLX5622 diet (PD), we examined the effects of CSF1R signaling on EAE clinical scores during onset and progression, and its role in modulating CNS and peripheral myeloid cell composition. Our data show that, upon EAE induction, PD mice exhibited milder classical neurological symptoms compared to CD mice. Moreover, a subset of PD mice developed atypical EAE symptoms, which were never observed in the CD group. Similarly to the changes detected in steady state, CSF1R antagonism increased neutrophil frequencies and decreased macrophage frequencies in the periphery. CSF1R antagonism also diminished the frequencies of monocyte-derived DCs (moDC), Tregs and T effectors (Th1, Th17, and Th1/Th17), and increased the frequencies of classical DCs (cDC) in the periphery. Furthermore, the CNS of PD mice was infiltrated by increased total numbers of peripheral cells compared to that of CD mice. The relative frequencies of neutrophils, inflammatory monocytes, Tregs, and cDCs were also elevated in the CNS of PD mice compared to CD mice during disease onset. Interestingly, during early clinical disease, CNS infiltrates in PD mice were localized in the cerebellum while in CD mice infiltrates were localized in the spinal cords. Our findings suggest that CSF1R antagonism modulates the cellular composition of myeloid cells both in the periphery and within the CNS, and affects the location of EAE lesions during the early stages of the disease.

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