# Graduate Group in Immunology


2020

UC DAVIS

# Index

# Friday Schedule

- January 31, 2020 –

| | |
|---|---|
| 8:30 a.m. | The Hilton Garden Inn Lobby, 110 F Street, Davis<br>(transportation provided to Vet Med 3B) |
| 9:00 a.m. | Convene in Vet Med 3B, Room 1105, UC Davis Campus<br>(light breakfast served) |
| 9:15 a.m. | Welcome with Dr. Huaijun Zhou, GGI Chair |
| 9:30 a.m. | Program Overview with Dr. Chuck Bevins, Former GGI Chair |
| 10:15 a.m. | Immunology Research at UC Davis with Dr. Nicole Baumgarth,<br>Academic Adviser & Former GGI Chair |
| 10:45 a.m. | Break |
| 11:00 a.m. | 15-min Research Talk with Dr. Scott Simon, GGI Faculty |
| 11:15 a.m. | 15-min Research Talk with Dr. Stefan Rothenburg, GGI Faculty |
| 11:30 a.m. | UCD Diversity Programs with Dr. Lillian Cruz Orengo, GGI Faculty |
| 11:45 a.m. | Leave for Botanical Conservatory Tour (transportation provided) |
| 12:00 p.m. | Tour the Botanical Conservatory<br>Enter at the North end of the middle Greenhouse, Klieber Hall Drive<br>Student Host – Tina Truong |
| 1:00 p.m. | Travel to 1023 Gladys Valley Hall (transportation provided) |
| 1:15 p.m. | Lunch with GGI student drivers<br>1023 Gladys Valley Hall (this room is available all afternoon) |
| 1:45 p.m. | Interviews in Vet Med 3B (Room 1001, 2003, 3003 or 4003) |
| 5:00 p.m. | Break (return to hotel, vans depart from Vet Med 3B parking lot) |
| 6:10 p.m. | Drive to dinner (vans depart Hilton Garden Inn, 110 F Street) |
| 6:30 p.m. | Dinner with students and faculty at the home of Dr. Huaijun Zhou<br>(2212 Reinecke Court, Woodland, CA) |
| 8:30 p.m. | Drive to Hilton Garden Inn (transportation provided) |
| 9:00 p.m. | Pub Party with current students (optional – walking from Hilton Garden Inn)<br>DeVeres Pub, downtown Davis<br>Student Hosts - Jasmine Labuda, Doug Akahoshi & Sonny Elizaldi |
| 11:45 p.m. | Walk back to the Hilton Garden Inn |

# Saturday Schedule

- February 1, 2020 -

| | |
|---|---|
| 7:45 a.m. | Vans depart the Hilton Garden Inn, 110 F Street, Davis<br>Current GGI student poster set-up (*Walter A. Buehler Alumni Center*) |
| 8:00 a.m. | Breakfast with GGI Students and Faculty<br>Walter A. Buehler Alumni Center |
| | ***Student, Alumni & Faculty Presentations*** |
| 8:45 a.m. | Welcome with Dr. Huaijun Zhou, GGI Chair |
| 9:00 a.m. | Alfredo Hernandez, 5th year GGI Student<br>*"Monocyte activation in cardiovascular disease through inflammatory signaling associated with CD11c function"* |
| 9:20 a.m. | Dr. Trang Nguyen, GGI Alumna, Postdoctoral Researcher<br>University of California, San Francisco<br>*"Identify the molecular pathways to reverse T cell anergy"* |
| 9:40 a.m. | Dr. Annie Mirsoian, GGI Alumna, Scientist,<br>UNITY Biotechnology, South San Francisco<br>*"Talk Title TBD"* |
| 10:00 a.m. | Dr. Bennett Penn, GGI Faculty, Department of Internal Medicine, Infectious Diseases<br>*"Talk Title TBD"* |
| 10:45 a.m. | Viewing of GGI student posters (group A) |
| 11:45 a.m. | Viewing of GGI student posters (group B) |
| 12:45 p.m. | Award presentations & closing with Dr. Huaijun Zhou |
| 1:15 p.m. | Lunch – candidates & student drivers<br>Walter A. Buehler Alumni Center Lobby |
| 1:30p.m. | Depart Alumni Center for UCD Medical Center<br>(transportation provided) |
| 2:00 p.m. | Tour of the UCD Medical Center, Sacramento |
| 3:30 p.m. | Depart the UCD Medical Center, Sacramento<br>(transportation provided) |
| 4:00 p.m. | Return to the Hilton Garden Inn & the Davis campus |

# Welcome, Prospective Students

Sofia Caryotakis
*University of California, Davis*
*Neurobiology, Physiology, & Behavior*

Shannon Clayton
*California State University, Sacramento*
*Microbiology*

Jacoby Clark
*North Carolina State University, Raleigh*
*Biological Sciences*

Michael Cremin
*University of California, Santa Cruz*
*Bioengineering*

Tram Dang
*University of California, Irvine*
*Biological Sciences*

Hannah Driks
*University of Michigan Ann Arbor*
*Biochemistry*

Loan Duong
*University of California, San Diego*
*Biochemistry & Cell Biology*

Jamie-Jean Gilmer
*Virginia Commonwealth University*
*Biology*

Chase Hawes
*University of California, Santa Barbara*
*Biochemistry*

Michelle Hsu
*University of California, San Diego*
*Biochemistry & Cell Biology*

Janna Johnson
*University of California, Davis*
*Global Disease Biology*

Jeanette Johnson
*University of British Columbia*
*Computer Science, Microbiology, & Immunology*

Tina Kwok
*University of California, Davis*
*Biological Sciences*

Melina Lanzar
*California State University, Stanislaus*
*Biological Sciences*

Alex Lee
*University of Hawaii Manoa*
*Microbiology*

Stephanie Lozano
*University of Illinois, Urbana*
*Molecular and Cellular Biology*

Nicole Ma
*College of William and Mary*
*Neuroscience*

Ashley Mello
*Xavier University of Louisiana*
*Biochemistry*

Jose Moran
*Cal Poly Pomona*
*Biotechnology*

Rachel Moreno
*Texas Woman's University*
*Biology*

Rasika Patkar
*University of California, Davis*
*Biochemistry & Molecular Biology*

Tyler Powell
*California State University, Los Angeles*
*Microbiology*
*California State University, Los Angeles*
*Biology (M.S.)*

Gabi Reeder
*University of California, Santa Barbara*
*Biochemistry & Molecular Biology*

Felipe Rodriguez
*University of California, Merced*
*Biological Sciences*

Stephanie Salazar
*University of California, Irvine*
*Biological Sciences*

Tina Sanchez
*Whittier College*
*Biology*

Nilang Shah
*Emory University*
*Biology & Chemistry*
*University of California, Davis (M.D.)*

Krista Thongphanh
*University of California, Davis*
*Microbiology*
*California State University, Sacramento*
*Stem Cell Biology (M.A.)*

Sadira Wang
*University of California, Davis*
*Neurobiology, Physiology, & Behavior*

Liz Waymire
*Montana State University, Bozeman*
*Biochemistry*


Douglas Akahoshi


Michelle Bagood


Jed Bassein


Nicholas Bates


Jaykumar Bhatt


Matthew Bruce


Ryan Bruneau


Antonio Cembellin-Prieto


Craig Collins

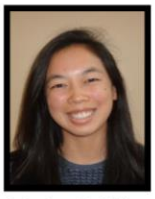

Claire Depew


Cordelia Dunai


Sonny Elizaldi


Kevin Fong


Marissa Franke


Katie Griffin


Nathan Haigh

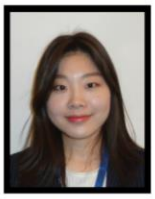

Elizabeth Hammond


Rian Harriman


Alfredo Hernandez


Heather Hughes

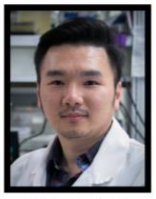

Chelsea Kelland


Danielle Kim


Jasmine Labuda


Jonathan Lam


Catherine Le


Jaewon Lee


Julianna Madigan

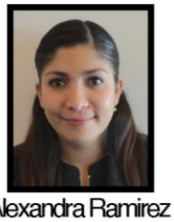

Hannah Miller


Alan Nguyen

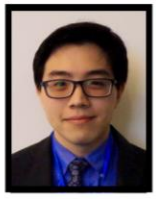

Harman Panesar


Karen Parra


Morgan Poindexter


Alexandra Ramirez


Jordan Rixon


Jamin Roh


Sara Rosero


Sharmila Sambanthamoorthy

# Immunology Graduate Group

2019-2020


Noah Siegel


Evelyn Sievert


Juan Tamayo


Allen Tu

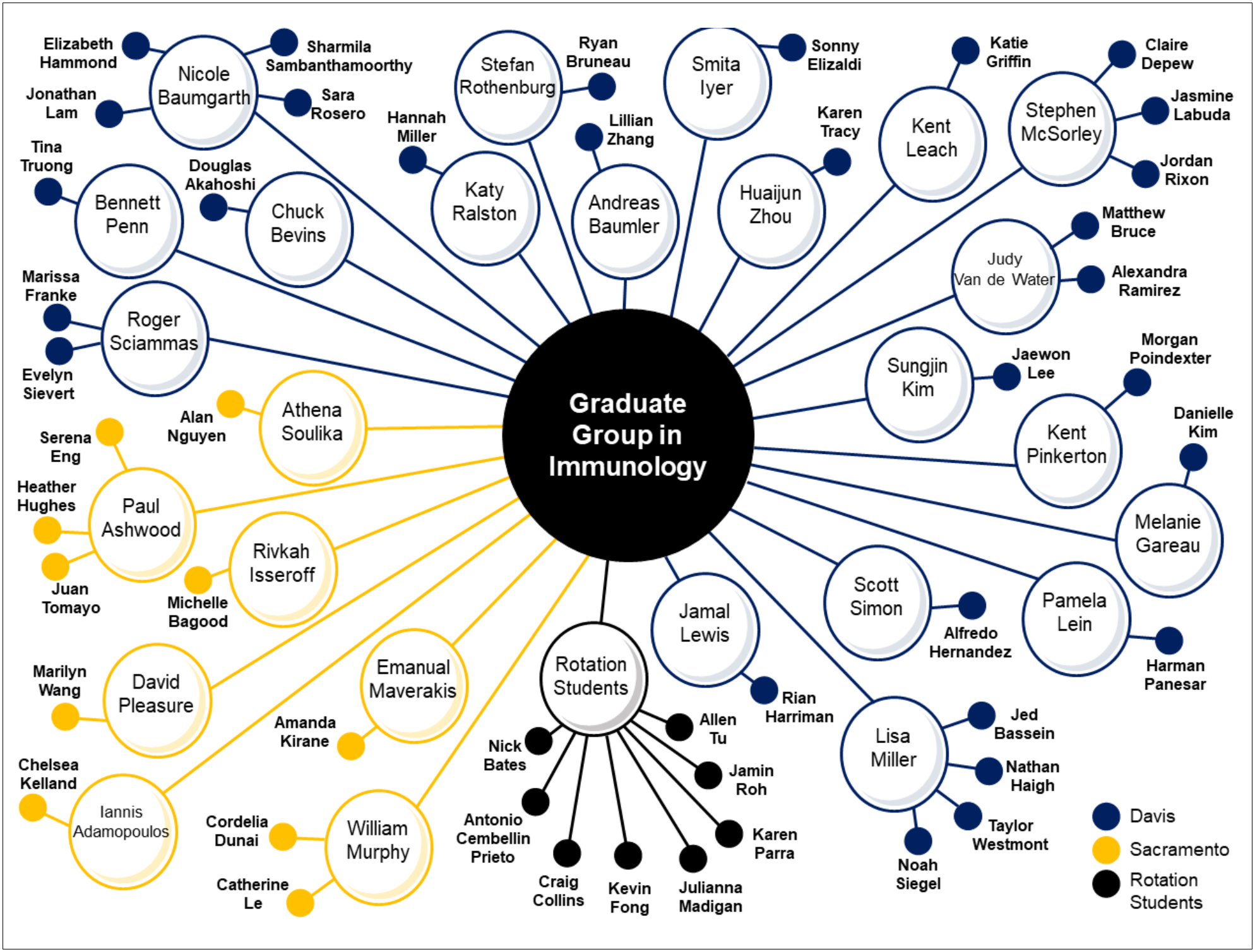

Karen Tracy


Tina Truong


Marilyn Wang


Taylor Westmont


Lillian Zhang


Graduate Group in Immunology
Nicole Baumgarth
Elizabeth Hammond
Jonathan Lam
Sharmila Sambanthamoorthy
Sara Rosero
Stefan Rothenburg
Ryan Bruneau
Hannah Miller
Katy Ralston
Andreas Baumler
Lillian Zhang
Smita Iyer
Sonny Elizaldi
Huaijun Zhou
Karen Tracy
Kent Leach
Katie Griffin
Stephen McSorley
Claire Depew
Jasmine Labuda
Jordan Rixon
Bennett Penn
Tina Truong
Chuck Bevins
Douglas Akahoshi
Roger Sciammas
Marissa Franke
Evelyn Sievert
Judy Van de Water
Matthew Bruce
Alexandra Ramirez
Sungjin Kim
Jaewon Lee
Kent Pinkerton
Morgan Poindexter
Danielle Kim
Melanie Gareau
Athena Soulika
Alan Nguyen
Paul Ashwood
Serena Eng
Heather Hughes
Juan Tomayo
Rivkah Isseroff
Michelle Bagood
Scott Simon
Alfredo Hernandez
Pamela Lein
Harman Panesar
Jamal Lewis
Rian Harriman
Rotation Students
Allen Tu
Jamin Roh
Karen Parra
Julianna Madigan
Kevin Fong
Craig Collins
Antonio Cembellin Prieto
Nick Bates
Lisa Miller
Jed Bassein
Nathan Haigh
Taylor Westmont
Noah Siegel
David Pleasure
Marilyn Wang
Emanual Maverakis
Amanda Kirane
Iannis Adamopoulos
Chelsea Kelland
William Murphy
Cordelia Dunai
Catherine Le
Davis
Sacramento
Rotation Students

# Why did you choose UCD?

## Antonio Cembellin Prieto

1st Year

"I was lucky to be able to visit Davis during my senior year of college, and I was instantly charmed by the city, campus, and most importantly, the phenomenal faculty and support staff. The university is fully bikeable and has striven to enable a fully sustainable campus. However, for me, it was the faculty and the constant curiosity and scientific passion that inspired me to choose UC Davis. I am grateful for those people, and as I have continued here, I have found the faculty to be nothing but supportive, knowledgeable, driven, and focused on pushing their research and students to groundbreaking discoveries".

## Sonny Elizadi

2nd Year

Lab of Dr. Smita Iyer
Department of Anatomy, Physiology, and Cell Biology
UC Davis School of Veterinary Medicine

"First and foremost, I chose to study Immunology at UC Davis because of the fantastic faculty. There is a good mix of well-established faculty with a proven track record and newer faculty with the potential to be leaders in their respective expertise. Second, the opportunity for interdisciplinary study and collaboration is unmatched. Having access to the premier veterinary school in the nation and the largest primate center in the nation are incredible resources you can't find anywhere else. Lastly, the students. They were all so welcoming and accommodating during my interview weekend here. Listening to the students talk about their projects, you could tell they were extremely driven and dedicated."

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## Claire Depew

3rd Year

Lab of Dr. Stephen McSorley
Department of Anatomy, Physiology, and Cell Biology
UC Davis School of Veterinary Medicine

"I applied to UC Davis because of the wide variety of research as well as the program's reputation. During recruitment weekend, everyone was so friendly and the faculty really seemed to care about the students. During my first year, everyone in the GGI has been very supportive and there to help you succeed and to give advice. I was worried that moving from the east coast to Davis would be a hard transition but with the close community, California already seems like home. I am so happy with my decision to come to UC Davis."

## Jonathan Lam

3rd Year

Lab of Dr. Nicole Baumgarth
Department of Pathology, Microbiology & Immunology
UC Davis School of Veterinary Medicine

"When I scouted UC Davis for their immunology program, I was impressed with the breadth of research topics that delved into how we fight disease- Ones that either sought to elucidate models of important immunological consequence or apply concepts conceived in the lab to the clinic as treatments. After interviewing and experiencing UC Davis as a first year student, the program has continued to exceed my expectations, from administration to academics to research. I was excited when I received my offer letter and now, after absorbing all that UC Davis has to offer, I can't imagine being anywhere else."

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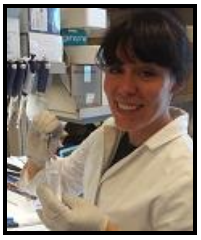
## Jed Bassein

5th Year

Lab of Dr. Lisa Miller
Department of Anatomy, Physiology, and Cell Biology
UC Davis School of Veterinary Medicine

"Imbued in a quiet little college town, UC Davis is a hot bed for veterinary science, plant biology, and clinical medicine. Additionally, the Graduate Group in Immunology at UC Davis offers a unique academic experience and a genuine interest in the growth of their students. Taking all these factors together made choosing UC Davis an easy decision."



## Heather Hughes

6th Year

Lab of Dr. Paul Ashwood
Department of Medical Microbiology and Immunology, School of Medicine
UC Davis MIND Institute

"I was fortunate to have an internship opportunity through UC Davis as a CSU undergraduate, and the quality of mentorship and supportive environment I experienced made me certain that I wanted to join the Graduate Group in Immunology. UC Davis offers excellent research opportunities in collaborative settings and has incredible resources available through the Graduate Groups, and Schools of Medicine and Veterinary Medicine. I have found the collaborative and interdisciplinary nature of the Graduate Groups beneficial both to students and to the expansion of scientific knowledge across the disciplines."

# Faculty

## Iannis E Adamopoulos

MPhil, DPhil
Associate Professor
Rheumatology, Allergy & Clinical Immunology
Shriner's Hospital
iannis@ucdavis.edu

**Keywords: arthritis, osteoimmunology**

**Research Interests:**

Novel treatments and therapeutic strategies for inflammatory arthritis and immune bone loss. Our laboratory studies the interface between the skeletal and immune systems, a newly emerging area of research called "osteoimmunology".

## Paul Ashwood

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

**Keywords: autism, neuroimmunology, neurodevelopment**

**Research Interests:**

Evaluating the interface between the immune system and the central nervous system and how altered immune responses can influence neurodevelopment and affect behavioral outcomes.

## Bryan (Bo) Barnhart

PhD
Senior Director
Immuno-Oncology Discovery
Bristol-Myers Squibb

**Keywords: drug discovery/development and translational research in immuno-oncology and oncology**

**Research Interests:**

He leads a team accountable for generating critical translational data, supporting multiple therapeutic candidates at all stages of drug development. His team also performs deep analysis of human tumor samples, producing data to establish and test clinical and translational hypotheses.

## Nicole Baumgarth

DVM, PhD
Professor
Pathology, Microbiology, & Immunology
Center for Comparative Medicine
nbaumgarth@ucdavis.edu

**Keywords: host-pathogen interaction, regulation of B cell responses, B-1 cells, natural IgM**

**Research Interests:**

The Baumgarth Lab investigates the signals that drive a protective B cell response to influenza infection and how these responses might be derailed during infection with *Borrelia burgdorferi*, the Lyme Disease agent. We are interested also in understanding the development, role, and function of B-1 cells in infectious immunity and how natural IgM regulates the adaptive immune response.

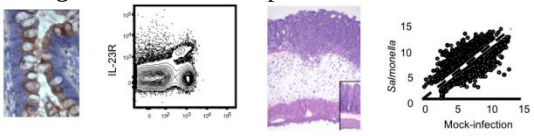
## Andreas Bäumler

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

**Keywords: host-pathogen interaction, *Salmonella***

**Research Interests:**

Pathogenesis and host response to Salmonella infections.




## Charles Bevins

MD, PhD
Professor
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.

# Faculty

## Marie Burns
PhD
Professor
Ophthalmology & Vision Science, Cell Biology
Center for Neuroscience
meburns@ucdavis.edu

**Keywords: microglia/monocyte, neurodegeneration, repair**

**Research Interests:**

Photoreceptor degeneration, like all neurodegenerative diseases, leads to microglial activation and neuroinflammation. We are trying to understand the regulation of neuroinflammation, the differential roles of tissue resident microglia and infiltrating monocytes in preserving neuronal and synaptic function in the CNS.

## Robert Canter
MD
Professor
Surgery
Comprehensive Cancer Center
rjcanter@ucdavis.edu

**Keywords: NK cells, translational research in immuno-oncology and oncology**

**Research Interests:**

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

## Sean Collins
PhD
Assistant Professor
Microbiology & Molecular Genetics
srcollins@ucdavis.edu

**Keywords: neutrophils, chemotaxis, signal transduction, NETosis**

**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
Assistant Professor
Anatomy, Physiology, & Cell Biology
cruzorengo@ucdavis.edu

**Keywords: blood-brain barrier, neuroimmune interactions, autoimmunity**

**Research Interests:**

My research focuses on the contribution of the neurovascular unit that conforms the blood-brain barrier to multiple sclerosis neuropathogenesis with the purpose of developing non-immunosuppressive and sex-specific therapeutic targets.

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

**Keywords: mucosal immunology, viral infections**

**Research Interests:**

HIV pathogenesis and gut mucosal immunology.
Persistent viruses and their influences on mucosal immune responses to co-infections, commensal microbiota and vaccines.

## Allison Ehrlich
PhD
Assistant Professor
Environmental Toxicology
akehrlich@ucdavis.edu

**Keywords: type 1 diabetes, AhR, and T cell differentiation**

**Research Interests:**

My research aims to identify the mechanisms by which AhR activation leads to divergent CD4+ T cell fates, and tests the hypothesis that the interaction between diverse AhR ligands, the host immune system, and the microbiome influences susceptibility to type 1 diabetes.

# Faculty

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

**Keywords: microbiota-gut-brain axis**

**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.

## Laurel Gershwin
DVM, PhD, DACVM
Professor
Pathology, Microbiology & Immunology
ljgershwin@ucdavis.edu

**Keywords: innate mechanisms of antiviral defense in the bovine lung**

**Research Interests:**

Our lab studies bovine respiratory disease, with particular emphasis on bovine respiratory syncytial virus infection (RSV) as a model for human RSV and as a component of bovine respiratory disease complex. We study polymicrobial interactions with emphasis on bacterial induction of host antiviral molecules, and the potential to employ probiotics to enhance vaccine efficacy for bovine RSV infection.

## Tzipora Goldkorn
PhD
Professor
Pulmonary & Critical Care Medicine
ttgoldkorn@ucdavis.edu

**Keywords: oxidative stress, lung disease**

**Research Interests:**

Our research is focused on understanding the molecular mechanisms of lung injury diseases and lung cancer. We study ceramide/sphingomyelin signal transduction in stress modulation and apoptosis; molecular mechanisms of nSMase2 and EGFR activation under oxidative stress and TKIs resistance development; and molecular mechanisms of EMT regulated by ceramide metabolites. We use transgenic mice models, animal exposures and imaging, and a range of cell biology and biochemistry methodologies.

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

**Keywords: lung physiology and immunology**

**Research Interests:**

Airway inflammation caused by environmental exposures (allergen, cigarette smoke, ozone inhalation, or psychosocial stress) in asthma and COPD. Innate and adaptive immune crosstalk and mechanisms of corticosteroid resistance. Lung physiology and a wide spectrum of immunological cell and molecular biology techniques.

## Volkmar Heinrich
PhD
Associate Professor
Biomedical Engineering
vheinrich@ucdavis.edu

**Keywords: ultrasensitive force microscopes, single-molecule interactions**

**Research Interests:**

Molecular-to-cellular bioengineering/biomechanics: Our multiscale approach uses the tools of mechanics and high-resolution optical microscopy to deepen the understanding of how nature does things in the nanoworld and where pathogens may attack our natural defenses. On the smallest scale, we characterize isolated single-molecule interactions using ultrasensitive force microscopes.

## Samuel Hwang
MD, PhD
Professor & Chair
Dermatology
sthwang@ucdavis.edu

**Keywords: cancer, cell trafficking**

**Research Interests:**

Leukocyte and cancer cell trafficking. Long standing interest in the role of chemokine receptors, including CCR6 and CXCR4 in immune cells as well as cancer cells.

# Faculty

## 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.

## Smita Iyer

PhD
Professor
Pathology, Microbiology, and Immunology
smiyer@ucdavis.edu

**Keywords: $T_{FH}$, HIV, vaccines**

**Research Interests:**

Our lab's primary research interests center around delineating immunological and molecular mechanisms of CD4 T cell help. Our ultimate goal is to use this information to design an effective HIV vaccine and in parallel understand mechanisms of HIV susceptibility and pathogenesis.

## Hong Ji

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

**Key words: epigenomics, gene regulation, chromosome biology**

**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.

## Sungjin Kim

PhD
Associate Professor
Medical Microbiology & Immunology
Center for Comparative Medicine
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.

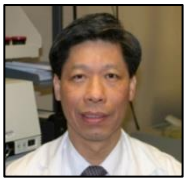
## Marcelo Kuroda

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.



## 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.

# Faculty

## J. Kent Leach

PhD
Professor
Biomedical Engineering
jkleach@ucdavis.edu

**Keywords: biomaterials, tissue engineering, cell and drug delivery**

**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.

## Pam Lein

PhD
Professor
Molecular Biosciences
pjlein@ucdavis.edu

**Keywords: neuroimmune interactions, autism, asthma**

**Research Interests:**

Determining the influence of inflammatory cells and cytokines on the structure and function of neurons in the brain and in the lung, and evaluating the role of such interactions in neuro-developmental disorders, neurotoxic syndromes and asthma.

## Patrick S. C. 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.

## Jamal Lewis

PhD
Assistant Professor
Biomedical Engineering
jamlewis@ucdavis.edu

**Keywords: immuno-engineering, biomaterials, dendritic cell biology, immunotherapy**

**Research Interests:**

The Immuno-modulatory Biomaterials Laboratory focuses on the development of novel biomaterial systems that can manipulate the immune system. Our primary goal is to design the next generation of immunotherapeutics.

## 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.

## Kimberley McAllister

PhD
Associate Professor
Neurobiology, Physiology & Behavior
Center for Neuroscience
kmcallister@ucdavis.edu

**Keywords: neurology, synapses, visual cortex**

**Research Interests:**

Cellular and molecular mechanisms of synapse formation, competition, and elimination in the developing visual cortex. The lab studies the formation, persistence, and elimination of individual synapses between dissociated, cultured visual cortical neurons using time-lapse imaging.

# Faculty

## Stephen J. McSorley

PhD
Professor
Anatomy, Physiology & Cell Biology
Center for Comparative Medicine
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.

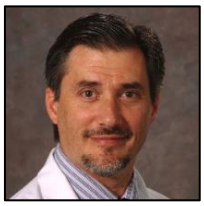
## Lisa Miller

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

**Keywords: respiratory, developmental, asthma, COPD**

**Research Interests:**

Our research is focused on understanding the relationship between early life environmental exposures and development of pulmonary disease, such as asthma. We study how mucosal and systemic immunity is established during infancy, and determine the impact of air pollutants, allergens, and infectious disease on childhood lung health.



## 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.

## Robert O'Donnell

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

**Keywords: radioimmunotherapy, cancer, apoptosis**

**Research Interests:**

Radioimmuotherapy 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.

## Bennett Penn

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

**Keywords: genetics, biochemistry, *M. tuberculosis***

**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.

## John Peters

MD
Associate Professor
Internal Medicine; Geriatric Medicine
Center for Aging
john.peters@ucdmc.ucdavis.edu

**Keywords: ECM, tissue injury and healing, aging**

**Research Interests:**

Define functional roles for extracellular matrix proteins, with emphasis on the fibronectin family of alternatively spliced proteins, in processes of tissue injury, inflammation and healing. Specifically, to define pathogenetic roles of ECM proteins in osteoarthritis and other chronic inflammatory disorders of aging.

# Faculty

## Kent Pinkerton

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

**Keywords: immunotoxicology, development, particle/host/pathogen interactions**

**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.

## David Pleasure

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

**Keywords: CNS, MS, EAE**

**Research Interests:**

Multiple sclerosis, experimental autoimmune encephalomyelitis, central nervous system innate immunity, development of the nervous system, neural stem cells.

## 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.

## Siba Raychaudhuri

MD
Professor
Internal Medicine; Rheumatology, Allergy & Clinical Immunology
sraychaudhuri@ucdavis.edu

**Keywords: psoriasis, arthritis, T cells**

**Research Interests:**

Neurogenic inflammation of the autoimmune diseases psoriasis, psoriatic arthritis, and rheumatoid arthritis. Cell trafficking and the activation of T cells by Nerve Growth Factor during inflammatory reactions. -SCID mouse-human skin chimera model of psoriasis.

## Colin Reardon

PhD
Assistant 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.

## 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.

# Faculty

## 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 Comparative Medicine
rsciammas@ucdavis.edu

**Keywords: Gene regulation in the control of antibody**

**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.

## 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-1 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 mucosa-associated invariant T-cells (MAIT cells), mucosal B-cells, and the functionality of cytotoxic T-cells. In an effort to broaden our emphasis on mucosal immunity, we are also beginning to study the pathogenesis of Endometriosis.

## Scott Simon

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

**Keywords: mechanosignaling, integrins, selectins, microfluidics**

**Research Interests:**

Inflammation in response to acute infection (Staphaureus 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.

## 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.

# Faculty

## 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.

## Jeffrey Stott

PhD
Professor
Pathology, Microbiology & Immunology
jlstott@ucdavis.edu

**Keywords: comparative immunology, development**

**Research Interests:**

Developmental, comparative, and clinical immunology with emphasis on bovine, equine, marine mammals, and zoo animal species. Viral and bacterial immunopathogenesis of the fetus and neonate. Immunology of the bovine mammary gland.

## Yoshikazu Takada

MD, PhD
Professor
Dermatology; Biochemistry & Molecular Medicine
ytakada@ucdavis.edu

**Keywords: integrins**

**Research Interests:**

Mechanism and regulation of integrin/ligand interactions. Role of integrins in growth factor signaling.

## 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.

## 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.

# Faculty

## Renée Tsolis

PhD
Professor
Medical Microbiology & Immunology
rmtsolis@ucdavis.edu

**Keywords: host-pathogen, immune evasion, innate immunity, co-infection**

**Research Interests:**

My research group studies interactions between bacterial pathogens and the innate immune system. We are particularly interested in how bacterial virulence factors interact with the host to evade immune clearance and elicit pathology.

## 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.

## Judy Van de Water

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

**Keywords: neuroimmunology, autoimmunity, autism, immune dysregulation**

**Research Interests:**

Immunopathology, neuroimmunology, and the cellular and molecular basis of autoimmunity. Current research addresses the biological aspects of autism spectrum disorders including immune function, cellular mechanisms of immune dysregulation, and autoimmunity.

## Andrew Vaughan

PhD
Professor
Radiation Oncology
andrew.vaughan@ucdmc.ucdavis.edu

**Keywords: fusion genes**

**Research Interests:**

I am interested in the mechanism whereby fusion genes are created. Such genes are classically the driving element in leukemia. However, their significance is expanding to a wider field and such fused genes have been implicated in the development of prostate cancer (TMPRSS2-ERG). Understanding the mechanism behind their creation opens possibilities to suppress the disease they cause.

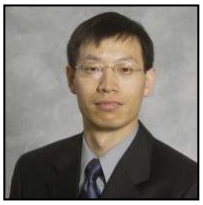
## Reen Wu

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

**Keywords: airway epithelial immunity**

**Research Interests:**

Roles of airway epithelial cells in lung diseases and airway mucosal immunity, embryonic stem cell biology and regenerative lung biology and medicine, epigenetic mechanism.



## Huaijun Zhou

PhD
Professor & Chair of Immunology Graduate Group
Chancellor's Fellow
Animal Science
hzhou@ucdavis.edu

**Keywords: gut microbiome, genomics, bioinformatics**

**Research Interests:**

Molecular mechanisms of colonization resistance in poultry using genomic approach. Understand genetic regulation of host response and basic mechanisms of pathogen virulence in poultry. Pathogens of interest include Salmonella, E coli., Newcastle disease virus, and avian influenza virus.

Dear Prospective Student:

Welcome to UC Davis and recruitment weekend! 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 competitive 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. 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!

# How does UC Davis Compare?

UC Davis consistently ranks among the top universities to attend for your graduate career, across multiple publications. Here's what others have to say about our university and programs:


- **Among the top 10 centers for biomedical research nationwide**
  *The Hartwell Foundation 2017*
- **11th in Top Public Schools**
  *U.S. News & World Report Rankings 2019*
- **1st in Agricultural Sciences Globally**
  *U.S. News & World Report Rankings 2019*
- **1st in Veterinary Medicine Globally**
  *U.S. News & World Report Rankings 2019*
- **3rd for global research impact in Life and Earth Sciences**
  *Centre for Science and Technology Studies at Leiden University 2015-2017*
- **1st in the nation for launching women into STEM professions**
  *"The 13 most important STEM Universities for Women," Forbes 2016*
- **39th out of 18,000 universities worldwide**
  *Center for World University Rankings 2019-2020*
- **7th for best student health services in the U.S.**
  *The Princeton Review 2017*
- **3rd Globally for campus sustainability practices**
  *UI GreenMetric World University Rankings 2019*
- **18th for best Graduate Biological Sciences Programs**
  *U.S. News & World Report Rankings 2019*
- **11th among public research universities nationwide**
  *U.S. News & World Report Rankings 2019*
- **5th in Best Public University in the United States**
  *Wall Street Journal/Times Higher Education College Ranking 2018*
- **3rd of 303 public and private national universities in contributions to the public good**
  *Washington Monthly Magazine*
- **Considered a "Best Value College"**
  *Princeton Review 2018*
- **10th Greenest College in the United States**
  *Princeton Review and Forbes "America's Top 'Green' Colleges," 2017*

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/)

# UC Davis Services & 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.

**UC Davis Genome Center (GBSF, Davis):**

- ☑ Bioinformatics Core: Matt Settles, core manager (settles@ucdavis.edu)
  - Provides expertise and infrastructure for the acquisition, curation, analysis, and distribution of large complex datasets, as well as develop and perform computations, analyses and simulations addressing a wide variety of biological questions from genomics to network biology.
  - Overlapping expertise in computing infrastructure, Web/database, scientific programming, biological annotation and statistics to provide bioinformatics support for the wetlab service cores as well as for researchers with individual bioinformatics needs.
- ☑ DNA Technologies Core: Dr. Lutz Froenicke, core director (lfroenicke@ucdavis.edu)
  - Provides high throughput sequencing, genotyping, microarray services, training, and consultation. NGS technologies include Illumina sequencing, PacBio (long read) sequencing, and Nanopore sequencing. 10X Genomics technologies include single-cell transcriptome and genome analyses.
  - Multiple platforms provide the capability to run low to very high throughput SNP assays with no requirements on the minimum or maximum number of samples or SNPs analyzed.
- ☑ Expression Analysis Core: Dr. Lutz Froenicke, core director (lfroenicke@ucdavis.edu)
  - Extends the services provided by the Genome Center/School of Medicine Affymetrix microarray facility.
  - This core focuses on ultra high throughput sequencing and Illumina gene expression arrays for studies in human, mouse, or rat.
  - Additional services include custom arrays, chromatin immunoprecipitation training, ChIP lab services, and comparative genomic hybridization using custom arrays. The Illumina Sequencers and downstream data analysis pipeline are also available for expression and ChIP-seq projects.
- ☑ Metabolomics Core: Dr. Oliver Fiehn, faculty director (ofiehn@ucdavis.edu)
  - Provides high-quality, cost-effective, state-of-the-art analytical services for metabolomics research and small molecule analysis.
  - The Core offers GC-MS and LC-MS lines for metabolic profiling using high quality standards, reagents, and solvents. It provides assistance with the experimental setup, design, data interpretation, and statistical analysis
- ☑ Proteomics Core: Dr. Brett Phinney, manager (bsphinney@ucdavis.edu)
  - Provides state-of-the-art analytical proteomic services with particular emphasis on label-free quantitative proteomic profiling, the analysis of macromolecular complexes, the post-translational modification of their constituents and standard protein identification from complex protein mixtures.
- ☑ Host-Microbe Systems Biology Core: Matt Rolston, manager (mrrolston@ucdavis.edu)
  - The HMSB Core's services include support for microbial phylogenetic studies, sample processing for Next-Generation Sequencing (NGS), functional analysis of NGS data sets, and gene expression profiling using Affymetrix GeneChips. The NGS analytical services offered utilize state-of-the-art open source software platforms and other customized scripts developed by the HMSB Core co-Director, Dr. Jonathan Eisen.

- The HMSB Core is designed to provide campus researchers with easily accessible, customized, and cost-effective resources for integrating analyses of microbial community structure and host-microbe interactions in health and disease.

☑ Center for Molecular & Genomic Imaging (CMGI): Dr. Abhijit J. Chaudari, director (ajchaudhari@ucdavis.edu)
- Provides dedicated, state-of-the-art, small animal imaging technologies to investigators at UC Davis as well as other research institutions. Imaging modalities include PET, SPECT, CT, MRI, ultrasound, autoradiography, and optical (fluorescence and bioluminescence). We offer assistance with study design, probe development and image analysis, in addition to providing imaging procedures with multiple imaging modalities.
- A satellite imaging suite is located at the California National Primate Research Center for PET imaging studies in non-human primates.

☑ TILLING Core: Dr. Luca Comai, manager (genome.tilling@gmail.com)
- Provides mutants for rice, hexaploid and tetraploid wheat, Arabidopsis thaliana, and tomato as well as other species on request.
- TILLING (Targeting Induced Local Lesions IN Genomes) is a reverse genetic technique that uses chemical mutagenesis to create libraries of mutagenized individuals that are subjected to high-throughput sequencing for discovery of mutations.

**Office of Primate Research (Davis):**

☑ California National Primate Research Center: Jenny Short, assistant director (jjshort@ucdavis.edu)
- The CNPRC has 4 service cores:
  1. Analytical & Resource Core: providing services in the areas of hematology, clinical chemistry, genetics, immunology, endocrinology, flow cytometry, and pathogen detection. Available resources include biological specimens, viral stocks, DNA, and species-specific reagents.
  2. Behavior Assessment Core: assists investigators interested in assessing brain function at the behavioral level. A variety of standardized tests are available onsite for developmental, cognitive, motor, sensory and social dimensions of behavior.
  3. Computational Imaging Core: provides microscopy, stereology, digital imaging, histology and consultation services to all campus departments
  4. Inhalation Exposure Core: capability for exposure of a wide variety of biological entities from cells to populations of organisms to a great range of compounds that can be delivered by inhalation (i.e. oxidant gases, reactive gases, aerosols, mixed gas and aerosols, allergens, microbes and various drug-containing entities). In addition, a pulmonary function unit has recently been established under the direction of a research physiologist to assess function in animals undergoing exposure.

**School of Veterinary Medicine & UC Davis Animal Services (Davis, Sacramento):**

☑ School of Veterinary Medicine:
- Provides a wide-range of services to the research community for both companion animal clinical trials and research animal diagnostics. As they are too numerous to list here, For a full list of services please refer to the following website: (http://www.vetmed.ucdavis.edu/ResServ.cfm)

☑ Mouse Model Creation Services:

- Generation of knockout and transgenic mouse strains, gene targeting by homologous recombination in ES cells, procurement, importation and rederivation to generate pathogen-free mice, cryopreservation, and resuscitation of embryos and germplasm, assisted reproduction procedures.

☑ Mouse Phenotyping Services:
- Gross and microscopic pathology, small animal imaging procedures.

☑ UC Davis-Jackson Laboratories Partnership:
- For the study of human tumors in mouse models.
- The collaboration seeks to establish a uniform and controlled testing process to integrate data from mouse cancer model studies with patient clinical trial studies. The approach will help identify biomarkers, molecules that provide targets for candidate drugs and help predict when these drugs will be most effective.

**UC Davis Health System, Clinical & Translational Science Center (Sacramento):**

☑ CTSC: Dr. Ted Wun, program director (twun@ucdavis.edu)
- Offers a full-fledged toolbox of resources that faculty and staff across the spectrum of scientific research can use to improve biomedical research. We encourage you to use the CSTSC website to explore services and resources that may benefit your research: (http://www.health.ucdavis.edu/ctsc)
- CTSC facilities include support services in:
  - Animal Models
  - Behavioral Assessment-Animal Models
  - Biostatics
  - Computer Graphics
  - Data Analysis
  - Drug Discovery
  - Endocrine and Other Assays
  - Flow Cytometry
  - Genetics
  - Image Analysis
  - In Vivo Imaging
  - Industry Collaborations
  - Informatics
  - Mass Spectrometry
  - Microarray
  - Microscopy and Imaging
  - Multiplex/Luminex
  - Pathology Services
  - Polyclonal Antibody Production
  - Proteomics and Metabolomics
  - Sequencing
  - Shops: Fabrication and Repair
  - Stem and Progenitor Cells
  - Taqman/PCR
  - X-Ray Crystallography

**Flow Cytometry: Davis & Sacramento**

☑ Flow Cytometry Shared Resource: Bridget McLaughlin, technical director (bmclaughlin@ucdavis.edu)
- Provides access to expertise and instrumentation for analytical flow cytometry, cell sorting, and laser scanning cytometry to all researchers at UC Davis, including members of the UC Davis Cancer Center, and to biotech companies and other research organizations.

# How do you plan to use your PhD?

## UC Davis Professional Development Opportunities

### 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**

### FUTURE Career Exploration for Graduate Students and Postdoctoral Scholars

**The mission of the FUTURE program is to enable and empower graduate students and postdoctoral fellows to develop their own educational portfolios and be the architects of their own successful career paths through career preparation and exploration.**

**http://future.ucdavis.edu/**

### 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.**

**http://gradstudies.ucdavis.edu/professional-development/professors-future**

### 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.**

**http://gsm.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.**

**http://gradstudies.ucdavis.edu/professional-development/gradpathways**

### 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.**

**http://icc.ucdavis.edu/mpp/**

*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.

*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 hour specials every day of the week! There are also special happy hours and weekly specials, such as "$6 beer & a slice" at Vito's Pizza, Whiskey Wednesday at DeVere's Irish pub, and trivia almost every day of the week at bar such as University of Beer, DeVere's, Sophia's, and Three Mile Brewing Co. 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!

Because Davis is a university-oriented city that caters to the needs and budget of students and their families, there are plenty of living options. House-hunting resources include UC Davis's Housing office, UCD Student Housing groups on Facebook, Davis Wiki, and Craigslist, which provide current listings of apartments, both on and off campus, at student- friendly prices. UC Davis offers various on-campus housing options for students with families, and several of these housing options may provide daycare services and afterschool programs. Together, these resources and activities makes living in Davis fun with all of the benefits and perks that allow students and families alike to enjoy what this great town has to offer!

*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-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. 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!

# Student Poster Abstracts

# Abstract Index

# III. Immune Regulation

# IV. Neuroimmunology

# I. Allergy and Autoimmunity

## 1. Early Life Tobacco Smoke Exposure Affects Bone Marrow Derived Dendritic Cells

Jed A. Bassein[1], Nathan E. Haigh[1], Alexa Rindy[2], Ross Allen[2], Chris Royer[2], Lisa A. Miller[1,2,3]

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Prenatal and postnatal exposure to environmental tobacco smoke (ETS) has been associated with increased risk of respiratory disease in children. ETS exposure can elicit remodeling of the respiratory tract and increase susceptibility to allergic asthma, however it is unknown whether the immune system is permanently influenced. Previous studies in humans and animal models have reported altered myeloid cell function in conjunction with antecedent cigarette smoke exposure. Because early life is a period of robust immune development, we hypothesized that neonatal ETS exposure can persistently manifest altered myeloid function by modulation of bone marrow stem cells populations. Neonatal mice and their associated dams were exposed to filtered air (FA) or ETS for 5 days at 5 h/day. For 6 weeks post-exposure, bone marrow was harvested from offspring on a weekly basis for cell culture studies. Bone marrow derived dendritic cells (BMDC) were cultured in the presence of GM-CSF for 12 days. Cultures were analyzed by flow cytometry for phenotypic and functional markers of dendritic cell activation. On day 3 post exposure, BMDC cultures from ETS exposed neonates had a greater frequency of CD11c+MHCIIhi cells relative to control animals, which was maintained at 2 and 3 weeks. At 4 weeks post ETS exposure, frequency of CD11c+MHCIIhi cells was reduced and subsequently stabilized relative to controls at 5 and 6 weeks. Early life ETS in mice results in altered MHCII expression on dendritic cells that is maintained for at least 3 weeks of exposure. Our findings suggest that modulated dendritic cell activation may influence T cell priming in response to a pathogen.
(Funding: T29DT0657, P51OD011107, T32ES007059)

## 2. Early-life environmental tobacco smoke disrupts the lung IL-22/IL-22Ra1 axis

Nathan Haigh[1,2], Alexa C. Rindy[2], Ross K. Allen[2], Chris M. Royer[2], Lisa A. Miller[1,3]

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Early-life pulmonary function deficits are predictive of lung disease in adulthood, including chronic obstructive pulmonary disorder (COPD). The absence of effective treatments for COPD makes understanding the molecular mechanisms of the disease of the utmost importance. Previous reports indicate that IL-22 is associated with psoriasis and inflammatory bowel disease and that IL-22 is elevated in COPD and healthy smokers. IL-22 receptor has been shown to be induced in the lung during injury, and IL-22 signaling has also recently been found to alter epithelial cell behavior. Given these data, we hypothesize that expression of IL-22 and its receptor are elevated by exposure to environmental tobacco smoke (ETS) during early life resulting in altered lung pathophysiology. We used C57BL/6J mice in an early neonatal ETS exposure protocol. Mice were exposed to filtered air (FA) or 1-2 mg/m3 ETS for 6 hr/day for 5 days starting at postnatal day 2 or 6 weeks. Mice were euthanized the day after exposure or after 5 weeks of recovery in FA. Early-life but not adult ETS exposure resulted in increased IL-22Ra1 in airways epithelium compared to FA animals. IL-22Ra1 partially overlapped club cells in early-life ETS treated mice. IL-22+ ILC3s were significantly increased immediately following neonatal but not adult exposure. No other immune cells demonstrated increased IL-22, and IL-22+ cells were not elevated following the 5 week rest period. Early-life ETS exposure also resulted in increased neutrophil frequency and increased protein concentration in the lavage fluid. These results indicate that early-life ETS exposure alters the IL-22/IL-22Ra1 axis at a critical juncture in lung development that may pose a risk for function decrements later in life.
(Funded by TRDRP 26IP-0045 and NIEHS T32 ES007059)

# 3. Augmentation of Oral Immunotherapy with Tolerance-inducing Nanoparticles

Rian Harriman[1,2], Kenneth Alvarez[2], Luke Mckibbin[2], Bahieh Noorafkan[2], Jamal S. Lewis[1,2]

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Roughly 15 million Americans suffer from food allergies which in severe cases can be life threatening. The underlying cause involves the stimulation of Th2 cells specific for normally harmless food allergens that orchestrate inappropriate and harmful reactions including anaphylaxis. Pacifying such responses without inhibiting overall immune function is critical for providing effective, safe therapies. To this end, researchers are devising novel biomaterial-based strategies to diminish problematic Th2 responses to specific food allergens. Although the inclusion of immunomodulatory factors such as CpG with allergen-encapsulated nanoparticles has been shown to shift problematic Th2 responses towards a Th1 phenotype and reduce allergic symptoms in mice, nanoparticle platforms designed to induce allergen-specific T regulatory (Tregs) responses has not been investigated. Several clinical studies indicate that sustained unresponsiveness after allergen oral immunotherapy in humans is correlated with increased Treg populations, suggesting that nanoparticles designed to induce Treg differentiation may have more therapeutic relevance than Th1-inducing nanoparticles. Polysaccharide A (PSA), a commensal molecule produced by the gut-symbiont Bacterorides fragilis, has been shown to have Treg-inducing capabilities and is protective in various inflammatory models through IL-10 dependent mechanisms. 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 NPs will show significant improvements in efficacy and safety over traditional allergen-only oral immunotherapy due to PSA NP 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. In this current study, we show that PSA NPs can be readily fabricated using water/oil emulsification with glutaraldehyde crosslinking and maintains immunoregulatory capability.
(Funding: NIAID R03AI138191)

# 4. MDL-1 Regulates Cytoskeletal Rearrangement and Bone Resorption in Inflammatory Arthritis

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Interleukin-23 (IL-23) and its cognate receptor interleukin-23R (IL-23R) play a critical role in the pathogenesis of many autoimmune diseases, including psoriatic arthritis. Although IL-23 has been extensively studies in lymphocytes, its role in myeloid cells remains understudied. We have previously shown that IL-23 induces osteoclast activation via MDL-1. MDL-1, also known as CLEC5A is a member of C-type lectin superfamily, which is exclusively expressed in myeloid cells. Myeloid cells differentiate to osteoclasts in the presence of MCSF and RANKL which upregulate bone lytic enzymes including TRAP, CATK, MMP9 to facilitate bone resorption. However, a key element in the bone resorption process is the cytoskeletal rearrangement within the osteoclast that allows adhesion, secretion and increased surface area during bone remodeling. The goal of this study was to demonstrate that MDL-1 signaling regulates the osteoclast cytoskeleton and affects bone resorption. To characterize the structure and functionality of MDL1-/- osteoclasts, we performed osteoclastogenesis, resorption assays, tubulin assays and western blot analysis as well as DNA microarray analysis of bone marrow cells isolated from WT and MDL-1-/- mice. Our data show that MDL-1-/-osteoclasts exhibit cytoskeletal impairment in the dysregulation of F-actin rings leading to a significantly impaired bone resorption in vitro and in vivo. Consistent with these observations, genes involved in the cytoskeleton and cytoskeletal processes were down-regulated in MDL-1-/-osteoclasts. Further, MDL-1-/-osteoclasts displayed aberrant microtubule dynamics as compared to WT osteoclasts. Collectively, our data contributes to the elucidation of mechanisms that control bone loss in inflammatory arthritis.
(Funding: National Psoriasis Foundation and NIH R01-AR-062173).

# II. Host-Pathogen Interactions

## 5. Can effector molecules of innate immunity target microbial motility?

Douglas T. Akahoshi[1,2], Dean E. Natwick[3], Sean R. Collins[1,3], Charles L. Bevins[1,2]

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Antimicrobial peptides are key effector molecules throughout nature responsible in part for the defense against microbial pathogens and influencing the composition of colonizing microbes. Defensins are the major antimicrobial peptides produced by Paneth cells in the mammalian small intestine and are essential for maintaining homeostasis between host and microbe. While mature defensin peptides typically have microbicidal activity, human alpha defensin 6 (HD6) lacks such activity yet provides protection from invasion by bacterial pathogens. Using a transgenic mouse model expressing HD6 in Paneth cells, we reported the importance of HD6 in preventing the translocation of pathogenic Salmonella Typhimurium (STM) across the small intestinal epithelium (doi:10.1126/science.1218831); however, the mechanism underlying the inhibition of invasion is not fully understood. We hypothesize HD6 binds to extracellular bacterial protein structures, such as flagella, and inhibits swimming motility through a process of direct binding and self-assembly. Using an agar based motility assay, we show STM radially swim at a slower rate when in the presence of HD6. In ongoing studies using live-microscopy to observe GFP-expressing STM in the presence of HD6, we observe a decrease in STM motility in a concentration dependent manner with some STM appearing to be completely immobilized, but without changes in bacterial viability. Unexpectedly, it appears the immobilization observed is influenced more by the expression of fimbriae than by the expression of flagella. With these results in mind, we plan to expand our investigation to elucidate key molecular determinants and include other microbes to test the broader relevance of this activity of HD6.
(Funding: NIH R37AI1032738 and U01AI125956)

## 6. A Chimeric Hamster PKR Inhibits Vaccinia Virus Replication

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The interaction between host innate immune pattern recognition receptors (PRRs) and their viral inhibitors offer a unique insight into the dynamics of infection, presenting the first major immune barrier to viral replication after transmission and cellular entry. Despite the importance of this interaction, the contribution of specific viral inhibitors of PRRs to viral infection of a specific host is poorly characterized. To address this lack of knowledge, we investigated the importance of two poxvirus inhibitors E3 and K3 from vaccinia virus (VACV) in the context of the PRR protein kinase R (PKR) from different hosts. Using a luciferase-based assay we identified two hamster species: Armenian and Syrian, which possess opposing sensitivities and resistance to VACV E3 and K3. We then created a chimeric hamster PKR possessing both species' resistance to E3 and K3. We hypothesized that the lack of PKR inhibition seen in our resistant phenotypes would correlate with a reduction in total viral replication, since PKR activation halts general translation causing apoptosis and arresting viral replication. To support this hypothesis, we generated cells lines on a T-REx HEK 293 PKR KO background, with Syrian, Armenian, and the chimeric PKR. With these cells we performed infections using vaccinia viruses containing both PKR inhibitors, one but not the other, or neither, and quantified the viral loads by titration. Our results support our hypothesis with luciferase-assay based resistance correlating with ~2-log fold lower viral titers in viruses containing an inhibitor that that specific PKR is resistant to compared to PKR sensitive viruses in vitro. The chimeric PKR was able to reduce viral titers of all viruses tested including the wildtype virus. Our results indicate the importance of poxvirus E3 and K3 inhibition of host PKR for viral replication, suggesting a role for these interactions in determining suitable hosts for viral infection.
(Funding: NIAID R01AI114851)

# 7. The role and formation of Tissue Resident Memory in protection against systemic *Salmonella* infection

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*Salmonella* vaccines are ineffective and are unable to protect individuals living in typhoid endemic areas. Understanding the mechanistic details involved in bacterial clearance and memory development is crucial for the design of effective vaccines. CD4 T cells are required for protection against systemic *Salmonella enterica* serovar Typhimurium (*ST*). While the adoptive transfer of splenic CD4 T cells from immunized mice did not protect naive recipient mice from systemic *ST* challenge, the adoptive transfer of hepatic CD4 T cells from immunized mice was protective. Therefore, a CD4 T cell memory population found in the liver is protective, but circulating memory is insufficient for protection against systemic *ST*. Using parabiosis to join naïve to immunized C57BL/6 mice, we demonstrate that non-circulating memory CD4 T cells are essential for optimal host resistance to systemic *ST* infection. Additionally, immunized mice have CD69+ P2RX7+ tissue resident memory CD4 T cells (CD4 Trm) present in their livers, the main non-lymphoid tissue infected by systemic *ST*. Thus, CD4 Trm in the liver are required for optimal protection against systemic *ST* and a vaccine needs to form this memory subset to be effective. However, the signals activated CD4 T cells need to become hepatic CD4 Trm is not known. To interrogate how to form hepatic CD4 Trm we will use a system in which *in vitro* activated TCR transgenic CD4 T cells are transferred into naïve mice. These adoptively transferred cells can form CD69+ P2RX7+ CD4 Trm in the liver which surface marker expression resemble that of hepatic CD4 Trm seen in immunized mice. The addition of sterile inflammation of the liver by acetaminophen overdose causes an increase in the number of hepatic CD69+ P2RX7+ CD4 Trm formed by the transfer of *in vitro* activated TCR transgenic CD4 T cells, indicating a role of liver inflammation in hepatic CD4 Trm formation. An effective vaccine against *Salmonella* needs to form CD4 Trm in the liver and by understanding the signals needed to form this memory population we can design more effective vaccines against systemic *ST*.

# 8. Neuroinflammation and CNS HIV-1 establishment following mucosal SHIV transmission in rhesus macaques

Sonny R. Elizaldi[1,2,3]*, Danielle Beckman[3]*, Sean Ott[3], Anil Verma[2], Brian A. Schmidt[2], Nancy N. Nguyen[2], Yashavanth S. Lakshmanappa[2], John H. Morrison[3,4], Smita S. Iyer[1,2, 3,5]

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HIV+ patients are at an alarmingly higher risk of developing HIV associated neurocognitive disorders (HAND). HAND is a spectrum of neurocognitive deficits linked to impairments in the prefrontal cortex (PFC) and hippocampus, areas controlling higher cognitive processes. Studies in HIV+ patients implicate acute viremia and inflammation in driving central nervous system (CNS) impairment. However, the timing and implications of viral dissemination to the CNS, particularly the PFC and hippocampus, remain undefined. We tested the hypothesis that HIV-1 is rapidly and actively established within areas of the CNS responsible for controlling cognition. We demonstrate HIV-1 dissemination within the CNS following vaginal transmission of the T cell tropic transmitted/founder SHIV.C.CH505. Strikingly, despite moderate systemic viremia (PVL range: 200-22,000 cp/ml), we found evidence of local HIV-1 replication within the cerebrospinal fluid (CSF) (23 - 900 cp/ml); an observation substantiated by HIV-1 within the choroid plexus. Presence of viral RNA and pro-viral DNA in the brain suggested active influx of infected CD4 T cells and/or monocytes into the CNS. Correspondingly, virus was disseminated within multiple brain regions including PFC, hippocampus, and superior temporal sulcus (STS). In further support of active CNS immune influx, CSF levels of interferon protein 10 and interleukin 6, central drivers of neuroinflammation, were markedly elevated. Presence of IgG against HIV-1 envelope in the CSF reflected equilibration between the systemic and CNS compartments during acute infection. In affirmation of these findings, high-resolution confocal microscopy showed blood-brain barrier disruption in multiple brain regions including: PFC, hippocampus, and STS. Notably, activated microglia and astrocytes, colocalized with p27 HIV-1, and surrounded disrupted blood vessels. Together, our data show rapid HIV-1 dissemination into the PFC and hippocampus following vaginal transmission. Acute HIV-1 establishment within the CNS has significant implications for functional neurological deficits in HAND and lays the foundation to identify mechanisms underlying HAND neuropathogenesis. (Funding: K01OD023034, R03AI138792 (SSI), RF1 RF1AG061001, P51OD011107-57S1 (SSI, JHM))

# 9. Local protection against Chlamydia depends on rapid mobilization of circulating memory to the female reproductive tract

Jasmine C. Labuda[1,2,3], Oanh H. Pham[2,3], Stephen J. McSorley[1,2,3]

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*Chlamydia trachomatis* is the most prevalent bacterial sexually transmitted infection worldwide and yet no vaccine currently exists to protect the public from this reproductive tract pathogen. Recent reports suggest that CD4 tissue resident memory cells ($T_{RM}$) are essential for vaccine-induced protection against *Chlamydia trachomatis* in a mouse infection model. Additionally, CD4 $T_{RM}$ in the female reproductive tract (FRT) have been shown to co-localize with APCs in memory lymphocyte clusters (MLCs) to enhance secondary adaptive immunity to reproductive tract infections. Here, we examine a requirement for CD4 $T_{RM}$ and MLCs in protective immunity against infection with *Chlamydia muridarum* (*Cm*). Using parabiosis of naïve and *Chlamydia*-immune mice, we demonstrate that although CD4 $T_{RM}$ form in the FRT after primary *Cm* infection, they are not required for protection. Furthermore, histological analysis of FRT tissue from parabionts revealed that circulating memory is sufficient for protection against intravaginal challenge with *Cm* in the absence of CD4 $T_{RM}$ or MLCs in the reproductive tract. Moreover, this protective circulating memory can be induced through intravaginal or intranasal challenge with *Chlamydia*, indicating that a strong mucosal immunization can generate circulating protection in a vaccine setting. Ongoing work using adoptive transfers and antibody depletions of CD4 T cells and B cells will reveal which memory lymphocytes are responsible for the observed circulating protection.
(Funding: NIAID RO1 AI103422).

# 10. g-NK cells are a novel subset that negatively impact immune reconstitution of HIV patients

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We have identified a novel subset of NK cells, called 'g-NK cells', which display adaptive immune features, including clonal-like expansion and long-term persistence. The presence of g-NK cells is associated with previous infection by cytomegalovirus and have enhanced response to broad range of viral-infected cells in the presence of virus-specific antibodies. We hypothesize that g-NK cells contribute to low CD4 counts in HIV patients and CD4 recovery during antiretroviral therapy (ART). In a cohort of 18 chronically infected HIV patients naive to treatment before and 12 months after starting ART, the presence of g-NK cells, as well as their frequencies and phenotypic characteristics, were measured by flow cytometry after intracellular staining of FcR-gamma signaling protein following cell surface marker staining. 17 HIV-negative control underwent identical procedures. Plasma biomarkers of inflammation were measured by ELISA and cytokine production by g-NK cells and conventional NK cells after stimulation with HIV-infected cells in the presence or absence of HIV-seropositive plasma. We observed that (1) HIV patients possessed higher frequencies of g-NK cells compared to HIV-negative control groups [39.9% and 10.33%, $p=0.0320$], (2) HIV patients with readily detectable g-NK cells show a trend toward lower CD4+ T cell count before [$p<0.08$] and 1 yr after ART [$p<0.01$]. g-NK cells did not change levels before and after the treatment, and (3) compared to conventional NK cells, g-NK cells produced greater amount of IFN-γ and TNF-α in response to HIV-infected cells in the presence of HIV-seropositive plasma. g-NK cells are more frequent in HIV-infected patients compared to controls and may contribute to low CD4 counts in HIV patients and poor recovery during ART. g-NK cells may be a useful biomarker for predicting how the CD4+ T cell population may recover during HIV treatment.
(Funding: NIAID 5R01AI110894-02)

# 11. Trogocytosis by Entamoeba histolytica mediates acquisition and display of human cell membrane proteins and evasion of lysis by human complement

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*Entamoeba histolytica* is the protozoan parasite responsible for amoebiasis, a potentially fatal diarrheal disease. We have previously shown that *E. histolytica* kills human cells through a mechanism that we termed trogocytosis (*trogo-:* nibble), due to its resemblance to trogocytosis in other organisms. One consequence of trogocytosis in mammalian immune cells is that cell membrane proteins from the nibbled cell can be acquired and displayed by the recipient cell. In this study, we tested the hypothesis that through trogocytosis of human cells, *E. histolytica* acquires and displays human cell membrane proteins. We demonstrate that *E. histolytica* displays human cell membrane proteins via trogocytosis leading to protection from lysis by complement-active human serum. We showed that protection is actin-dependent, requires direct cell-cell contact and only occurs from trogocytosis of live human cells but not phagocytosis of dead human cells. Likewise, mutant amoebae defective in phagocytosis, but not trogocytosis, were protected from human complement. We also demonstrate that amoebae are protected complement after trogocytosis of both human Jurkat cells and erythrocytes in a dose-dependent manner, and that ingestion of human cells results in less deposited C3b protein on the amoebae surface. Finally, we show that amoebae acquire CD59 via trogocytosis, a key complement regulatory protein. Currently, we are testing the contribution of CD59 and other acquired proteins to protection from complement. Our studies are the first to demonstrate that amoebae can display human cell membrane proteins and suggest that acquisition and display of membrane proteins is a general feature of trogocytosis that is not restricted to trogocytosis between mammalian immune cells. These studies have major implications for interactions between *E. histolytica* and the immune system and also reveal a novel strategy for immune evasion by a pathogen.
(Funding: NIH NIAID # AI108814, The Pew Charitable Trusts, Hellman Fellows Fund)

# 12. Effective clearance of Chlamydia from the female reproductive tract in the absence of T-bet+ Th1 cells

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Protective immune responses to *Chlamydia* infection within the female reproductive tract (FRT) are incompletely understood. MHC class II-restricted CD4 Th1 responses are thought to be vital for bacterial clearance, due to their capacity to secrete IFN-γ. However, other studies suggest protective or pathogenic roles for additional CD4 T helper subsets. We used a variety of gene-deficient mice to re-examine bacterial clearance following primary genital infection of C57BL/6 mice with *Chlamydia muridarum*. As seen previously, IFN-γ-, and IFN-γR-deficient mice resolved much of FRT infection, but experienced systemic dissemination and 100% mortality with an average median survival of approximately 4 weeks. Mice lacking the Th1 subset defining transcription factor T-bet or the Th2 transcription factor STAT6 both effectively cleared infection from the reproductive tract, suggesting that neither Th1 nor Th2 cells are essential for local bacterial control. In contrast, RORγt mutant mice selectively deficient in Th17 responses exhibited a week delay in clearance compared to wild-type mice. While systemic responses in T-bet-/- mice exhibited increased Th17 markers, Th1 subsets were minimally upregulated in RORγt mutant mice, indicating that compensation between these subsets does not explain bacterial clearance. In conclusion, timely local clearance of *Chlamydia muridarum* from the reproductive tract requires Th17 CD4 T cells, but will ultimately clear independent of classical T-bet+ Th1 and RORγt+ Th17 cells individually. Studies are underway to examine which alternative CD4 T cell mechanisms contribute to bacterial clearance within the FRT.
(Funding: NIAID RO1A1103422, NIAID T32AI060555)

# 13. IgM-secreting cells in non-human primates

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Secretion of IgM occurs spontaneously in the absence of microbial encounter, as so-called "natural IgM". IgM is also produced rapidly by antigen-stimulated B cells following their differentiation to plasmablasts. While in mice the responsible cells have been identified as belonging to two distinct B cell subsets, B-1 and B-2, respectively, whether such subset distinctions exist also in humans or in non-human primates has been the subject of much debate. Using known functional differences in antigen- and TLR-responsiveness of murine B-1 and B-2 cells, we aim to determine the antigen-induced and natural IgM secreting cells in the rhesus macaque, the most commonly used pre-clinical non-human primate model for vaccine and infectious disease research. For this we used a set of cell surface markers, namely CD20, CD21, CD27 and CD38, to distinguish major B cell subsets in the spleens of rhesus macaques. Simultaneous staining for surface IgM-, IgD- and IgG-B cell receptor helped to separate class-switched from non-switched B cells. The various identified subsets are then isolated by flow cytometry and tested by ELISPOT analysis for IgM secretion, either spontaneously, i.e. in the absence of stimulation, or in response to anti-IgM, and/or TLR-agonists. Future studies are aimed at identifying the antigen-induced IgM producing cells by probing for virus-specific B cells in PBMC from rhesus macaques vaccinated 7 – 28 days prior with canine-distemper virus, as identified using a fluorescently-tagged recombinant distemper virus H-protein. This study will provide novel information to help distinguish natural and antigen-induced IgM in immune protection from infections.
(Funding: NIH U19AI109962)

# 14. 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 intracellularly. 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 protein CBL, signifying the potential importance of CBL for antibacterial responses. Moreover, our lab made the unexpected discovery that *Cbl*$^{-/-}$ BMDMs infect with *Mtb* displayed a hyperactive antiviral phenotype as indicated by increase 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 U937, using short hairpin RNA. These knockdown cell lines were stimulated with either viral mimetics, viruses, or *Mtb*. Antiviral response was quantified by detecting for mRNA levels of IFNβ and IFIT-1 through qRT-PCR. A two/three-fold difference was detected between the IFNβ/IFIT-1 levels of the knockdown versus the wildtype group. This result suggests that knocking down CBL might not have a robust impact on antiviral responses in human cells. To determine the functional impact of knocking down CBL, we infected macrophages with *Mtb* strains carrying a Lux operon that would allow us to measure *Mtb* replication through bioluminescence. Our function assay demonstrated a significant increase in bacteria growth in the CBL knockdown macrophages compared to wildtype, suggesting an important role for CBL in inhibiting *Mtb* replication.

# 15. Neonatal Antibiotic Treatment Alters Normal Lung Development And Physiology During The First Year Of Life

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Antibiotics are commonly administered to human infants, which may result in changes to the microbiome that persist with maturity. It is currently unknown whether disruption of progressive commensal colonization can modulate normal development and physiology of the lung in the first year of life. Because the microbiome has been reported to influence pulmonary immunity and response to pulmonary injury in animal models, we hypothesized that antibiotic administration in infants may alter the normal growth and function of the lung during postnatal development. To test our hypothesis, we investigated whether antibiotic treatment of infant rhesus macaque monkeys can result in differential expression of developmental genes in the respiratory tract and pulmonary function. Indoor housed infant monkeys were treated with an antibiotic cocktail consisting of ampicillin, gentamicin and vancomycin during the first week of life. Saline-treated infant monkeys served as controls. All infant monkeys were breast-fed by their dams until weaned at 5 months of age. At 6 months of age, pulmonary function testing was conducted and lung specimens were collected following necropsy. Gene expression in the airways was assessed using qRT-PCR. Genes associated with growth and development, including WNT3A and SOX2, were decreased in proximal airways of antibiotic-treated animals relative to controls. MMP16 expression was increased in airways of antibiotic-treated animals. Vital capacity and expiratory reserve volume were reduced in antibiotic-treated animals relative to controls. When separated by sex, changes in lung volumes were more pronounced; inspiratory capacity was decreased in antibiotic-treated males compared to control males while there were no significant differences between females. These results indicate that the administration of antibiotics to neonatal monkeys can cause changes in developmental gene expression and lung function. This suggests that neonatal disruption of the microbiome may alter normal growth and function of the lung.
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# 16. Understanding the Role of the Salmonella Typhi Vi Capsular Polysaccharide in Neutrophil and Macrophage Phagocytosis

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*Salmonella* Typhi is the causative agent of typhoid fever, which is a life-threatening, systemic disease, with an estimated global disease burden of 21.6 million cases annually, resulting in about 220,000 deaths. Due to the absence of convenient animal models to study *S.* Typhi, our understanding of typhoid fever pathogenesis is still incomplete. One major virulence factor of *S.* Typhi is the Vi polysaccharide capsule, which, like many other bacterial capsules, has long been thought to play a role in preventing phagocytosis and complement killing. However, like other *Salmonella* serovars, *S.* Typhi is taken up by host macrophages by phagocytosis and survives and replicates intracellularly within these cells. It is not well understood why *S.* Typhi, which survives and replicates within macrophages, also possesses an anti-phagocytic capsule, which is more characteristic of an extracellular pathogen. Here, we demonstrate that the *S.* Typhi Vi capsule selectively prevents phagocytosis and uptake of the bacteria depending on the host cell type. We found that interestingly, the Vi capsule prevents phagocytosis of *S.* Typhi by neutrophils, which typically generate a potent reactive oxygen species response to facilitate killing of bacteria. In contrast, the Vi capsule does not prevent uptake of the bacteria by macrophages, which remain the site of *S.* Typhi growth and replication. This suggests that there exists a receptor that is present on macrophages, but not on neutrophils, that is able to bind to and recognize the Vi capsule and facilitate this selective phagocytosis. We found that the C-type lectin receptor DC-SIGN, which is more highly expressed on macrophages than on neutrophils, functions as a receptor for binding to the Vi capsule, leading to uptake of *S.* Typhi. Interestingly, there are eight genetic homologs of DC-SIGN in mice, with no clear DC-SIGN ortholog. Because DC-SIGN appears to be important for interaction of human

macrophages with capsulated *S.* Typhi, this difference in DC-SIGN expression and function between mice and men could shed light as to why *S.* Typhi remains a human restricted pathogen. These findings that the Vi capsule of *S.* Typhi interacts differently with different host phagocytes represents a step forward in our understanding of how typhoidal *Salmonella* serovars interface with host immunity and will provide important new insights into the pathogenesis of typhoid fever.
(Funding: Public Health Service Grants F30AI136309, AI088122 and AI096528, UL1 TR 000002 and linked award TL1 TR 000133)

# III. Immune Regulation

## 17. Challenging The Paradigm For Impaired Healing In Aging

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The generally accepted clinical dogma is that wound healing is delayed in aged individuals, however supporting evidence and mechanistic understanding are conflicting and incomplete. Older patients are known to have systemic inflammation and diminished immune responses, both of which may contribute to impaired healing. We hypothesized full-thickness cutaneous wounds would heal more slowly because of increased inflammation in aged (2+ yrs, equivalent to 69+ y.o. humans) compared to young (10-12 wks, equivalent to 20-25 y.o. humans) BALB/c mice. Contrary to our hypothesis, we found that aged mice trended toward better healing compared to young mice despite having greater weight loss. While the aged mice did show increased pro-inflammatory mediator gene and protein expression, they initiated pro-reparative immune responses such as increased wound IL-10 and TGFβ gene expression earlier than young mice, which combined may account for the comparable healing. Also potentially contributing to healing in aged animals was their elevated systemic level of dopamine, a catecholamine known to attenuate IL-8 effects, inhibit superoxide anion production, and induce neutrophil apoptosis, which are known to impair healing in sterile wounds. When repeated in male and female C57BL/6 aged and young mice to rule out sex and strain dependence, we found the same trend of equivalent healing with greater weight loss. While our results do not agree with popular consensus, it is evidence that wounds have deleterious effects on the overall health of the older wounded individual. An additional stress, such as wound infection, may overwhelm the organism's reparative functions, and result in impaired healing.
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# 18. The effect of mouse cytomegalovirus infection on natural killer cell development following hematopoietic stem cell transplant

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Hematopoietic stem cell transplant (HSCT) is a treatment for patients with hematological malignancies who are not eligible to receive intensive cytoreductive therapy and for patients experiencing relapse. Cytomegalovirus (CMV) is an extremely prevalent infection and in immune-compromised patients, it is a significant cause of morbidity and mortality. Approximately two-thirds of seropositive patients experience CMV reactivation following HSCT. Interestingly, there have been reports that CMV reactivation causes increased activation of NK cells which actually benefits graft-versus-tumor effects. Our study objective is to delineate the kinetics of this effect and determine whether there are long-term functional differences of NK cells exposed to CMV early on in development. We hypothesized that immune reconstitution is impacted by CMV infection and that the lymphopenic and inflammatory environment post-HSCT detrimentally affects the immune response to CMV infection. Using a syngeneic HSCT model in C57BL/6 mice (total body irradiation followed by bone marrow cell rescue), we studied de novo NK cell repopulation. At 8 days post-transplant, mice were inoculated with a low dose of mouse CMV. We found a significantly higher viral burden in the HSCT recipients compared to control mice. We found that CMV-specific NK cells (Ly49H+) rapidly expanded following CMV infection post-HSCT, but experienced a population collapse after two weeks. This is possibly due to exposure to a primary virus infection early on in development and/or the increased viral burden in the HSCT environment. There was a higher frequency of mature NK cells and IFN-gamma producing NK cells following CMV infection in the HSCT environment, suggestive of increased activation and accelerated differentiation. The disproportionate loss of the Ly49H+ NK cells may cause long-term functional defects in the HSCT recipient immune response.
(Funding: R01 HL140921)

# 19. Altered composition of CD14++CD16-, CD14++CD16+, and CD14+CD16++ monocyte subtypes in ASD

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Autism spectrum disorders (ASD) are a collection of neurodevelopmental disorders that are characterized by impairments in social communication and restricted repetitive behaviors. ASD has been associated with chronic inflammation resulting from disturbances of the regulatory immune system controlling the overall immune response. Monocytes are key regulators of the inflammatory response derived from precursors in the bone marrow and can be subdivided into subsets that differ in size, trafficking, and receptor expression. Classical CD14++CD16- monocytes are involved in the production of inflammatory cytokines, intermediate CD14++CD16+ monocytes are involved in the production of anti-inflammatory cytokines and reactive oxygen species in addition to proinflammatory mediators, and non-classical CD14+CD16++ monocytes are patrolling cells involved in tissue repair and removal of debris. To assess the composition of these monocyte subtypes in ASD, PBMCs isolated from whole blood from typically-developing and ASD participants were phenotyped by flow cytometry. Preliminary data suggest that consistent with previously-reported immune regulation deficits, a greater proportion of inflammatory classical CD14++CD16- monocytes were found to be present in the peripheral blood of individuals with ASD. This altered composition of monocyte subsets could contribute to the pathophysiology observed in children with these disorders.
(Funding: NIH R01HD090214)

# 20. Role of the SET-like domain of Blimp-1 in plasma cell differentiation

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Secreted immunoglobulin (Ig), which is vital for neutralizing pathogens yet detrimental in autoimmune diseases, is predominantly produced by plasma cells (PCs). Blimp-1 is both necessary and sufficient for PC fate and induces Ig secretion by regulating alternative polyadenylation (APA) of the Ig heavy chain transcript. Through structure/function experiments in cell lines, we showed that APA of the Ig heavy chain transcript is dependent on a unique Blimp-1 domain, named PR, that remains to be characterized. Intriguingly, this domain resembles evolutionarily conserved lysine methyltransferase domains known as SET. Whether Blimp-1's SET-like domain also acts as a lysine methyltransferase is unknown. To further study this, we developed a novel mouse model (PR*) which has a B cell specific, inactivating mutation in the SET-like domain of Blimp-1. We found that mice harboring this mutation display low levels of serum Ig both at steady-state and in response to immunization. In fact, the diminished levels of serum Ig are comparable to levels seen in Blimp-1 null mice. We also used a TLR ligand stimulation of B cells *in vitro* and found that cells from PR* mice exhibit lowered Ig secretion, comparable to the secretion defect of Blimp-1 null B cells. Importantly, we confirmed that the defect in Ig secretion occurs at the RNA level. These results lead us to conclude that the SET-like domain of Blimp-1 is critical for its function in promoting the switch to secreted Ig. Whether the PR domain affects other aspects of PCs or global APA will be examined by comparing the transcriptomes from WT, PR*, and Blimp-1 null cells. Since the PR domain resembles the lysine methyltransferase SET domains, we will also incubate nuclear extracts with radioactively labeled S-adenosylmethionine (SAM) to track methylation reactions. Overall, this mouse model will allow us to separate out the role of the PR domain to determine its effect on APA as well as its role in PC differentiation.
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# 21. Allosteric shifts in CD11c affinity activate a pro-atherogenic state in arrested intermediate monocytes

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Circulating intermediate monocytes (iMo; CD14+CD16+) increase in number during coronary artery disease (CAD) and their recruitment to inflamed arteries is implicated in mortality following myocardial infarction (MI). Shear resistant monocyte arrest is regulated by □2-integrin (CD11c/CD18) that activates □1-integrin (VLA-4) to bind VCAM-1 that facilitates diapedesis across endothelium. To assess the role of integrin activation in pro-inflammatory monocyte recruitment and changes in phenotype that contribute to MI in cardiac patients. Methods- Whole blood samples were obtained from patients treated for coronary artery disease (CAD) and non-ST elevated myocardial infarction (NSTEMI), along with aged matched healthy controls. Monocyte subset identity based upon chemokine, integrin, and CD14/CD16 expression was quantified by flow cytometry. Real time phenotyping of monocyte activation following recruitment on a substrate of inflamed human aortic endothelium or recombinant VCAM-1 under fluid shear stress was assessed using an arterial mimetic microfluidic device (A-Chip). Distinct inflammatory activation states were then assessed using affinity modulating allosteric antibodies to CD11c. Results- iMo CD11c receptor expression, activation of VLA-4 dependent arrest, and diapedesis across inflamed arterial endothelium was highest in NSTEMI patients. Conversion to an IL-1β+ pro-atherogenic phenotype coincided with a downshift in CD11c affinity that triggered membrane shedding of CD16 in a majority of iMo from cardiac patients but not healthy age matched subjects. Conclusion- Mechanotransduction via high affinity CD11c activated VLA-4 dependent arrest and conversion of iMo to a pro-atherogenic phenotype, which correlated directly with the extent of myocardial injury and the onset of MI.

# 22. TLR adaptors MyD88 and TRIF are critical for extrafollicular B cell responses to influenza

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Antibodies produced during primary influenza infection can be protective and form rapidly. This occurs independently of germinal centers (GCs) in extrafollicular B cell (EF) responses, where antibody-secreting cells (ASCs) blast and produce antibodies in the medulla of the mediastinal lymph node. While the EF response to influenza is known to be mostly T-dependent, it is unknown why B cells are shunted away from a GC fate and what factors lead to generation of EF ASCs. We show that absence of both Toll-like receptor (TLR) adaptors MyD88 and TRIF (double knockout, DKO) cause severe, B cell-intrinsic reductions in EF responses to influenza. Observing a reduction of the B cell differentiation factor IRF4 in DKO plasmablasts *in vivo*, we used *in vitro* culture systems to assess BCR signaling and T cell help by stimulating B cells with anti-IgM$(Fab)_2$ and CD40L and/or BAFF, respectively. DKO B cells showed reduced survival in culture, which was rescued by providing either CD40L or BAFF. Strikingly, DKO B cells barely proliferated in response to any dose of anti-IgM, with or without CD40L/BAFF. High-dose BCR stimulation further reduced the viability of DKO B cells, which correlated with reduced IRF4 induction and altered NFkB signaling. Specifically, we show by image flow cytometry reduced nuclear localization of NFkB c-Rel, a positive regulator of IRF4, following BCR stimulation of DKO compared to wild type B cells. We propose that EF responses during influenza infection require not only antigen and T cell help, but also MyD88 and/or TRIF signaling to drive activation of c-Rel. This enhances antigen-specific B cell survival, proliferation, and the strong upregulation of IRF4 required for plasmablast differentiation.

# 23. PD-1 regulates response to bystander activation of memory CD8 T cells

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Inflammatory cytokines, released in virally infected tissues, activate bystander memory T cells, expressing CD132 and CD122, in an antigen non-specific manner through signal 3 alone to provide early anti-viral protection in an NKG2D-dependent manner. We have previously observed that IL-2 stimulation expands bystander memory CD8 T cells that are NKG2D+/Programmed cell death protein 1(PD-1)-/CD25-. However, it is unclear if the presence of PD-1 regulates the ability of memory T cells to respond to signal 3 alone. In our study, IL-2 *in vitro* culture for 3 days results in proliferation of memory T cells in human PBMCs and preferential expansion of memory CD8 over CD4 T cells. PD-1- CD8 T cells had greater cycling of proliferation compared to PD-1+ CD8 T cells, as observed by dilution of CPeFluor670 staining. Similarly, mouse splenocytes proliferate in response to IL-2 *in vitro*. Ki67+ CD8 T cells were found to be predominantly PD-1-, while ConA-stimulated Ki67+ CD8 T cells were predominantly PD-1+. Adoptively transferred memory OTI CD8 T cells but not naïve OTI CD8 T cells expanded in vivo in the liver at 3-4 days post-infection with 2x10^4 PFU murine cytomegalovirus (MCMV), and a greater percentage of PD-1- OTI CD8 T cells were Ki67 positive compared to PD-1+ OTI CD8 T cells. We conclude that the expression of PD-1 on memory CD8 T cells can regulate response to signal 3 alone. Future studies will examine the impact of PD-1 blockade on the bystander response in anti-viral protection.
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# 24. Cysteinyl leukotrienes (CysLTs) promote burn wound healing

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Burn wounds are severe cutaneous injuries that are characterized by intense inflammation marked by infiltration of the wound site by a multitude of immune cells from the periphery including: neutrophils, monocytes, and lymphocytes. The immune milieu of the burn site consists of elevated amounts of inflammatory mediators such as cytokines, chemokines, and leukotrienes. This leads to prolonged inflammation resulting in delayed healing. Leukotrienes are derived from the 5-lipoxygenase pathway and include LTB4, LTC4, LTD4, and LTE4; with the latter three being categorized as the cysteinyl leukotrienes (cysLTs). LTB4 is a potent chemoattractant and activator of neutrophils, and the cysLTs are classically known to be involved in allergic inflammatory responses. Interestingly, previous *in vitro* studies have suggested that cysLTs exert pro-healing functions by inducing proliferative signals in endothelial cells, and mediating contractile forces by myofibroblasts. Therefore, our study aims to investigate the role of cysLTs in wound healing through an *in vivo* murine burn injury model. We employed C57BL/6 mice, treated either with montelukast, an FDA-approved cysLT receptor antagonist, or vehicle as control. When compared to vehicle control, we found that montelukast treatment resulted in decreased re-epithelialization, associated with a reduction in angiogenesis and proliferation of keratinocytes. Furthermore, we observed that montelukast-treated wounds exhibited decreased mature collagen content, indicating a perturbation in healing. Inhibition of cysLT signaling also resulted in downregulation of growth factors that are crucial for wound healing. Collectively, we conclude that cysLTs promote burn wound healing by inducing expansion of keratinocytes, revascularization, and regulating the expression of reparative genes in the wound site. This study uncovers a potential in exploiting the functions of cysLTs in driving burn wound healing.
(Funding: Shriners Hospitals for Children)

# 25. Effects of E-Cigarette Vapor on the Pulmonary Immune System

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E-cigarettes are nicotine delivery devices that have rapidly gained popularity in recent years. It is not well understood how the use of these devices impact the pulmonary immune system and its ability to defend against respiratory viral infection. To this end, BALB/c mice were exposed to e-cigarette aerosols for 3 hours per day, 5 days per week for 2 weeks. Lung tissue and serum were collected following 1, 3, 5 and 10 days of exposure. Average serum nicotine and cotinine concentrations during the 10-day exposure were 133 ± 46 ng/mL and 712 ± 302 ng/mL, respectively, which is consistent with levels found in active tobacco smokers. Compared to filtered air controls, e-cigarette exposure significantly increased total cells and macrophages in bronchoalveolar lavage fluid on days 1 and 5, and significantly decreased neutrophils on day 1, suggesting that e-cigarette vapor may change the cellular infiltrate of the lungs. mRNA expression of IL-1β, IL-6, TNFα and IL-10 in right lung tissue was significantly decreased at all timepoints, suggesting possible dampening of the pulmonary immune response. To investigate how these cellular changes may affect the response to viral stimuli, human Type II epithelial cells were treated with e-cigarette conditioned media 24 hours prior to poly(I:C) stimulation. Compared to controls, e-cigarette treatment of type II epithelial cells resulted in significantly decreased expression of the critical interferon pathway genes IRF3, IFNα, and IL-1β following poly(I:C) stimulation. E-cigarette media alone was able to significantly decrease the expression of IRF3 in these cells, suggesting e-cigarette vapor may impair key genes necessary for the recognition of and sufficient response to respiratory viruses.
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# 26. Correlating B Cell RNA Signatures in Solid Tumors with Immunotherapy-Treatment Free Survival Times

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B cells are multifunctional lymphocytes that play important roles in immune defense. Loss of B cell tolerance to self-antigens contributes to several disease pathologies including autoimmune diseases and cancer. While B cell targeting is a promising approach to combat autoimmune diseases, their role in anti-tumor immunity is incompletely understood. In this study, we investigated the prognostic significance of B cell RNA signatures of a large number of solid tumors with human patient survival and B cell infiltration. The study was performed by systematically analyzing The Cancer Genome Atlas (TCGA) datasets for mRNA expression of three B cell specific proteins: CD19, CD79A, and CD20 and binning high and low mRNA expression to correlate with overall patient survival. The study showed significant differences in overall survival between the two groups. High B cell mRNA presence correlated with improved clinical outcome for two tumors: Head and Neck (n=523): HR=0.526, 95% CI 0.38-0.72 and Lung Adenocarcinoma (n=1059): HR=0.753, 95% CI, 0.59-0.95. The clinical metadata and the survival analysis herein provides the first evidence for a favorable prognostic role of B cells in these two types of cancers.

# 27. Attenuation Of Muc5b Expression In Infant Airway Epithelium Is Intrinsically Regulated With Developmental Stage

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Mucins play an important innate immune role in pulmonary host-pathogen defense. MUC5B is one of two major mucins in the lung. Dysregulated expression of MUC5B is linked to chronic respiratory disease in humans. Using a primate model of lung development and RNA-seq analysis, we determined that tracheobronchial epithelial cells (TBEs) derived from infant rhesus monkeys have reduced expression of MUC5B relative to adult monkeys. We hypothesized that MUC5B is developmentally and intrinsically regulated within the respiratory tract. We used primary TBE cultures established from infant (n=3) or adult (n=3) macaque lung biospecimens obtained from the California National Primate Research Center Pathology Unit. Upon confluence, cultures were differentiated under air-liquid interface conditions for two weeks. Following differentiation, MUC5B mRNA expression in cultures was measured weekly for three weeks. Immunofluorescence staining for MUC5B in both infant and adult lung tissue sections was conducted with a rabbit anti-human MUC5B polyclonal antibody. We found that adult monkey TBEs displayed a progressive increase in MUC5B mRNA during the evaluation period, with a significant peak of expression at three weeks. Relative to adult cell cultures, infant monkey TBEs showed reduced expression of MUC5B mRNA *in vitro* for the 3-week period. MUC5B expression was detected in large airway epithelium and submucosal glands of monkey lung tissue sections. Expression of MUC5B was attenuated in infant monkey lungs compared to adult lungs, with a reduction in immunofluorescence detected in the proximal airways. These studies demonstrated that the attenuation of MUC5B expression in infant cell cultures is maintained over a 3-week period *in vitro*, suggesting an irreversible developmentally intrinsic regulation. Future studies will investigate transcriptional mechanisms during development that regulate MUC5B expression *in vivo*.

## 28. Role of SAM in Plasma Cell Differentiation and Function

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Plasma cells (PCs) are terminally differentiated B cells which secrete high levels of immunoglobulin (Ig). While Ig is essential for neutralizing and clearing pathogens, an excess of Ig is detrimental in autoimmune conditions. The transcription factor Blimp-1 is necessary and sufficient for this transition to PCs and is known to regulate Ig secretion. PC differentiation is reliant on multiple levels of regulation - epigenetic, post-transcriptional, and translational, which we hypothesize are dependent on methyltransferase activity for dynamic methylation. PCs also upregulate high levels of CD98, which functions as a membrane transporter for amino acids such as methionine, and thus initialization of the methionine cycle. In this cycle, methionine adenosyltransferase (MAT) coordinates the production of the methyl donor S-adenosylmethionine (SAM) from methionine. We are interested in determining whether this strong expression of CD98 is dependent on Blimp-1 or regulated by PCs, and to understand the role of SAM is this differentiation event. Utilizing a Blimp-1-YFP reporter mouse line, we are able to detect the transition to PCs in-vitro and study the requirement for SAM during this transition. Depletion of the precursor to SAM, methionine, resulted in a loss of PC number and secretory capacity. To specifically target the role of SAM for PCs, we treated in-vitro cultured PCs with inhibitors of MAT2A. Preliminary data provides evidence that inhibition of SAM reduces PC phenotype, function, and viability. We aim to determine the role of SAM in Ig secretion through transcriptional analysis and metabolomics, and hypothesize that Ig post-transcriptional regulation in PCs is controlled by methyltransferase activity.

# IV. Neuroimmunology

## 29. *In Vivo* Magnetic Resonance Imaging and Spectroscopy Detect Alterations in Brain Structure and Metabolites in a Rat Model of Maternal Autoantibody-Related Autism

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Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by altered social, communicative, and repetitive behaviors, though of unknown etiology. The Van de Water lab has previously identified a set of potentially pathogenic autoantibodies (aAb), specific to ASD, in the plasma of ~20% of mothers of ASD children. We have termed this phenomenon maternal autoantibody-related (MAR) ASD. These aAb have specific reactivity to key developmental proteins, such as lactate dehydrogenase A and B (LDH-A/B), collapsin response mediator protein 1 (CRMP1) and stress-induced phosphoprotein 1 (STIP1). However, mechanisms linking these aAb to altered neurodevelopment is still unclear. To understand the effects of these aAbs, *in vivo*, we have created an active immunization model in rats, whereby we induce endogenous aAb production in rat dams to specific epitopes related to ASD diagnosis in the clinical population. To assess broad effects of maternal aAb on offspring neurodevelopment, we used longitudinal magnetic resonance imaging (MRI) to evaluate volumetric changes in global and regional brain structure in MAR-treated animals (N=12) compared to control animals (N=16). Simultaneously, we also collected *in vivo* spectroscopic data from the prefrontal cortex (PFC) of rat brains using proton nuclear magnetic resonance ($H^1$ NMR). The PFC being a brain region of significance in ASD based on clinical studies and symptomology. In this manner we could compare differences in levels of key neurometabolites as a result of MAR treatment and correlate these findings with changes in regional brain volume. Analysis of MRI results revealed treatment-induced volumetric increases in several brain regions including sensory and motor cortices as well as white matter

regions. Furthermore, MAR-treated rats displayed altered levels of neurometabolites in the PFC compared to controls. Specifically, an increase in the amino acid taurine and a decrease in the level of choline was observed in MAR offspring compared to control animals. These results were seen at both timepoints of analysis, in both juvenile and young adult rats. Moreover, taurine levels in MAR-treated animals appeared to correlate strongly with cingulate cortex volume – the closest region to the PFC in the brain atlas used for this study. This being of particular interest as taurine is a known osmolyte and important for early neuronal signaling. No correlations were seen between these neurometabolites and brain volume in control animals. Additionally, cingulate cortex development in MAR-treated animals appeared to follow an altered trajectory compared to control animals. Overall these data reveal alterations in brain structure as well as region-specific metabolite levels in our MAR rat model. Further studies are needed to deduce mechanisms underlying these changes and how they may relate to clinical ASD findings.
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# 30. Dysregulated immune gene expression in monocytes in children with autism spectrum disorders.

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Autism spectrum disorders (ASD) are a collection of heterogeneous developmental disorders that are characterized by deficits in social interactions, communication, and stereotypical behaviors. Immune dysfunction is a common co-morbidity seen in ASD, with innate immune dysfunction seen both in the brain and periphery. We previously identified significant differences in peripheral blood monocyte cytokine responses after stimulation with lipoteichoic acid and lipopolysaccharide, which activate toll-like receptors (TLR) 2 and 4 respectively. However, an unbiased examination of monocyte gene regulation in response to these stimulants had not yet been performed. To identify how activation of TLRs impacts gene expression in ASD monocytes, we isolated peripheral blood monocytes from 27 children with ASD and 23 typically developing (TD) children and cultured them with LTA or LPS for 24 hours, then performed RNA sequencing to profile mRNA responses between non-treated and treated samples for each diagnosis. We identified genes with differential expression in non-treated compared to stimulated cells for both TD and ASD samples and then compared the responses between the two diagnoses. Activation of both TLR2 and TLR4 induced expression of immune genes, with a subset that were differentially regulated in ASD compared to TD samples. In response to TLR4 activation, monocyte cultures from ASD patients showed a unique increase in a KEGG immune pathway that includes key immune regulator genes such as FAS cell surface death receptor (*FAS*), nuclear factor kappaB (*NFKB1*), Interleukin Receptor Type1 (*IL1R1*), and TGF beta Kinase 3 (*TAB3*) in ASD. Notably, monocytes from TD patients uniquely showed a consistent decrease in expression of genes associated with translation and rRNA metabolism in response to both TLR2 and TLR4 activation. A similar decrease was not observed in the ASD samples, suggesting a failure to properly regulate a prolonged immune response. As monocytes are involved in early orchestration of the immune response, our findings will help elucidate the mechanisms regulating immune dysfunction in ASD.
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# 31. Myelin as a novel signaling factor in long-term regulation of the microbiota-gut-brain axis

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Myelination in the peripheral and the central nervous system is critical in regulating motor, sensory, and cognitive functions. As myelination is rapid during early life, neonatal gut dysbiosis can potentially alter proper myelination by dysregulating immune responses and neuronal differentiation. Despite common usage of antibiotics (Abx) in infants, the impact of neonatal Abx-induced dysbiosis on the development of microbiota, gut, brain (MGB) axis, including myelination and behavior is unknown. We hypothesized that neonatal Abx-induced dysbiosis chronically dysregulates myelination in both the gut and the brain altering the MGB axis. Neonatal C57BL/6 mice were orally gavaged (50ul) daily with an Abx (neomycin [1mg/ml], vancomycin [0.5mg/ml], ampicillin [1mg/ml]) cocktail or water (vehicle) from postnatal day 7 (P7) until weaning (P23) to induce dysbiosis. Behavior (cognition [novel object recognition [NOR] task; light/dark [L/D] box), microbiota (16S Illumina sequencing), and qPCR (ileum, colon, hippocampus and pre-frontal cortex [PFC]) were performed in adult mice (6-8 weeks). Neonatal Abx administration led to behavioral alterations (cognitive deficits and anxioloytic behavior) coupled with persistent intestinal dysbiosis in adulthood, characterized by decreased Shannon alpha-diversity and altered Bray-Curtis beta-diversity versus shams. Expression of myelin genes (*Mag, Mog, Mbp, Mobp, Plp*) and transcription factors (SOX10, MYRF) related to promyelinating and myelinating oligodendrocytes were significantly increased only in the PFC region of Abx- treated mice, potentially supporting a PFC-specific cognitive deficit. This was supported by increased immunofluorescence of SOX10 in PFC of Abx-treated mice compared to sham. Ileum samples in Abx-treated mice displayed significant downregulation of these same myelin-associated genes and transcription factors, suggesting paralleled altered myelin-related system in the gut. Increased neurogenesis was found in Abx-treated mice, with increased immature hippocampal neurons. Taken together, we identified a long-lasting impact of neonatal Abx administration on the MGB axis, specifically on myelination, likely contributing to impaired cognition function.
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# 32. Effect of Polychlorinated Biphenyl (PCB) 95 on NF-κb Activation in Primary Rat Neurons and Astrocytes

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Polychlorinated biphenyl (PCB) 95 is a non-dioxin-like PCB linked to adverse neurodevelopmental outcomes in preclinical and epidemiologic studies. PCB 95 interferes with normal patterns of dendritic growth in developing brain, which is thought to underlie the cognitive and behavioral deficits associated with developmental exposure to non-dioxin-like PCBs. PCBs also modulate cytokine release and NF-κB activation. NF-κB plays a critical role in not only inflammation, and cell-survival in the brain, but also neural development and neurite outgrowth. In neuronal cell cultures, inhibition of NF-κB reduces dendritic complexity. Here, we test the hypothesis that PCB 95 modulates dendritic growth by altering NF-κB activation in neurons and/or astrocytes. To test this hypothesis, we are using immunocytochemical analyses of NF-κB nuclear localization to quantify NF-κB activation in rat primary neuron-glia co-cultures and purified astrocyte cultures exposed to fM-μM concentrations of PCB 95. Results from these studies will elucidate the role of neuroimmune mechanisms in the concentration-dependent effects of PCB 95 on dendritic growth.
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# 33. Peptides of neuron specific enolase as potential ASD biomarkers: from discovery to epitope mapping.

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Autism spectrum disorder (ASD) is an important health issue and affects 1 in 59 children in the US. Prior studies determined that maternal autoantibody related (MAR) autism is thought to be associated with ~23% of ASD cases. We previously identified seven MAR-specific autoantigens including CRMP1, CRMP2, GDA, LDHA, LDHB, STIP1, and YBX1. We subsequently described the epitope peptide sequences recognized by maternal autoantibodies for each of the seven ASD-specific autoantigens. The aim of the current study was to expand upon our previous work and identify additional antigens recognized by the ASD-specific maternal autoantibodies, as well as to map the unique ASD-specific epitopes using microarray technology. Fetal Rhesus macaque brain tissues were separated by molecular weight and a fraction containing bands between 37 and 45 kDa was analyzed using 2-D gel electrophoresis, followed by peptide mass mapping using MALDI-TOF MS and TOF/TOF tandem MS/MS. Using this methodology, Neuron specific enolase (NSE) was identified as a target autoantigen and selected for epitope mapping. The full NSE sequence was translated into 15-mer peptides with an overlap of 14 amino acids onto microarray slides and probed with maternal plasma from mothers with and ASD child and from mothers with a Typically Developing child (TD) (ASD= 27 and TD=21). The resulting data were analyzed by T-test. We found 16 ASD-specific NSE-peptide sequences for which four sequences were statistically significant ($p<0.05$) using both the t-test and SAM t-test: DVAASEFYRDGKYDL ($p=0.047$; SAM score 1.49), IEDPFDQDDWAAWSK ($p=0.049$; SAM score 1.49), ERLAKYNQLMRIEEE ($p=0.045$; SAM score 1.57), and RLAKYNQLMRIEEEL ($p=0.017$; SAM score 1.82). We further identified 5 sequences that were recognized by both ASD and TD antibodies suggesting a large immunodominant epitope (DYPVVSIEDPFDQDDWAAW). While maternal autoantibodies against the NSE protein are present both in mothers with ASD and mothers of TD children, there are several ASD-specific epitopes that can potentially be used as MAR ASD biomarkers. Further, studies including analysis of NSE as a target protein in combination with the previously identified MAR ASD autoantigens are currently underway.
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# 34. Maternal Allergic Asthma and Iron-Soot Exposure During Fetal Development

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Autism spectrum disorders (ASD) are neurodevelopmental disorders characterized by impaired social interactions and communication skills, and repetitive or stereotyped behaviors. Rates of ASD diagnoses have risen in recent years with current estimates of ASD at 1 in 59 children in the US. Epidemiological studies have suggested a link between maternal allergic asthma (MAA) and an increased likelihood of having a child diagnosed with ASD. Additionally, air pollution, has been linked to both ASD and asthma severity/frequency. Despite these links, there is a lack of mechanistic laboratory models investigating the combination of these phenomenon. The Ashwood and Pinkerton lab developed a novel mouse model of MAA in combination with ultrafine iron-soot (UIS) exposure. Our previous data on MAA alone reported that offspring from these mothers exhibit behavioral differences compared to controls, as well as trends in increased inflammatory cytokines in fetal brain tissue. In the current study, adult female C57B/6 mice were primed with either PBS or ovalbumin, then mated. MAA was induced by administering aerosolized ovalbumin to pregnant dams at gestational days 9.5, 12.5, and 17.5, while control mice received aerosolized PBS. Following asthma induction, pregnant dams were exposed to UIS particles for four hours. At postnatal day 15, brains from offspring were collected. Brains homogenates were measured for changes in cytokine levels using Luminex multiplex bead assay. Elevated inflammatory cytokines were found in MAA-UIS brains compared to controls, specifically, MIP-1α, IL-7, IL-13, and IL-2 appear to be significantly increased. These changes are in line with our previous data collected from fetal MAA exposure, however the response seems to be exacerbated by iron-soot exposure. While these profiles suggest biological differences, studies must be done to investigate how these changes translate to behavior.
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# 35. SHP1 Activity Regulates EAE Severity

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Multiple Sclerosis (MS) is a debilitating demyelinating autoimmune disease in which there is currently no cure. To study this disease, we use a mouse model called Experimental Autoimmune Encephalomyelitis (EAE) which consists of three phases- the first one is Pre-onset, in which there is peak peripheral immune response and lymphocyte proliferation; the second one is Acute, in which there is peak CNS infiltration of peripheral myeloid cells and lymphocytes and activation of CNS resident microglia. The last phase is Chronic, in which disease progression is stabilized, inflammation quiesces, and inflammatory infiltration slows. Moreover, it has been found that MS patients are deficient in Src Homology 2 Domain-Containing Phosphatase 1 (SHP1), which is an important inhibitor of inflammatory cascades in various immune cells. Since SHP1 knockout mice succumb to granulocytic skin lesions and pneumonitis, we elected to use a SHP1 heterozygous mouse to explore EAE. We hypothesize that SHP1 controls EAE pathogenesis through regulation of inflammatory infiltration. We will test our hypothesis by inducing EAE in C57BL/6 mice and running flow cytometry and performing immunohistochemistry on the brain, spinal cord, spleen, and lymph nodes. We expect SHP1 heterozygous mice to exhibit increased peripheral macrophage and CNS resident microglial activation, and increased neutrophilic infiltration as compared to wildtype mice during the chronic phase of the disease. Next, we will elucidate the cell type through which SHP1 is modulating EAE severity using the Cre-Lox system. This project will elucidate SHP1's role in EAE and uncover potential clinical applications for MS treatment.
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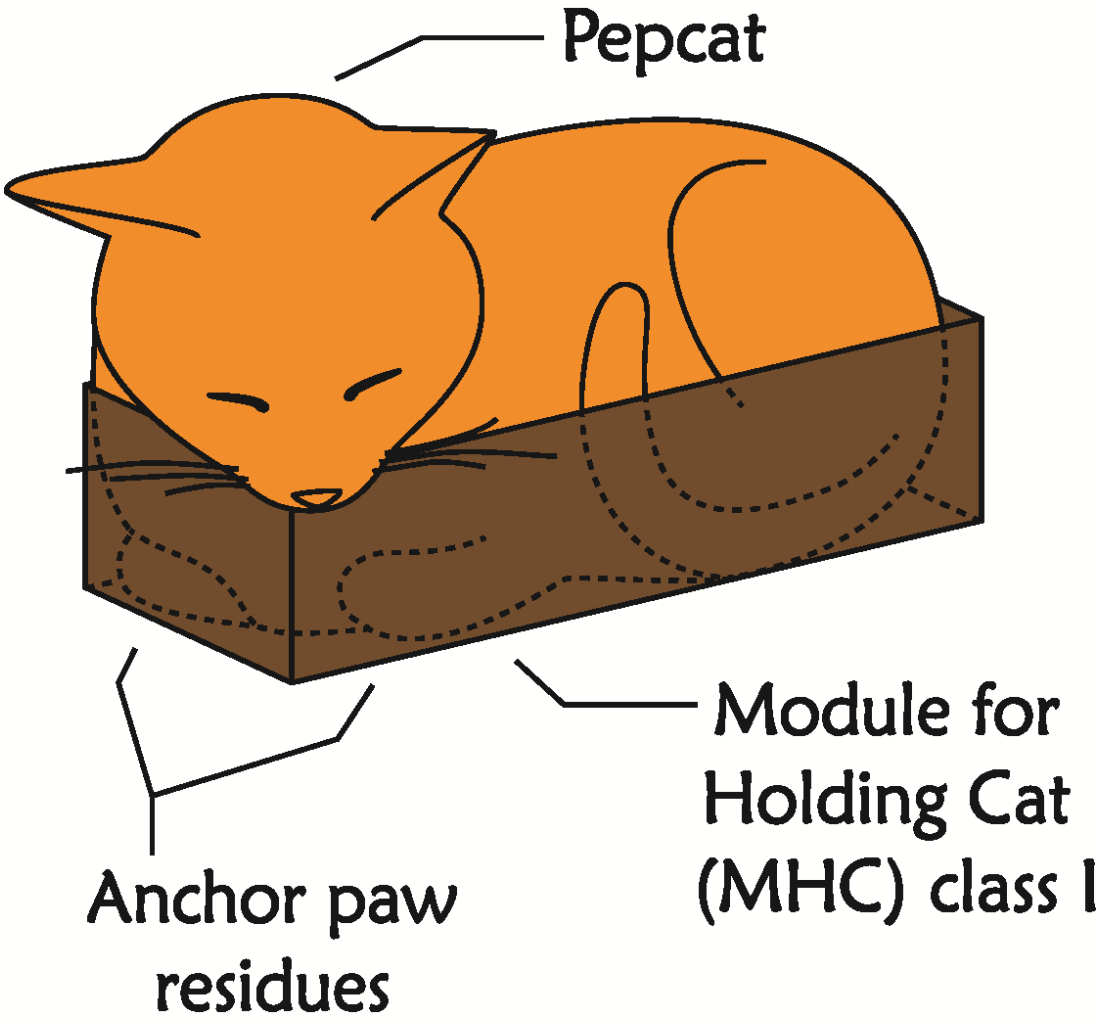
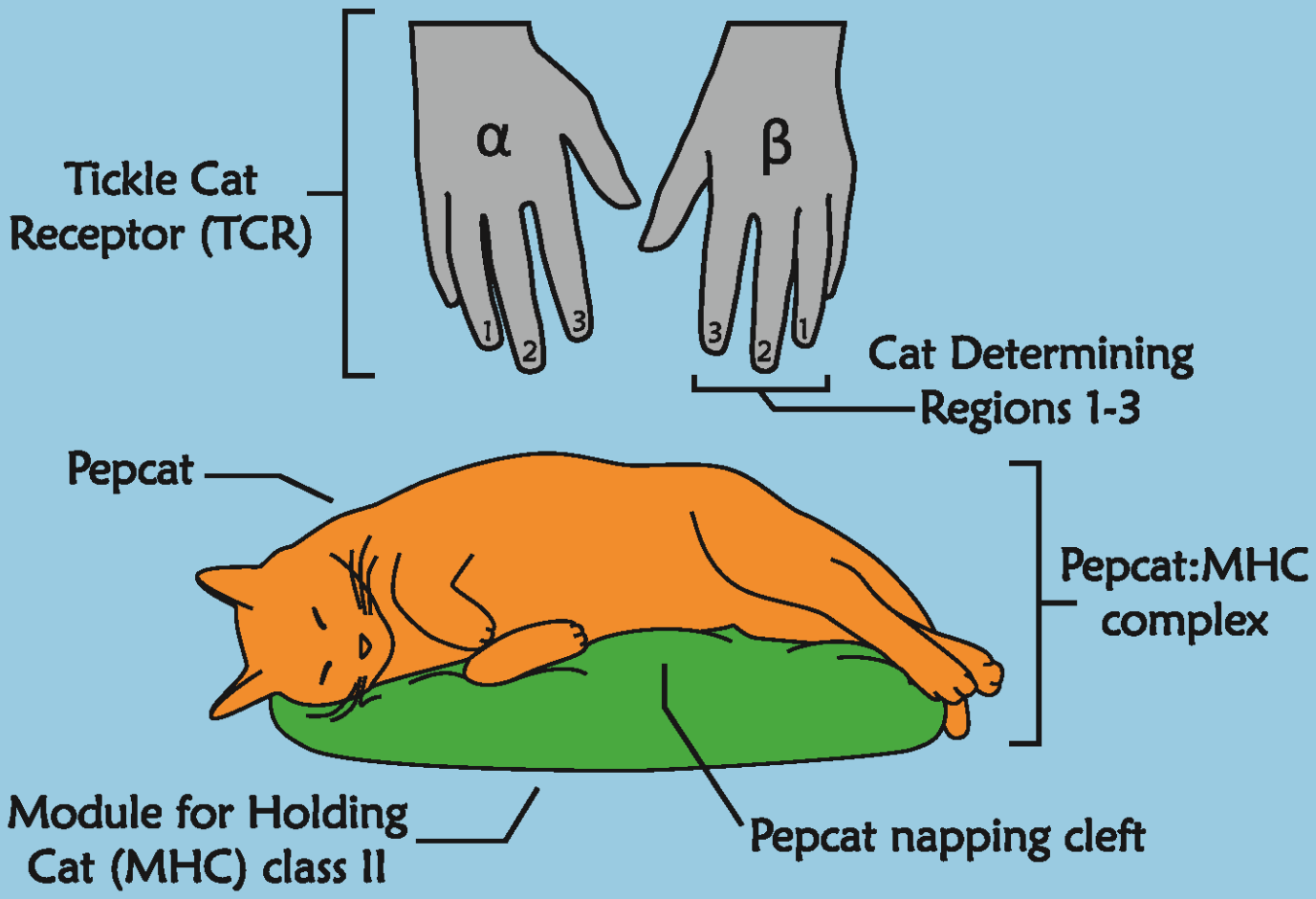

Pepcat
Module for Holding Cat (MHC) class I
Anchor paw residues




*Pepcat must be present in context of MHC for recognition and proper cat tickling