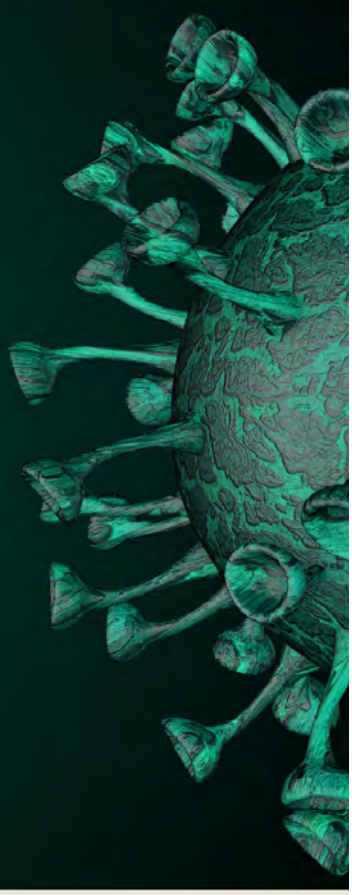
3rd Annual GCC Future of Immunology Symposium



March 7-8, 2023

Houston, Texas

Gulf Coast Consortia
QUANTITATIVE BIOMEDICAL SCIENCES

The Gulf Coast Consortia (GCC), located in Houston, Texas, is a dynamic, multi-institution collaboration of basic and translational scientists, researchers, clinicians, and students in the quantitative biomedical sciences, who benefit from joint training programs, topic-focused research consortia, shared facilities and equipment, and exchange of scientific knowledge. Working together, GCC member institutions provide a cutting-edge collaborative training environment and research infrastructure beyond the capability of any single institution. GCC research consortia gather interested faculty around research foci within the quantitative biomedical sciences, and currently include Immunology, Antimicrobial Resistance, Cellular and Molecular Biophysics, Innovative Drug Discovery and Development,, Mental Health Research, Regenerative Medicine, Single Cell Omics, Theoretical and Computational Neuroscience, and Translational Pain Research. GCC training programs currently focus on Biomedical Informatics, Cancer Therapeutics, Computational Cancer Biology, Molecular Biophysics, Pharmacological Sciences, Precision Environmental Health Sciences, and Antimicrobial Resistance. Current members include Baylor College of Medicine, Rice University, University of Houston, The University of Texas Health Science Center at Houston, The University of Texas Medical Branch at Galveston, The University of Texas M. D. Anderson Cancer Center, The Institute of Biosciences and Technology of Texas A&M Health Science Center and Houston Methodist Research Institute.

GCCIMM Executive Steering Committee

David Corry
Baylor College of Medicine
Chair

Roza Nurieva
MD Anderson Cancer Center
Co-*Chair*

Caleb Bashor, Rice Univ.
Yingzi Cong, UT Medical Branch Galveston
Michael Diehl, Rice Univ.
Isaac Hilton, Rice Univ.
Nancy Huang, IBT TAMU
Cynthia Ju, UTHealth
Katherine King, Baylor College of Medicine
Maksim Mamonkin, Baylor College of Medicine

Ricardo Rajsbaum, UT Medical Branch
Joel Sederstrom, Baylor College of Medicine
Omid Veiseh, Rice Univ.
Jin Wang, Houston Methodist Research Institute
Momoko Yoshimoto, UTHealth
Shaun Xiaoliu Zhang, Univ. of Houston
Yubin Zhou, IBT TAMU

Follow us on Twitter:

@GCCIMM

For today's conference use hashtag:

#GCCIMM23

Follow us on LinkedIn:

Gulf Coast Consortia - Research

Agenda

March 7, 2023

Day 1

1:30-2:00 Registration and poster set-up

2:00-2:05 Welcome
David Corry, **MD,** Baylor College of Medicine
Suzanne Tomlinson, **PhD, MBA,** Gulf Coast Consortia

2:05-2:50 Keynote Presentation
Mast Cells and IgE Orchestrating the "Good Side" of Allergy: Defense Against Venoms and Staphylococcus aureus
Stephen J. Galli, MD
Stanford Univ.

Session 1: Mast Cells and Organ Specific Immunity
Convenors: **Cynthia Ju, PhD,** Univ. of Texas Health Science Center
Kelsey Mauk, **BS,** Baylor College of Medicine

2:50-3:10 *IL7R Marks Embryo-derived Mast Cells*
Michihiro Kobayashi, PhD
Univ. of Texas Health Sciences Center Houston

3:10-3:30 *Host Gastric Microenvironment Facilitates Ascaris Suum Larval Infection*
Jill Weatherhead, MD, PhD
Baylor College of Medicine

3:30-3:50 *Macrophages in Vitamin E Acetate Induced Lung Injury*
Yun "Alex" Zhang, BS
Baylor College of Medicine

3:50-4:10 *Developing a Chronic Model of Candida albicans Cerebral Mycosis through Gut Colonization*
Lynn Bimler, PhD
Baylor College of Medicine

4:10-5:15 pm Poster session (event hall)

March 8, 2023

Day 2

8:30 Welcome
David Corry, **MD,** Baylor College of Medicine

Session 2: Molecular Control of Immunity
Convenors: Roza Nurieva, PhD, MD Anderson Cancer Center
Dominique Armstrong, BS, Baylor College of Medicine

Agenda

Keynote introduction
Roza Nurieva, PhD, MD Anderson Cancer Center

8:35-9:20 Keynote Presentation
Ligand-dependent Regulation of Nuclear Receptors in Inflammation
Laura Solt, PhD
Univ. of Florida Scripps Biomedical Research

9:20-9:40 *Epigenetic Changes in Hematopoietic Stem and Progenitor Cells as the Basis for Trained Immunity*
Brandon Tran, BS
Baylor College of Medicine

9:40-10:00 *The let-7 microRNA is a Multi-Faceted Regulator of Chronic Lung Inflammation, Lung Injury and Advanced Lung Disease*
Antony Rodriguez, PhD
Baylor College of Medicine

10:00-10:20 *Platelet Derived Dickkopf-1 (Dkk-1) Mediates T Cell Responses in Severe COVID-19*
Yifan Wu, MD, PhD
Baylor College of Medicine

10:20-10:40 *The Immunological Effect of DAS181 in Smoking*
Cheng-Yen Chang, PhD
Baylor College of Medicine

10:40-11:00 Break

Session 3: Cancer Immunobiology
Convenors: Maksim Mamonkin, PhD, Baylor College of Medicine
Lynn Bimler, PhD, Baylor College of Medicine

11:00-11:20 *Clinically Translatable Cytokine Factories for Cancer Immunotherapy*
Omid Veiseh, PhD
Rice Univ.

11:20-11:40 *Comparative Effects of Combustible Cigarette versus Electronic Cigarette Exposures on Lung Microenvironment and Microbiome of Kras Mutant Lung Cancer*
Seyed Javad Moghaddam, PhD
MD Anderson Cancer Center

11:40-12:00 *MAGE-A4 Induces Tumor-Promoting Plasma Cells in NSCLC*
Dominique Armstrong, BS
Baylor College of Medicine

12:00-12:20 *The Role of Nucleophosmin 1 Mediated Caspase-2 Activation in Acute Myeloid Leukemia*
Dharaniya Sakthivel, BS
Baylor College of Medicine

Agenda

12:20-1:30 Lunch

Session 4: **General Immunology-Part I**
Convenors: Jin Wang, PhD, Houston Methodist Research Institute
Bashir Uddin, DVM, MS, PhD, Univ. of Texas Medical Branch

1:30-1:50 *Clearance of HIV Infection by Selective Elimination of Host Cells Capable of Producing HIV*
Min Li, MD, PhD
Houston Methodist Research Institute

1:50-2:10 *Elevated Plasma Cytokines/Chemokines Predict and Provide Evidence of a Persistent Inflammatory Basis for Breast Cancer-Related Lymphedema*
Melissa Aldrich, PhD
Univ. of Texas Health Sciences Center Houston

2:10-2:30 *A Parasite Derived Protein that can Inhibit Human IL-5 and Host Immune Activation*
Rojelio Mejia, PhD
Baylor College of Medicine

2:30-2:50 *Of Stress, Inflammation and Programmed Cell Death*
Parimal Samir, PhD
Univ. of Texas Medical Branch

2:50-3:05 Break

General Immunology-Part II
Convenors: Momoko Yoshimoto, PhD, Univ. of Texas Health Science Center Houston
Cheng-Yen Chang, PhD, Baylor College of Medicine

3:05-3:25 *Lipid Dysregulation of Immune Responses to Intestinal Injury*
Andrea McAlester, PhD
Baylor College of Medicine

3:25-3:45 *Long-Term Persistence of Candida albicans in the Murine Gastrointestinal Tract*
Kelsey Mauk, BS
Baylor College of Medicine

3:45-4:05 *Let-7 microRNA controls AT2 Progenitor Stemness and Prevents Interstitial Lung Disease*
Matthew Seasock, BS
Baylor College of Medicine

4:05 Closing remarks

Presenters in alphabetical order

Melissa B. Aldrich, PhD
Associate Professor
Center for Molecular Imaging
Univ. of Texas Health Science Center
Houston

Elevated Plasma Cytokines/Chemokines Predict and Provide Evidence of a Persistent Inflammatory Basis for Breast Cancer-Related Lymphedema

Melissa B. Aldrich received degrees from the University of Texas at Austin (B.A., Biochemistry), the University of Houston-Central (M.B.A.), and the MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences (Ph.D., Immunology). Her research focuses on clinical studies of lymphatic dysfunction in lymphedema. She and colleagues recently completed a five-year study of breast cancer-related lymphedema, and are presently working on a project investigating reparative microsurgeries for lymphedema.

Dominique Armstrong, BS
Graduate Student
Baylor College of Medicine

MAGE-A4 Induces Tumor-Promoting Plasma Cells in NSCLC

Dominique graduated from Whitworth University with a BS in Biology and minors in Chemistry and Music. Before coming to Baylor College of Medicine, she worked in environmental microbiology and in clinical pathology. She is currently in the Translational Biology and Molecular Medicine graduate program at Baylor College of Medicine in Dr. Farrah Kheradmand's lab studying plasma cells in lung cancer.

Lynn Bimler, PhD
Postdoctoral Fellow
Baylor College of Medicine

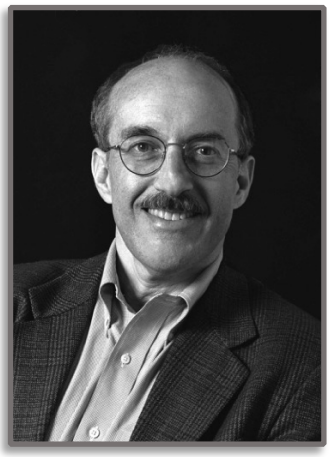
Developing a Chronic Model of Candida albicans cerebral mycosis Through Gut Colonization

Lynn Bimler is a postdoctoral fellow in the lab of Dr. David Corry. For her PhD, Lynn worked in the laboratory of Dr. Silke Paust at Baylor College of Medicine studying a novel vaccine and therapies directed towards the M2e peptide of influenza. Through her work on this project, her interest in pathogen-host interactions and aging increased. Leading to her current focus on developing a chronic murine model of Candida Albicans induced cerebral mycosis to determine its relationship to the pathogenesis of Alzheimer's Disease.

Abstract: Recent evidence suggests that Alzheimer's Disease (AD) is linked to fungal brain infections. We have previously established an acute model of cerebral mycosis by intravenously (IV) injecting the pathogenic yeast Candida albicans. The resulting infection induces mild transient memory deficits and fungal induced glial granulomas (FIGGs) consisting of microglia and amyloid β (aβ) deposits surrounding yeast aggregates. This structure essentially duplicates AD's characteristic senile plaque. AD involves numerous senile plaques and tauopathy that presumably accrue over many years potentially from chronic infection. This raises the key possibility that C. albicans might persist in a remote tissue, such as the intestines, from which it periodically mobilizes to chronically re-infect the brain. As both C. albicans colonization of the GI tract and low-level candidemia deriving from the GI tract have been documented in humans, we hypothesize that chronic C. albicans enteritis leads to low-level transmission of fungal cells into the bloodstream and persistent cerebral mycosis. To test this hypothesis and establish a more translationally relevant chronic model, we administered yeast from C. albicans to wildtype C57BL/6 mice via oral gavage. Live yeast are recoverable from the brain as soon as 2 days post gavage and out to at least two months. Additionally, these colonies were polymicrobial, consisting of both yeast and bacteria, an observation that is consistent with recent published analysis and our own cultures of AD brains. Through this study we will establish if this infection produces an AD phenotype. This research is groundbreaking for the AD field, producing an unprecedented model that could be used for critical AD therapeutic and mechanistic studies.

Cheng-Yen Chang, PhD
Postdoc
Baylor College of Medicine
The Immunological Effect of DAS181 in Smoking

Cheng-Yen is a postdoc in the laboratory of Dr. Farrah Kheradmand at Baylor College of Medicine (BCM). Her Ph.D. work at BCM was to understand how environmental airborne carbon black particles reprogram lung macrophages to accelerate lung cancer. Now she is investigating the role of a novel recombinant protein therapeutic, DAS181, in the lung microenvironment.



Stephen J. Galli, MD
Professor
Pathology and of Microbiology and Immunology
Stanford University

Mast Cells and IgE Orchestrating the "Good Side" of Allergy: Defense Against Venoms and Staphylococcus aureus

Stephen J. Galli, MD, is the former Chair of Pathology (1999-2016) and current Professor of Pathology and of Microbiology and Immunology at Stanford University. He investigates the roles of mast cells and basophils in health and disease, including allergic disorders and resistance to venoms. He was President of the American Society for Investigative Pathology (ASIP, 2005-2006) and belongs to several honorary societies including the Collegium Internationale Allergologicum (President, 2010-2014), Pluto Club (American Association of University Pathologists; President, 2018-2019), the National Academy of Medicine (currently, Chair of Section 4), and the Accademia Nazionale dei Lincei in Rome. Dr. Galli received a MERIT Award from the NIAID/NIH (1995-2006), Scientific Achievement Awards from the International Association of Allergy & Clinical Immunology (1997) and the World Allergy Organization (2011), the Rous-Whipple Award of the ASIP (2014), and the Karl Landsteiner Medal of the Austrian Society for Allergology and Immunology (2014).

Keynote Presenter

Michihiro Kobayashi, MD, PhD
Assistant Professor, Center for Stem Cell and Regenerative Medicine
Univ. of Texas Health Science Center

IL7R Marks Embryo-derived Mast Cells

Dr. Kobayashi got M.D. / Ph.D. at Mie Uni. Sch. Med. (in Japan) and worked as Pediatric Hematology/Oncologist at National Cancer Center Hos. (Tokyo) and Kyoto Univ. After moving to the US for basic research (Indiana Univ. School of Med.), he has been focusing on Hematopoietic stem cells, leukemia, and cytokine receptor signaling. In 2016, he moved to UTH (IMM) as an assistant Prof. and keep focusing on developmental immunology/ hematology, Hematopoietic stem cells.

Abstract: The mast cell (MC) is a unique immune cell displaying a wide variety of functions. Recent breakthroughs well illustrated multiple waves of MC generation provided by embryonic Yolk Sac (YS) and AGM, and adult BM HSC does not supply MC in unperturbed conditions (HSC-independence). While post-natal HSC doesn't reconstitute MC, it was unknown whether the first emerging HSC in the AGM region or fetal liver (FL) possesses MC repopulation capacity. We investigated the MC potential of those cells by transplant and fate-mapping study. By the transplant into (neonatal) NSG, E11.5 AGM (Pre-)HSCs and E12.5 FL HSCs repopulated MC with multi-lineage reconstitution, but HSCs of E14.5 FL and later did not. HSC-labeling by injecting TAM into E14.5 or p2 revealed almost no contribution (< 5%) of MC from labeled HSCs, supporting our transplant results.

Now, it is widely known that all blood cells are produced via hemogenic endothelial cells (HEC), and one of the earliest their products, YS erythro-myeloid progenitors (EMP), provide the earliest tissue-resident macrophage (brain microglia, etc.) and MC together. Since one report shows a part of tissue-resident macrophages are marked by IL-7 receptor (IL-7R), an essential molecule for early lymphoid differentiation, we thought that MC could be also marked by IL-7R. We tested by utilizing IL-7Rcre/RosaLSL-dTom model and found that more than 90% of MCs in various tissues exhibited dTom positive (90.8 ± 3.1%). IL-7R protein was not expressed on the Peritoneal cavity (PerC), skin MCs, and FL MC progenitors. To confirm functional IL-7R involvement in MC development, we measured MCs in IL-7Rcre/+ (Het) and IL-7Rcre/cre (KO) mice. Despite marked reductions of T/B cell counts, PerC MC count was comparable (WT: 2.4 ± 1.6 vs KO: 4.1 ± 2.3 x 10e4), suggesting that IL-7R is temporarily expressed in the early EMP stage in only a short period and IL-7 signaling is not actively used for development/expansion of MC in vivo. We also observed MC

differentiation from the adult BM dTom-neg Lin-Sca+Kit+ (LSK) cells. MC production was comparable between Het and KO and interestingly, both WT/KO LSK-derived MCs showed the least dTom positivity (3.4± 2.5 vs 4.7 ± 3.1 %) whereas more than 70% of macrophages turned dTom+, suggesting embryonic and adult MC differentiation utilize different program respectively. Transplantation of dTom- HSCs from E12.5 FL successfully reconstituted dTom positive MCs. In the old mice (1 year), the %dTom in PerC MC was reduced (79.2 ± 8.1 %), suggesting that post-natal de novo MC production is minimum without IL-7R use.

Taken together, IL-7R is temporarily expressed shortly after the endothelial-hemogenic transition that can mark the vast majority of MCs. Embryonic- and HSC-derived IL-7R could be regulated by different program.

Min Li, MD, PhD
Research Associate
Immunology and Transplant Sciences Center
Houston Methodist Research Institute

Clearance of HIV Infection by Selective Elimination of Host Cells Capable of Producing HIV

Dr. Li is a Research Associate in the Immunology and Transplant Sciences Center at Houston Methodist Research Institute. He received his MD from Harbin Medical University, China and his PhD from Peking University, China. Min was a Postdoctoral Associate at Baylor College of Medicine. He has previously held Instructor positions at Baylor College of Medicine and MD Anderson Cancer Center. He has a board of certification of MB(ASCP)^{CM} from the American society for clinical pathology.

Kelsey Mauk, BS
Graduate Student
Baylor College of Medicine

Long-Term Persistence of Candida albicans in the Murine Gastrointestinal Tract

Kelsey is a fourth-year graduate student in the laboratory of Dr. David B. Corry at Baylor College of Medicine. In the Corry Lab, Kelsey studies how human-associated fungi interact with the host, and how these host-pathogen interactions influence chronic inflammation.

Andrea McAlester, PhD
Instructor
Pathology and Immunology Department
Baylor College of Medicine

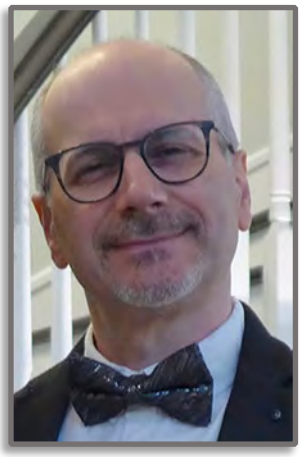
Lipid Dysregulation of Immune Responses to Intestinal Injury

Dr. McAlester received her BS. in biology at Clark Atlanta University. She completed her Ph.D. at Vanderbilt University in the department of Molecular Physiology and Biophysics, focusing on immunometabolism. She came to BCM as a postdoc in the MVM department, where she studied the impact of diet on intestinal immune responses. Dr. McAlester is a K01 recipient and is now an instructor in the department of Pathology and Immunology at BCM, continuing her studies to understand the role of diet in intestinal tissue repair.

Rojelio Mejia, MD
Assistant Professor of Infectious Diseases and Tropical Medicine
Laboratory of Human Parasitology
National School of Tropical Medicine
Baylor College of Medicine

A Parasite Derived Protein that can Inhibit Human IL-5 and Host Immune Activation

Dr. Mejia is dedicated to improving the understanding and treatment of parasitic infection through advancing systems of their diagnoses. The laboratory's work involves defining the prevalence and parasitic burden in endemic populations and improving healthcare outcomes. The Southern USA has been plagued with unacceptable levels of poor sanitation, poverty, and parasites in the community. Dr. Mejia is committed to decreasing the prevalence and burden of these parasites among the poor and disenfranchised population. Parasites disproportionately impact people of color and further continue the cycle of poverty. Research studies include New York, Maryland, Texas, Louisiana, Mississippi, Alabama, and South Carolina.



Seyed Javad Moghaddam, MD, ATSF
Associate Professor
Pulmonary Medicine, UT MD Anderson Cancer Center
Director of Immunology Program, MD Anderson UTHealth Houston Graduate School of Biomedical Sciences

Comparative Effects of Combustible Cigarette versus Electronic Cigarette Exposures on Lung Microenvironment and Microbiome of Kras Mutant Lung Cancer

Dr. Seyed Javad Moghaddam is an Associate Professor (tenured) at the Department of Pulmonary Medicine, UT MD Anderson Cancer Center, and director of the Immunology Graduate Program at MD Anderson UTHealth Houston Graduate School of Biomedical Sciences, Houston, TX. He also serves as a faculty member and lecturer for other training programs such as the CPRIT-CURE Training Program, CPRIT Postdoctoral Fellowship in Cancer Prevention Program, and King Foundation Summer Program.

Dr. Moghaddam has received numerous awards including Lung Cancer Discovery Award (American Lung Association), Research Scholar Award (American Cancer Society), and Cyrus Scholar Award in Basic/Translational Research (Cyrus Family Foundation). He is the 2017 recipient of the American Thoracic Society Early Career Achievement Award in Thoracic Oncology where he currently serves as an executive committee member on its Thoracic Oncology Assembly. Recently, he was elected as a Fellow of the American Thoracic Society for his dedication to the Society and his significant contributions to the fields of pulmonary, critical care, and/or sleep medicine locally, nationally, and internationally.

Overall, his research program is focused on airway inflammation, intrinsic (e.g. oncogene driven) and extrinsic (e.g. smoke or infection induced), and its role in airway epithelial tumorigenesis. His research team has developed and interrogated various human-relevant mouse models that closely emulate the molecular pathobiology of human airway inflammation, COPD, and lung cancer. His group is working on understanding the cell type specific roles of inflammatory signaling pathways in lung carcinogenesis. These studies have the potential to detect and target important pathways in lung tumorigenesis, which could have major impacts on the prevention and treatment of lung cancer. They will also lay the groundwork to develop predictive and prognostic biomarkers to identify responders and non-responders. He has actively published, been well-funded, and trained several postdoctoral fellows, medical students, as well as college, and graduate students in this field.

Antony Rodriguez, PhD
Assistant Professor
Immunology, Allergy & Rheumatology
Baylor College of Medicine

The let-7 microRNA is a Multi-Faceted Regulator of Chronic Lung Inflammation, Lung Injury and Advanced Lung Disease

Dr. Rodriguez's lab is interested in microRNAs as potheyrful genetic and epigenetic modifiers of advanced lung injury and disease. Their approach is multipronged and they work with genetically modified mice and clinical samples to decipher the mechanism of action of microRNAs. The scope of their research is wide and for example, they have shown the importance of miRNAs in adaptive and/or innate immunity (i.e. miR-155, miR-22), heart failure (i.e. miR-22), and lung injury (i.e. miR-22). Their most recent projects focuses on the let-7 miRNA as a master regulator of inflammation in immune cell compartments (T cells and macrophages) as theyll as alveolar progenitor stem cells (AT2 cells). They have found that genetic manipulation of let-7 miRNA in immune cells compartment sensitizes mice to lung inflammation and chronic obstructive pulmonary disease. On the other hand, they found that let-7 miRNA they found that conditional inactivation of let-7 microRNA clusters specifically in alveolar AT2 cells in mice promotes spontaneous age-dependent parenchymal remodeling with features of interstitial lung disease. Current work Based on transcriptomic data suggests that let-7 serves as an essential coordinator of AT2 cell survival, progenitor stem cell renewal, and AT1 differentiation. Their combined work will elucidate a fundamental repair and regeneration process in the lung and pave the way for new targetable pathways for drug discovery in advanced lung disease(s).

Dharaniya Sakthivel, BS
Graduate Student
Genetics & Genomics
Baylor College of Medicine
The Role of Nucleophosmin 1 Mediated Caspase-2 Activation in Acute Myeloid Leukemia

Dharaniya is a CPRIT scholar, currently pursuing a Ph.D. in the laboratory of Dr. Lisa Bouchier-Hayes, Division of Hematology-Oncology, Department of Pediatrics at Baylor College of Medicine (BCM). Her research focuses on understanding the role of caspase-2, a cell-death initiator in acute myeloid leukemia harboring nucleophosmin 1 mutation. Her recent work reveals the importance of exploring the non-traditional roles of caspase-2 in regulating the cell cycle and DNA repair of cancer cells.

Prior to BCM, Dharaniya did her postgraduate research in the laboratory of Dr. Indranil Sinha at Harvard Medical School. In collaboration with Dana Farber Cancer Institute, Dharaniya studied the molecular mechanism underlying hypoxia signaling in sarcopenic obesity and cancer models. Dharaniya hopes to establish a long-standing scientific career in developing efficient therapeutic interventions for liquid and solid tumors.

Parimal Samir, PhD
Assistant Professor
Microbiology and Immunology
Univ. of Texas Medical Branch
Of Stress, Inflammation and Programmed Cell Death

Parimal received his Ph.D. in Biochemistry from Vanderbilt University where he studied proteomic regulatory mechanisms in yeast and humans. He moved to St. Jude Children's Research Hospital for his postdoctoral training where he was part of the team that discovered cross-regulation of innate immune, programmed cell death and stress signaling by each other. He established his own lab in the Department of Microbiology and Immunology at UTMB in the Spring of 2022 and is continuing to study this cross-regulation of different arms of host response against microbial infections.

Matthew Seasock, BS
Immunology & Microbiology Graduate Program
Clinical Translational Research Program
Baylor College of Medicine

Let-7 microRNA controls AT2 Progenitor Stemness and Prevents Interstitial Lung Disease

Matthew Seasock received his Bachelor of Science in Cell & Molecular Neuroscience at Temple University. His undergraduate research focused on traumatic brain injuries and the blood-brain barrier, and he published a method for modeling the blood-brain barrier by growing micro-vessels on a microfluidic chip. This bioengineered "brain-on-chip" was used to study the development of the fetal brain during injury. Matthew then worked as a technician and lab manager for 3 years in a genetics lab at the University of Pennsylvania Perelman School of Medicine. During this time he grew the largest human kidney biorepository in North America in addition to his research on chronic kidney disease. He published 5 high impact papers which included two genetic screens for risk alleles in diabetic nephropathy in Nature Medicine and Nature Genetics. Now Matthew is a 4th year graduate student in the Immunology & Microbiology Program at BCM in Dr. Antony Rodriguez's lab where he studies how microRNAs affect pulmonary stem cells, the innate immune system, and pulmonary fibrosis. During his time at BCM, he won Best Basic Science Poster at the Department of Medicine Housestaff Symposium. He received a T32 award and a certificate of added qualification for Clinical Translation Research.

Laura A. Solt, PhD
Associate Professor
Immunology and Microbiology
UF Scripps Biomedical Research

Ligand-dependent Regulation of Nuclear Receptors in Inflammation

Laura A. Solt, Ph.D., is an Associate Professor in the Department of Immunology and Microbiology at UF Scripps Biomedical Research in Jupiter, Florida (formerly Scripps Florida). She received her B.A. from Boston College and her Ph.D. in Immunology from the University of Pennsylvania. After completing her postdoctoral research at the Scripps Research Institute's Jupiter, Florida (Scripps Florida) campus, she started her independent laboratory at Scripps Florida in 2013. Dr. Solt's research is focused on understanding the roles of nuclear receptors in the immune system, with a specific focus on TH17 cells, and how their expression, function, and activity affects disease. As ligand-regulated transcription factors, nuclear receptors serve as excellent targets for the treatment of a variety of diseases. Therefore, her lab also works in close collaboration with medicinal chemists to design and develop small molecule ligands to nuclear receptors to further probe their functions and evaluate their therapeutic potential. Using these approaches, her lab described a negative regulatory role for the nuclear receptor REV-ERBα in TH17 cell development and autoimmunity as well as the design and synthesis of newer, more potent synthetic REV-ERB modulators that target TH17 cells in vivo. Additionally, her lab further elucidated the essential, pathogenic role for the nuclear receptor RORα in TH17 cells as well as the characterization of RORα -selective small molecules targeting TH17 cells to treat TH17-mediated autoimmunity. Thus, her lab aims to gain insight into the transcriptional regulation of nuclear receptors and their ligand(s) to better understand signaling pathways that govern TH17 cell homeostasis vs. pathogenicity, which may aid in the rational design of therapeutics for specific disease indications.

Keynote Presenter

Brandon Tran, BS
Graduate Student
Graduate School of Biomedical Sciences,
Baylor College of Medicine

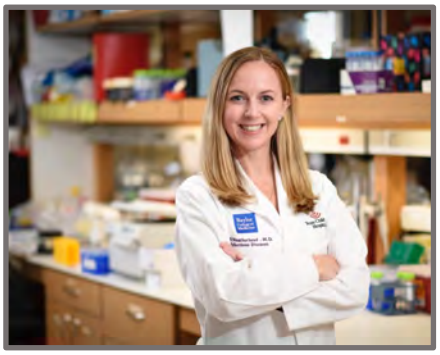
Epigenetic Changes in Hematopoietic Stem and Progenitor Cells as the Basis for Trained Immunity

Brandon Tran is a 4th year Ph.D. candidate in Dr. Katherine Y. King's lab in the Graduate School of Biological Sciences (GSBS) at Baylor College of Medicine. Prior to joining Dr. King's lab, Brandon graduated with a Bachelor of Science in Biology from the University of Texas at Dallas in May 2019. While earning his Bachelor, Brandon worked with Dr. Mario Romero-Ortega to determine the effects of neuregulin I type III on peripheral nerve regeneration. Currently, his thesis focuses on determining the mechanisms of inflammation-induced epigenetic reprogramming of hematopoietic stem and progenitor cells (HSPCs). Particularly, his work focuses on determining how chronic interferon gamma (IFNy) signaling via Mycobacterium avium alters histone modifications and chromatin open-ness of HSPCs to promote myeloid differentiation and altered innate immune responses, also known as central trained immunity.

Omid Veiseh, PhD
Assistant Professor
CPRIT Scholar in Cancer Research
Rice University

Clinically Translatable Cytokine Factories for Cancer Immunotherapy

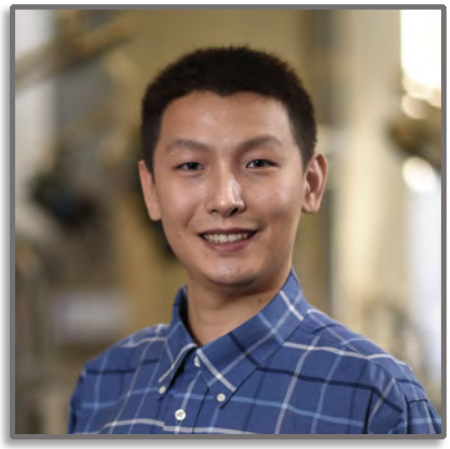
Dr. Omid Veiseh, Ph.D. is a professor of Bioengineering at Rice University where he leads a research program aimed at engineering next generation treatments for a wide range of human diseases by leveraging the latest techniques in synthetic biology, immunoengineering, and materials science to develop innovative cell-based platforms for real-time production of biologics. He is also a serial entrepreneur who has co-founded Sigilon Therapeutics (Nasdaq: SGTX), Avenge Bio, Pana Bio, and Curada Bio.



Jill Weatherhead, MD, PhD
Assistant Professor
Tropical Medicine and Infectious Disease
Baylor College of Medicine

Host Gastric Microenvironment Facilitates Ascaris Suum Larval Infection

Jill Weatherhead is a physician-scientist at Baylor College of Medicine and Texas Children's Hospital. She went to Michigan State University for medical school and completed her residency, fellowship and PhD at Baylor College of Medicine. She is board certified in internal medicine, pediatrics, infectious diseases and pediatric infectious diseases with a sub-specialty certification in Tropical Medicine and Travelers Health. She is the Director of the adult and pediatric tropical medicine clinics in Harris Health System and Texas Children's Hospital where she provides medical care to uninsured and underinsured patient's with parasitic infections. She is the Assistant Dean at the National School of Tropical Medicine at Baylor College of Medicine and teaches on parasitology, immunology and global health. Her research investigates the impact of parasites on host immune responses, mechanisms of larval migration through the host and the long-term morbidity associated with parasite infections.



Yifan Wu, PhD
Postdoctoral Associate
Pediatrics
Baylor College of Medicine

Platelet Derived Dickkopf-1 (Dkk-1) Mediates T Cell Responses in Severe COVID-19

Yifan Wu is currently a postdoctoral associate in the Department of Pediatrics, Baylor College of Medicine with Dr. Jill Weatherhead. He completed his medical degree at Shanghai Jiao Tong University School of Medicine in 2015 and obtained his PhD in immunology from Baylor College of Medicine in 2020. Yifan has been focusing on the organ-specific host immune response to a variety of pathogens, including fungi and parasites, and has discovered novel infectious mechanisms, pathologies, and immune pathways involved. Now he is working on establishing a new project studying platelet related mechanisms in SARS-CoV-2 infections.

Yun (Alex) Zhang, BS
Graduate Student
Baylor College of Medicine
Macrophages in Vitamin E Acetate Induced Lung Injury

Yun Zhang (Alex) is currently a 6th-year immunology program graduate student in Professor Farrah Kheradmand MD's laboratory at Baylor College of Medicine.

Alex received his bachelor's and master's degrees from Harbin Medical University in northeast China in 2017.

In Prof. Kheradmand's laboratory, his work focuses on the innate and adaptive immunity in the respiratory immunity in cigarette smoking and vaping associated lung injuries as well. He also works on respiratory mucosal immunity against influenza.

Prior to joining Baylor, Alex worked on the role of macrophage and atherogenesis and the role of B lymphocytes in the pathogenesis of murine experimental autoimmune encephalomyelitis.

Poster presenters
In alphabetical order of presenter

First Name	Last Name	Institution	Title of Submission	Poster Number
Aditi	Aditi	Univ. of Texas Medical Branch	Generation Of Reporter Cell Lines For Computational Modelling Of Innate Immune Signaling	1
Werner	Braun	Univ. of Texas Medical Branch	Breaking the Sertotype Barrier with Broad-Spectrum, PCPcon Antigens Against Alphaviruses.	2
Sarah	Browning	Univ. of Texas Medical Branch	Dysregulation of C-type Lectin Receptors in HIV and Mycobacterium tuberculosis Co-infection	3
Yong	Du	Houston Methodist Research Institute	Apex1 Restrains p53 Signaling in Activated T Cell and Potentiates Systemic Lupus Erythematosus Development	4
Annamalai	Govindhan	Baylor College of Medicine	Epithelial cGAS Mediates Allergen-induced Neutrophil and Dendritic Cell Recruitment in the Early Stages of Allergic Airway Inflammation	5
Koa	Hosoki	Baylor College of Medicine	Allosteric Inhibition of CXCR1/2 Chemokine Receptors Attenuates Th2/Th17 Allergic Lung Inflammation	6
Mohamed	Kady	Baylor College of Medicine	Engineered Probiotic for Oral Delivery of a Joint-Targeted Peptide Therapy for Rheumatoid Arthritis	7
Dan	Kennedy	Baylor College of Medicine	Dnmt3a-/- Leukocyte Migration, Expansion Are Accelerated In Response To Acute Viral Pneumonia	8
Hoa Nhu	Le	Univ. of Houston	Structural Modeling T Cells Receptor Interactions for Immunotherapy Applications	9
Jaila	Lewis	Univ. of Houston	Investigating the Accuracy of Alternative Scoring Functions on the Ranking of Docked Peptide-HLA Conformations	10
Siyao	Liu	Texas A&M Institute of Biosciences and Technology	Optogenetic Engineering of STING Signaling to Remotely Control anti	11
Yikai	Luo	Baylor College of Medicine	A Spatiotemporal Cell Atlas of Human Gastric Malignancy Reveals Mechanisms Underlying Metastasis and Immunotherapy Response	12
Arushana	Maknojia	Baylor College of Medicine	Microbiome-Driven Type I Interferon Signaling Regulates the Survival of B-cells	13
Joselyn	Rojas-Quintero	Baylor College of Medicine	Role of B Cells in the Progression of Emphyser	14
Jorge	Tovar Perez	Texas A&M Institute of Biosciences & Technology	Epigenetic Targeting of PRC2 Complexes Upregulates MHC Antigen Presentation Components in Gastrointestinal Cancer Cells	15
Ravi	Verma	Baylor College of Medicine	Diverse Immune Responses of Fecal Microbiota Transplantation Suggest Differences in Enterotype of Microbiota	16
Yang	Yang	Univ. of Texas Health Science Houston	Eosinophil Orchestrates Tissue Repair After Hepatic Ischemia Reperfusion Injury	17

Poster 1

Generation of Reporter Cell Lines for Computational Modelling of Innate Immune Signaling

Aditi*[1], Lamichhane PP*[1], Samir P[1]

1. Department of Microbiology and Immunology, The University of Texas Medical Branch, Galveston, TX 77555

Innate immune response is the first line of defense against viral infections. A complex array of intracellular signaling pathways such as, stress response, innate immune and programmed cell death signaling, are activated in response to viral infection to mount an efficient host response. Extensive cross talk exists between these pathways. To study the connection between these signaling pathways and cellular phenotype, single-cell reporters can be used to probe signaling dynamics and generate computational models of innate immune response. Here, we report the generation of florescent signaling reporter cell lines based on kinase translocation reporters (KTR). KTR system was invented by the Markus Covert lab and is based on conversion of phosphorylation of a reporter into a nucleocytoplasmic translocation. These biosensors are shown to be rapid, specific and quantitative reporters for various kinases, including MAPKs. We have generated stable mammalian reporter cell lines for ERK, JNK, p38 and PKA kinases, and validated these using LPS mediated signaling. Our future studies will focus on quantifying signaling pathways and cellular phenotypes in response to viral infection and build computational models of innate immune signaling. This work will greatly expand our knowledge of host cell responses to viral infections and guide future therapeutics.

Poster 2

Breaking the Sertotype Barrier with Broad-Spectrum, PCPcon Antigens Against Alphaviruses

Schein CH[1], Rafael G[2], Baker WS[1], Anaya ES[3], Schmidt JG[3], Weaver SC[2], Negi SS[1], Braun W[1]

1. Department of Biochemistry and Molecular Biology, UTMB Galveston, TX 77555
2. Department of Microbiology and Immunology, UTMB Galveston, TX 77555
3. Department of [6]Biochemistry and Biotechnology, Bioscience Division, Los Alamos National Laboratory, NM 87545
Corresponding authors: Catherine Schein chschein@utmb.edu; Werner Braun, webraun@utmb.edu

Background: The mosquito-borne alphaviruses (AV) cause epizootic encephalitic outbreaks with high mortality (eastern and Venezuelan equine encephalitis (EEEV and VEEV), Madariaga virus (MADV)) or chronic arthralgia and heart problems (Chikungunya virus, CHIKV). As many AV co-circulate, there is a pressing need for safe, broad-spectrum vaccines to prevent debilitating encephalitis and arthralgia. Human trials have shown immune interference when mixing antigens. We produced PhysicoChemical Property Consensus (PCPcon) protein and peptide antigens to epitope-rich regions of the E2 protein of all AV. Protein/peptide antigens are molecularly defined and easily stored requiring no animal cell culture.

Goals: Demonstrate PCPcon protein/peptide protect against challenge with encephalitic AV. Test computationally derived PCPcon E2-B domain antigens combined with peptides to surface exposed areas of the E2-A domain for protection against VEEV and EEEV challenge.

Methods: Rabbits were inoculated 1x with 200 ug each protein/10 ug each of 4 A-region peptides in specially formulated FCA, and boosted 3x with 100 µg protein/10 µg each peptide in FIA. CD1 mice were inoculated with 3 x 20µg doses in ASO3 adjuvant, 3 weeks apart, of species-specific proteins antigens $VEEV_{con}$, $EEEV_{con}$, $CHIKV_{con}$, a PCPcon based on all three of these (EVC_{con}) or $Mosaic_{con}$, $AllAV_{con}$ of 24 AV reference strains altered to contain known epitopes of VEEV and CHIKV. A mixture of 5 µg each of 4 peptides representing surface-exposed regions of the E2-A domain was administered 2x at weeks 4 and 7 to each protein-vaccinated animal. Negative controls were adjuvant only, positive were IRES-attenuated whole AV expressing the E proteins of VEEV or EEEV[4]. Challenge used wild-type strains VEEVZPC738 or EEEV93939, three weeks after the third inoculation.

Results: 9/10 inoculated with $EEEV_{con}$+peptides survived EEEV challenge with no weight loss or viremia 2 days after challenge. All protein vaccinations reduced viremia 2 days after challenge against both EEEV and VEEV. For those vaccinated with the recombinant protein antigens plus peptides, 4 of 5 $CHIKV_{con}$,3 of 5 $VEEV_{con}$, 3 of 5 $Mosaic_{con}$ and 2/5 EVC_{con} mice survived. Only 2/5 $VEEV_{con}$ and 1/5 $EEEV_{con}$ inoculate survived VEEV challenge.

Conclusions: All the protein/peptide inocula induced serotype specific or broad-spectrum protective antibodies in inoculated rabbits. They also reduced viremia 2 days post challenge in inoculated CD1 mice but had mixed effects on survival. Further vaccination studies will use different adjuvants and optimized protein/peptides to enhance broad spectrum protection.

Acknowledgements: The project was supported by the NIH R01 AI137332 grant to WB, CHS and SW.

Poster 3

Dysregulation of C-type lectin Receptors in HIV and Mycobacterium tuberculosis Co-infection

Browning S[1], Paez R[1], Endsley M[1], Naqvi K[2], Huante M[1], Chauhan S[1], Gelman B[3], Endsley J[1]

1. Department of Microbiology and Immunology, University of Texas Medical Branch, Galveston, TX 77555
2. Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA.
3. Department of Pathology, University of Texas Medical Branch, Galveston, TX 77555

Corresponding author: Janice Endsley, Department of Microbiology and Immunology, University of Texas Medical Branch, Galveston, TX 77555, Email: jjendsle@utmb.edu

Background Infection with *Mycobacterium tuberculosis* (Mtb) is a serious and potentially life-threatening condition, especially in people with HIV (PWH). According to the WHO, there were 10.6 million new tuberculosis (TB) cases in 2021, and 700,000 of those cases were among PWH. Macrophages are a host cell for both pathogens and play an important innate immune role in determining the outcome of disease. C-type lectin receptors (CLR) are pattern recognition receptors (PRR) abundantly expressed on the macrophage surface that orchestrate the innate immune response to microbial insults.

Hypothesis/Goals The purpose of this project is to investigate the signaling pathways involved in regulation of MGL expression and to identify mechanisms that HIV exploits to disrupt this process.

Methods Human tissue samples used for imaging and other experiments were obtained from the National NeuroAids Tissue Consortium. In vitro experiments were carried out using monocyte-derived macrophages (MDM) from the THP-1 cell line or from primary human PBMC isolated from healthy donors. THP-1 MDM were differentiated using PMA before being stimulated with the designated treatments.

Results We previously identified a role for the macrophage galactose-type lectin receptor (MGL) CLR in protection against TB. In subsequent studies, we observed suppression of MGL in tissues of HIV-infected decedents and in human macrophages following in vitro infection with HIV. In human THP-1 cells and a humanized mouse model, we observe that HIV infection markedly impairs activation of MGL by mycobacteria in comparison to other CLRs with defined roles in antimycobacterial immunity including DC-SIGN and Dectin 1. We further determine roles for TLR2/6 heterodimer, TLR4, and TGF-β signaling pathways for transcriptional regulation of MGL. Importantly, these pathways have roles in innate immunity and pathogenesis following Mtb or HIV infections.

Conclusions We report a differential expression of the CLR MGL in the setting of TB and HIV infections, as well as a defect in Mtb-mediated upregulation in the setting of co-infection. We also identify PRR signaling pathways that contribute to activating expression of this receptor. These findings advance our understanding of MGL regulation as part of the CLR repertoire, as well as its role in the response to Mtb and to Mtb/HIV co-infection.

Acknowledgements NIH R31AI138328, R61AI138328

Poster 4

Apex1 Restrains P53 Signaling in Activated T Cell And Potentiates Systemic Lupus Erythematosus Development

Du Y[1], Xing J[1], Yuan R[2], Fang M[1], Lu W[1], Zhang A[1], Zhang Z[1, 3]

1. Department of Surgery and Immunobiology and Transplant Science Center, Houston Methodist Research Institute, Houston, TX, 77030, USA.
2. HSS Research Institute and David Z. Rosensweig Genomics Research Center, Hospital for Special Surgery, New York, NY, USA.
3. Department of Surgery, Weill Cornell Medical College of Cornell University, New York, NY, 10065, USA.

Correspondence: Zhiqiang Zhang, Department of Surgery and Immunobiology and Transplant Science Center, Houston Methodist Hospital, 6670 Bertner Ave, Houston, TX 77030, zzhang@houstonmethodist.

ABSTRACT

Background: Systemic lupus erythematosus (SLE) is an incurable autoimmune disease with multiple organ damage. Elimination of pathogenic autoreactive T cells in SLE is presumed to ameliorate autoimmune inflammation. Elevated Apex1 auto-antibodies were found in serum samples of human lupus patients. However, whether Apex1 plays a role in lupus development is not characterized.

Results: In this study, we report that global or T cell specific depletion of Apex1 in lupus-prone mice (Lpr, Ape^{CD4Cre}) reversed the disease progression, with the failure to develop splenomegaly, swollen lymph nodes, much lower autoantibodies, compromised nephritis and completely reversed the autoimmunity-induced death. Lpr, Ape^{CD4Cre} mice have diminished aberrant Th1, CD4-CD8- T cell, CD44+ memory T cells and Tfh cell and decreased abnormal B cell populations and autoantibodies production. Mechanistically, we demonstrated Apex1 deficiency compromised IFN gamma production but marginally impact cell proliferation by TCR stimulation. However, Apex1 deficiency impaired IL2-STAT5 signaling in activated T cells, which leads to dramatically decreased cell expansion ability and decreased viability. RNASeq and ATACSeq analysis revealed Apex1 is a strong epigenetic suppressor of chromatin accessibility of p53 target genes in activated T cells in response to IL2, resulting in the upregulation of p53 target genes such as p21, the powerful cell cycle arrest gene.

Conclusion: Altogether, we have shown Apex1 plays an indispensable role in both T cell function and expansion. Our study reveals an undefined role of Apex1 in lupus development and provides a potential drug target to cure lupus disease.

Acknowledgement: The work is supported by R01AI155488 and the Lupus Research Alliance grant 519418.

Poster 5

Epithelial cGAS Mediates Allergen-induced Neutrophil and Dendritic Cell Recruitment in the Early Stages of Allergic Airway Inflammation

Govindhan A[1], Hosoki K[1], Rodriguez A[1], Hazra T[2], Sanjiv S[1*]

1. Department of Medicine, Immunology Allergy and Rheumatology, Baylor College of Medicine, Houston, Texas
2. Department of Medicine, University of Texas Medical Branch, Galveston, Texas, USA

Corresponding author: Sanjiv Sur, Department of Medicine, Immunology Allergy and Rheumatology, Baylor College of Medicine, Houston, Texas, Email ID: sanjiv.sur@bcm.edu

Background: Exposure of the airways to allergens rapidly induces oxidative DNA damage in the airway epithelium. Cyclic-GMP-AMP synthase (cGAS) is an immune-surveillance DNA-sensor that senses damaged DNA and induces innate inflammation. We hypothesized that sensing of allergen-induced damaged DNA by epithelial club cell cGAS stimulates an innate neutrophilic immune response. To test this hypothesis, we investigated the in vivo role of epithelial cGAS expression in allergen challenge-induced innate neutrophilic airway and lung inflammation.

Methods: We developed conditional knockout $cGAS^{flox/flox}$; Clara cell secretory protein $(CCSP)^{Cre}$ mice ($cGAS^{flox/flox}/CCSP^{Cre}$) with loss of epithelial cGAS and wildtype littermate control $cGAS^{flox/flox}$ mice with wild-type levels of epithelial cGAS. Mice were sensitized with multiple challenges of cat dander extract (CDE) and challenged a week later with either phosphate-buffered saline (PBS) or CDE to elicit an allergic airway inflammation. To assess the early wave of neutrophil and dendritic cell recruitment after the CDE challenge, mice were euthanized 28h after these challenges. Neutrophils and dendritic cells in lung single-cell were quantified by gating $CD45^+$ $CD11b^+$ $Ly6g^+$ Siglec F- and $CD45^+$ $CD11b^+$ $CD11c^+$ IA/IE^+ cells using high-parameter flow cytometry.

Results: As expected, PBS challenge in wild-type $cGAS^{flox/flox}$ mice and conditional epithelial knockout $cGAS^{flox/flox}/CCSP^{Cre}$ recruited very few and similar numbers of neutrophils and dendritic cells into the lungs. By contrast, compared to $cGAS^{flox/flox,}$ CDE challenge in $cGAS^{flox/flox}/CCSP^{Cre}$ recruited about 40% fewer neutrophils ($p<0.0001$) and dendritic cells ($p<0.01$).

Conclusions: cGAS expression in clara club epithelial cells is rate limiting and mediates allergen-induced innate transmigration of neutrophils and dendritic cells into the lungs. Additional studies are required to elucidate the molecular mechanisms by which epithelial cGAS regulates the recruitment of neutrophils and dendritic cells during the early stages of allergic airway inflammation.

Acknowledgments:
Funding: National Heart, Lung, and Blood Institute (5R01HL145477-02 and 3R01HL145477-01S1)
Department of Defense (PR171425 W81XWH-18-1-0743)

Poster 6

Allosteric Inhibition of CXCR1/2 Chemokine Receptors Attenuates Th2/Th17 Allergic Lung Inflammation

Hosoki K[1], Govindhan A[1], Knight M[1], Hazra T[2], Sur S[1]
1. Department of Medicine, Baylor College of Medicine
2. Department of Medicine, University of Texas Medical Branch

Corresponding author: Sanjiv Sur, Department of Medicine, Baylor College of Medicine, One Baylor Plaza, Houston, Texas, E-mail: Sanjiv.Sur@bcm.edu

Background: Asthma is characterized by chronic eosinophil and/or neutrophil infiltration to the airways mediated by T helper 2 (Th2) and T helper 17 (Th17) cells. A series of publications have shown that CXC chemokines are elevated in allergic inflammation, but their role in induction of Th2 and Th17-mediated allergic eosinophilic airway have not been reported. CXCR1 and CXCR2 are G protein-coupled chemokine receptors for CXCL CXCL1, CXCL2, CXCL3, CXCL5, CXCL6, CXCL7, and CXCL8 chemokines. We reported that administration of CXCR2 small molecule inhibitor SB225002 or dual CXCR1/2 inhibitor reparixin suppressed allergen-induced eosinophilic allergic airway inflammation in mice. Here we explored the gap in knowledge about the role of CXC chemokines in cytokine production from Th2 and Th17 using ladarixin, an allosteric inhibitor of CXCR1/2.

Hypothesis/Goals: We hypothesized that CXCR1/2 ligand CXC chemokines stimulate Th2 and Th17 cytokine synthesis from T cells in the lungs of allergic mice, and induction of allergic inflammation. To test this hypothesis, we utilized ladarixin, a second generation orally bioavailable dual CXCR1/2 inhibitor that binds an allosteric pocket of the trans-membrane region of both receptors with a 100-fold higher affinity than first generation CXCR1/2 inhibitors.

Methods: Naïve C57BL/6 mice were sensitized to cat dander extract (CDE), then challenged with intranasal phosphate buffered saline (PBS) or CDE with or without administration of oral ladarixin via gavage. Induction of allergic lung inflammation, serum IgE, mRNA expression of chemokines and chemokine receptor were examined. Cytokine generation from lung T-cells and inflammatory cells were elucidated using high-parameter flow cytometry.

Results: CDE-challenge in sensitized mice induced allergic lung inflammation characterized by increases in the numbers of BAL and lung macrophages, neutrophils, eosinophils, serum total IgE and serum CDE specific IgE. Oral administration of ladarixin blocked these increases. CDE-challenge upregulated mRNA expression of *Il4, Il5, Il13, Il6, Il1β, Tgfβ1, Il17, Il23, Gata3,* and *Rorc* in bronchioalveolar lavage (BAL) cells, and oral administration of ladarixin inhibited these upregulations. CDE-challenge increased the number of T-cells producing IL5 or IL17, and IL-23-producing neutrophils, epithelial cells and T-cells, and oral administration of ladarixin inhibited these increases.

Conclusions: These observations indicate that oral ladarixin attenuates Th2/Th17-associated allergic lung inflammation. We suggest that additional studies should be performed in humans to assess whether it is an effective therapeutic strategy in asthma.

Acknowledgements: This research was supported in parts by the National Heart, Lung, and Blood Institute (grant nos. 5R01HL145477-02 and 3R01HL145477-01S1) and the Department of Defense (grant no. PR171425 W81XWH-18-1-0743).

Poster 7

Engineered Probiotic for Oral Delivery of a Joint-Targeted Peptide Therapy for Rheumatoid Arthritis

Kady MR[1], Laragione T[2], Gulko PS[2], Beeton C[3], Britton RA[1]

1. Department of Molecular Virology and Microbiology, Baylor College of Medicine
2. Division of Rheumatology, Icahn School of Medicine at Mount Sinai
3. Department of Integrative Physiology, Baylor College of Medicine

Corresponding Author: Mohamed Ryan Kady, Department of Molecular Virology and Microbiology, Baylor College of Medicine, 1 Baylor Plaza, Houston, Texas, E-mail: kady@bcm.edu

Background:
While peptide drugs often have high specificity, oral peptide administration is a challenge due to the harsh environment and tight mucosal barrier of the gut. Oral delivery of therapeutics via bioengineered live microbes has emerged as a promising strategy to overcome this hurdle. Oral gavage of *Limosilactobacillus reuteri* engineered to secrete the immunomodulatory peptide ShK-235 has been successful in treating rat models of autoimmune disease. We sought to extend this exciting finding to other peptide drug candidates.

Hypothesis/Goals:
Iberiotoxin (IbTX), a peptide found in scorpion venom, is a specific and potent blocker of the $K_{Ca}1.1$ ion channel. This channel is necessary for proliferation of the inflammatory fibroblast-like synoviocyte (FLS) cells which drive rheumatoid arthritis (RA). Injected IbTX treats arthritis in animal models by blocking inflammatory FLS proliferation and invasion. Our hypothesis is that IbTX can be functionally detected in the supernatant of *L. reuteri* engineered to secrete it and in the serum of rats orally gavaged with the bacteria, as a potential alternative to injection.

Methods:
A construct for secretion of IbTX was designed with an inducible vector and transformed into *L. reuteri* ATCC PTA 6475, yielding LrIbTX. Healthy 8-week-old Lewis rats were orally gavaged with 10^9 CFU of induced LrIbTX and their serum collected 6 hours later. *In vitro* proliferation of pristane-induced arthritic rat FLS cells exposed to LrGusA or LrIbTX supernatants as well as corresponding gavaged rat sera was measured by ^{3}H-thymidine incorporation.

Results:
LrIbTX showed no growth deficits before or after induction as compared to wild type (n = 6 independent colonies). Supernatants from induced LrIbTX significantly decreased proliferation of pristane-induced arthritic rat FLS cells *in vitro* compared to those from induced LrGusA control (87.3% decrease, $p = 0.0286$ by Mann-Whitney test, representative of n = 2 independent experiments) Sera of rats gavaged with LrIbTX also inhibited proliferation versus control to a lesser degree (15.4% decrease, $p = 0.0271$ by unpaired t test, n = 4 rats per group). This suggests that oral IbTX secreted by *L. reuteri* present in the gut is absorbed into the bloodstream, and may be useful as a therapy for RA.

Conclusions:
L. reuteri was engineered to secrete iberiotoxin, a promising peptide drug candidate for treatment of rheumatoid arthritis. *In vitro* assays on arthritic rat joint cells validated that bacterial supernatant as well as serum of rats orally administered the bacteria significantly blocked proliferation, suggesting absorption of functional peptide from the gut into the bloodstream. This platform may serve as a useful way to orally administer other targeted peptides for autoimmune disease therapy, including RA.

Acknowledgements:
This work was funded by Department of Defense award WS00664401.

Poster 8

Dnmt3a$^{-/-}$ Leukocyte Migration, Expansion are Accelerated in Response to Acute Viral Pneumonia

Kennedy II DE[1], Le DT[1], Florez MA[1], Tran BT[1], Wathan TK[1],. Maknojia AA[1], Fernandez-Sanchez JV[1], Cao R[1], Thatavarty A[1], Maknojia AA[1], Morales-Mantilla DE[1], King KY[1]

1. Department of Pediatrics, Division of Infectious Diseases, Baylor College of Medicine, 1102 Bates Street, Suite 1150, Houston, TX 77030

Corresponding author: Daniel E. Kennedy II, Department of Pediatrics, Baylor College of Medicine, 1102 Bates Street, Houston, TX, E-mail: daniel.kennedyii@bcm.edu

Background: Clonal hematopoiesis (CH) results from expansion of a mutant hematopoietic stem cell in the bone marrow. Mutations in the gene encoding DNA methyltransferase 3 alpha (*DNMT3A*) constitute ~60% of mutations associated with CH. CH increases the risk of negative health outcomes to infection (Bolton et al, 2019). Germline and age-related *DNMT3A* mutations in monocytes, neutrophils, and lymphocytes have been implicated in the dysregulation of immune responses (Youngblood et al, 2011; Tovy et al, 2022).

Hypothesis: Our ***central hypothesis*** was that loss-of-function *Dnmt3a* mutation leads to attenuated myeloid immune responses. To investigate this, we screened broadly for altered immune cell responses to respiratory infection in a conditional mouse model of *Dnmt3a* CH.

Methods: Wild-type (WT) and *Dnmt3a$^{-/-}$* (KO) mice were intranasally challenged with IAV at doses of 1X- and 2X LD_{50} or PBS sham-challenged at 10-16 weeks old. Mice were weighed daily and euthanized 40 h or five days post-infection (PI). Blood, lungs, and spleens were analyzed by flow cytometry for differences in cell type populations.

Results: There was no significant change in body mass of KO mice compared to WT 40 h or five days PI. However, neutrophil infiltration 40 h PI in the lungs of KO mice was significantly more rapid than in WT mice. Kinetic studies of neutrophil migration significantly showed mature neutrophils ($CXCR4^+$ $CD62L^-$) were nearly absent from peripheral blood of uninfected and challenged KO mice 40 h PI compared to WT mice. Mature neutrophils trended higher in the lungs of KO mice 40 h PI than in WT mice, and immunophenotyping of lung neutrophils showed an increase in $CD49d^+$ $CD69^+$, suggesting a more robust migration into the airways. We detected a lower number of dendritic cells in the KO lungs compared to WT lungs at 40 hours. Furthermore, DC numbers were significantly higher in KO spleens than WT 40 h PI with no significant difference in DC in either tissue five days PI. A significant expansion of B lymphocytes was observed in KO spleens compared to WT at 40 PI. However, the B cell expansion was short lived and splenic B cell numbers were low in both KO and WT mice by five days PI.

Conclusions: Given that DCs typically migrate from pulmonary tissues to draining lymph nodes within 24 h PI in viral infections (Belz et al, 2004; Moltedo et al, 2011), we speculate that pulmonary DC migration is accelerated in *Dnmt3a* KO mice compared to WT. Acceleration of DC migration and lymphocyte expansion may be sufficient for initial exposure. However, clinical observations suggest memory responses are impaired (Bolton et al, 2019). We will investigate whether changes in DC kinetics correspond to enhanced antigen-presentation or generation of antigen-specific T and B cells.

Acknowledgements: Funding was provided by the following grants: NIH grant # 5T32HL092332-20; NIH grant # R35 HL155672; NIH grant # 1 P01 CA265748. We thank BCM CCSC, TCH CCCL, CAGT, and WTS Center for expertise in flow cytometry.

Poster 9

Structural Modeling T Cells Receptor Interactions for Immunotherapy Applications

Le HN[1], Freitas MV[1], Antunes DA[1, *]

1. Department of Biology & Biochemistry, University of Houston, USA

* Corresponding Author: Dinler Antunes, Department of Biology & Biochemistry, University of Houston, 3517 Cullen Blvd. Science & Engineering Research Center (SERC) Bldg 545, Suite 3007. Houston, TX 77204-5056, antunesda@central.uh.edu

Background: T cell lymphocytes play a central role in triggering cellular immune responses against "non-self" peptide-targets. T cells recognize these peptide-targets via the T cell receptors (TCR) located on their membrane. These receptors recognize only peptides bound to Major Histocompatibility Complex (MHC) molecules. Each TCR is specific to one peptide-MHC (pMHC) complex, and this specificity is important to prevent off-target toxicity in cellular responses. However, in some cases, a TCR can recognize more than one pMHC, which is known as T-cell cross-reactivity. Therefore, the characterization of the molecular interactions driving T-cell specificity (i.e., TCR fingerprints) has become extremely important in diagnosis of autoimmune diseases and for immunotherapy treatment of several diseases. There are a few methods proposed to predict 3D structure of TCR-pMHC complexes, including ImmuneScape (IS) and TCRpMHCmodels (TCRpMHC). There are also some general-purpose modeling methods, such as AlphaFold2 (AF), which could be tailored for this application.

Goal: In this context, our project mainly focused on benchmarking the accuracy of 24 models created by three different well-known methods: IS, TCRpMHC and AF, against experimentally determined crystal structures of the same complexes.

Methods: Models were evaluated regarding the Root Mean Square Deviation (RMSD) of 5 distinct groups of atoms of the TCR-pMHC complex: all proteins, peptide, MHC chain, TCR chains and six complementarity determining region (CDR) loops.

Results: Our preliminary results suggest that all methods are reasonably capable of producing the overall structure of the MHC and the TCR, but IS is the method with greater accuracy for modeling the peptide (Median RMSD of 1.96 Amstrong) and the flexible CDR loops (Median RMSD of 1.93 Amstrong). Our future analysis will include a detailed comparison of the network of interactions between the CDR loop residues and the peptide residues, and the stability of these contacts when submitted to molecular dynamics simulations.

Conclusions: This could be further applied in improving the accuracy of the structure-derived TCR fingerprints from amino acid sequences. Our long-term goal is to define the best modeling/simulation protocol to accurately predict the molecular fingerprint for a given TCR of interest, which could be used to guide the design of better and safer TCR-based immunotherapies.

Poster 10

Investigating the Accuracy of Alternative Scoring Functions on the Ranking of Docked Peptide-HLA Conformations

Lewis JD[1], Conev A[2], Vaz de Freitas M[1], Hall-Swan S[2], Kavraki LE[2], Antunes DA[1]

1. Department of Biology and Biochemistry, University of Houston
2. Department of Computer Science, Rice University

* Corresponding Author: Dinler Antunes, Department of Biology & Biochemistry, University of Houston, 3517 Cullen Blvd. Science & Engineering Research Center (SERC) Bldg 545, Suite 3007. Houston, TX 77204-5056, antunesda@central.uh.edu

Background: Cellular immunity requires the participation of diverse mechanisms to combat infections and cellular diseases. Human-Leukocyte Antigen (HLA) receptors play a vital role in cellular immunity due to their ability to present peptides to T-cell lymphocytes. The recognition of peptide-HLA (pHLA) complexes leads to T-cell activation, elimination of the diseased cell (e.g., tumor or virally infected cells), and the generation of immunological memory against the recognized, irregular peptide. This mechanism is used to boost the cellular immunity against a specific peptide via innovative immunotherapy methods like cancer vaccines and CAR-T immunotherapy. Sequence-based techniques, paired with computational methods, are used as the gold-standard to identify peptides that bind to HLAs for direct applications in immunotherapy. However, these methods have limitations (e.g., lack of data for less prevalent HLA alleles). Because of this, structure-based methods (e.g., molecular docking) have been proposed as a general approach for studying and predicting pHLA interactions. These methods are still limited by the efficiencies of their sampling algorithms, and the accuracy of the scoring functions used to rank predicted conformations. Our group developed the meta-docking approach DINC (Docking INCrementally), which outperformed other docking tools, to address this sampling challenge. However, we still need to identify an accurate scoring function.

Goals: Compare crystallographic pHLA conformations docked by DINC to the ranked crystal pHLA conformations of 11 different scoring functions and determine the most accurate scoring function.

Methods: We tested 11 existing scoring functions to identify the best option for ranking peptide conformations produced by DINC. In order to benchmark the scoring functions, we selected a dataset of 25 pHLA complexes for which we have (i) an experimentally-determined crystal structure, and (ii) an ensemble of 100 alternative conformations that were sampled by DINC in a self-docking experiment. The experimentally-determined crystal structures provide us a reference for ranking all predicted conformations in terms of their distance to the *correct answer* (i.e., compute the RMSD for all heavy atoms of the peptide). In order to account for and correct potential packing effects and other artifacts of crystallization, we also ran a control experiment using energy minimized structures as a reference for RMSD calculations.

Results: Our preliminary benchmark included 11 alternative scoring functions: Vina, Vinardo, AutoDock4, 3pHLA, DOPE, GradDock, FoldX, Bach, Pisa, Zrank, and Irad. Among those, DOPE and AutoDock4 were the best options. As more conformations were introduced, all scoring functions performed at similar levels.

Conclusion: DOPE outperformed all other scoring functions. Our future actions include expanding our dataset to 836 pHLAs (all available pHLA crystal structures), and including outputs made by other validated molecular docking tools. We will also evaluate the potential usage of consensus scoring methods. If successful, this project will have direct applications to antiviral vaccine development and cancer immunotherapy by providing the means for accurate structure-based screening of HLA binders.

Acknowledgments: CNRCS at the Biology and Biochemistry Department of the University of Houston, and the Department of Computer Science at Rice University.

Poster 11

Optogenetic Engineering of STING Signaling to Remotely Control anti-Tumor Immunity

Liu S[1], Dou Y[1,*], Chen R[1,*], Lee Y-T[1], Jing J[1], Zhou Y[1,2,#], Huang Y[1,2,#]

1. Institute of Biosciences and Technology, Texas A&M University, Houston, TX, USA
2. Department of Translational Medical Sciences, School of Medicine, Texas A&M University, Houston, TX 77030, USA

Corresponding author: Yubin Zhou and Yun Huang, Institute of Biosciences and Technology, Texas A&M University, 2121 W Holcombe Blvd, Houston, TX 77030, USA. E-mail: yubinzhou@tamu.edu (Y.Z.) or yun.huang@tamu.edu (Y.H.)

Background and Aim: The cGAS-STING signaling pathway is regarded as a promising target for cancer therapeutics. STING activation has been shown to promote the maturation and antigen-presenting capability of dendritic cells (DCs), which enhances T cell priming and its cytotoxicity against tumor cells. However, the intratumoral injection of STING agonists has a number of drawbacks such as enhancing tolerogenic immune response, promoting the apoptosis of T cells and B cells, and causing systemic inflammation. These limitations point to a need to develop a method that allows temporal and spatial control over STING signaling.

Methods and results: Here we present an ultra-light-sensitive optogenetic device, designated LiSmore for light-inducible SMOC-like repeats, that remotely controls STING activation and downstream gene expression in antigen-presenting cells to mount innate immunity. We demonstrate that noninvasive light-triggered STING modulation effectively promotes dendritic cell (DC) maturation and antigen presentation, allowing T cells to be effectively sensitized to engage tumor antigens, thereby photo-boosting anti-tumor immune response. Importantly, combining LiSmore with immune checkpoint blocker (ICB) synergistically enhances antitumor efficacy in an immunosuppressive lung cancer model, which otherwise remains largely unresponsive to ICB treatment.

Conclusion: Our findings establish that targeted optogenetic activation of STING signaling allows for the remote control of DC functions by boosting anti-tumor immunity at the tumor sites. Hence, LiSmore sets the stage for the development of wireless optogenetic immunomodulatory therapies in a light-switchable manner.

Acknowledgment: This work was supported by the Welch Foundation (BE-1913-20220331 to Y.Z.), the Cancer Prevention and Research Institutes of Texas (RP210070 to Y.Z.), and the National Institutes of Health (R01GM144986 to Y.Z., R01HL134780 to R01 Y.H., R01HL146852 to Y.H., and R01CA240258 to Y.H.). Images were created by Biorender.com.

Poster 12

A Spatiotemporal Cell Atlas of Human Gastric Malignancy Reveals Mechanisms Underlying Metastasis and Immunotherapy Response

Luo Y[1,2], Kang M[3], Liu W[2], Wang L[4], Chen J[3], Liang H[2,1,5]

1. Graduate Program in Quantitative and Computational Biosciences, Baylor College of Medicine
2. Department of Bioinformatics and Computational Biology, MD Anderson Cancer Center
3. Department of Gastrointestinal Surgery, Second Affiliated Hospital, Zhejiang University
4. Institute of Immunology and Bone Marrow Transplantation Center, Zhejiang University
5. Department of Systems Biology, MD Anderson Cancer Center

Corresponding author: Han Liang, Department of Bioinformatics and Computational Biology, MD Anderson Cancer Center, 1400 Pressler Street, Houston, TX, E-mail: hliang1@mdanderson.org

Background
Cellular heterogeneity in the tumor immune microenvironment (TIME) of gastric cancer (GC) is progressively molded in pre-malignant lesions and has a profound impact on disease progression and responses to therapeutics, in particular those based on immune checkpoint blockade (ICB).

Hypothesis/Goals
We aim to characterize for the first time the single-cell kinetics of tumor-infiltrating immune populations in gastric cancer patients treated with ICB.

Methods
Here, we generated for the first time single-cell RNA sequencing (scRNA-seq) and TCR sequencing (scTCR-seq) profiles of ICB- treated primary GC tumors, as well as liver and ovary metastases. When integrated with public scRNA-seq datasets, our data capture a full trajectory of GC malignancy comprising more than 300,000 cells derived from 73 samples. We further performed bulk TCR-seq, cytometry by time of flight (CyTOF), and multiplex immunofluorescence (mxIF) on independent GC samples to orthogonally validate the key observations from the scRNA-seq cohort and unbiasedly search for more in-depth and spatial- relationship-focused features of ICB-responsive immune population

Results
Built upon this multi-omic atlas of GC cell states, we identified remarkable transformation in the abundance and clonal dynamic of distinct immune populations and their population-specific transcriptional programs. Most importantly, we observed the rejuvenation of exhausted CD8+ T cells induced by anti-PD-1 treatment, which is associated with the enhanced immunogenicity of gastric cancer cells. In addition, we found the enrichment of NK-like terminally differentiated CD8+ T cells in metastases independent of migration destinations.

Conclusions
Our single-cell ICB-perturbed spatiotemporal GC landscape reveals how neoadjuvant checkpoint-blockade induces local and systemic tumor immunity. As a cellular and molecular reference, it also enables high-resolution interpretation of future single-cell omics data in gastric cancer that may be masked by de novo analysis.

Acknowledgements
This study was supported by grants from the National Natural Science Foundation of China (Nos. 32030035, 31870874, 32000623, and 32100693)

Poster 13

Microbiome-Driven Type I Interferon Signaling Regulates the Survival of B-cells

Maknojia AA[1,2], Walker F[5], Nolan L[4], Yan H[3], Baldridge M[5], King KK[1,2]

1. Immunology and Microbiology, Graduate School of Biomedical Sciences, Baylor College of Medicine, Houston, TX
2. Pediatric Infectious Diseases, Baylor College of Medicine, Houston, TX
3. Immunology, Graduate School of Biomedical Sciences, Baylor College of Medicine, Houston, TX
4. Department of Pediatrics, Washington University School of Medicine, St. Louis, MO
5. Division of Infectious Diseases, Department of Medicine, Edison Family Center for Genome Sciences and Systems Biology, Washington University School of Medicine, St. Louis, MO

Corresponding author: Katherine Y. King, Pediatric Infectious Diseases, Baylor College of Medicine, 1 Baylor Plaza, Houston, TX 77030, kyk@bcm.edu.

Background: Prior studies have shown that 10-15% of patients treated with antibiotics for 2 weeks or longer develop hematological complications such as neutropenia, lymphopenia, and other cytopenias. The King lab recently discovered that depletion of the microbiome on prolonged antibiotics results in impaired hematopoiesis. We discovered that microbiome-induced type I interferon (IFN-I) production promotes steady-state hematopoiesis. We found that B cells were strongly and reproducibly suppressed upon antibiotic treatment in specific pathogen free mice. However, the pathways utilized by the microbiome to induce tonic IFN-I signaling and their role in the maintenance of B cell populations remain elusive.

Hypothesis: Here, we investigated the mechanism by which the microbiome regulates B cell homeostasis. We hypothesized that microbiome-driven basal IFN-I signaling regulates the B cell survival.

Methods: We treated C57BL/6 WT mice with an antibiotic cocktail (Abx) consisting of vancomycin, ampicillin, metronidazole, and neomycin or flavoring alone in the water for 2 weeks *ad libitum*. To determine if B cells suppression on antibiotics is attributed to impaired proliferation, we first harvested whole bone marrow from Abx or mock-treated mice and performed BrdU staining to quantify B cell proliferation via flow cytometry. Next, we tested the effect of antibiotic-mediated IFN-I suppression on the survival of B cell populations via Annexin V staining and FLICA (fluorescently labeled inhibitor of caspase assay), which quantify apoptotic cells and polycaspase activation, respectively. To further investigate the immune signaling pathway responsible for IFN-I-mediated B cell regulation, we characterized B cell defects in *Nod1*$^{-/-}$, *Myd88*$^{-/-}$, *Sting*$^{-/-}$ and *Mavs*$^{-/-}$ mice.

Results: Our findings suggest that microbiome-driven basal IFN-I signaling is not required to regulate the cell cycle dynamics but is required for the survival of lymphoid progenitors and B cell populations in blood, bone marrow, and spleen. Our data from the FLICA assay validated the Annexin V staining results by showing increased polycaspase activation in B cells from Abx-treated mice compared to the controls. Preliminary analysis also shows that NOD1-RIPK2, cGAS-STING, RIG-I-MAVS, and TLR-MYD88 signaling pathways, all of which are shown to produce type I IFN upon microbial stimulation, are dispensable for B cell homeostasis.

Conclusions: In summary, we showed that microbiome-driven tonic IFN-I signaling regulates B cell survival. By identifying the immune signaling pathways that promote IFN-I-mediated hematopoiesis, we hope to devise ways to ameliorate or prevent cytopenias in patients who require long-term antibiotics.

Acknowledgements: This project is funded by NIH R01AI147514, and CTR-CAQ T32 grant (GM 136554-3). This project depended on the support of flow cores at TCH and Center for Human Immunobiology as well as members of the King lab.

Poster 14

Lymphoid Follicle Transcriptome Reveals Maladaptive Immune Responses In Severe Chronic Obstructive Pulmonary Disease (COPD)

Rojas-Quintero J[1], McKenna N[2], Ochsner SA[2], Cala-Garcia J[1], Kheradmand F[1], Rosas IO[1], Polverino F[1]
1. Pulmonary, Critical Care and Sleep Medicine Department. Baylor College of Medicine. Houston, Texas.
2. Molecular and Cellular Biology, Baylor College of Medicine, Houston, Texas

Rationale: Increases in the number and size of lymphoid follicles (LFs) are present in severe stages of COPD and have not been fully characterized. HLA complex is crucial in enabling the immune system to recognize "self" versus "non-self" antigens, and plays a major role in the innate and adaptive immune responses to foreign antigens such as CS.

Methods: Lung follicles from COPD patients with milder (GOLD I-II) and more severe (GOLD III-IV) COPD were sampled using GeoMX® Digital Spatial Transcriptional Profiling. Data were analyzed and normalized using GeoMx® DSP Analysis Suite. Followed by unbiased enrichment, GO pathways and KEGG pathways analyses were performed using PANTHER classification system.

Results: Across all LFs from all COPD patients, the GO PANTHER pathway analysis showed that B cell activation pathways had the highest fold enrichment. GOLD I-II compared to GOLD III-IV COPD patients had the highest expression of *HLA-C* and its ligands (*KIR2DS2*, *KIR2DS1*, *KIR3DL1*; $p<0.0001$) which facilitate CD8-mediated cytotoxicity, and *HLA-G* and its receptor *LILRB4* ($p=0.01$) which are key modulators of immune tolerance. GOLD III-IV COPD patients had the highest HLA enrichment in LFs, with upregulation of genes associated with the transcription (*HIF1A*, *IRF1*, *NFYB* and *NFYC*) and assembly (*CALR*, *TAPBP*, *ERP27*, *MARCHF1*, *B2M*, and *CIITA*) of HLA ($p<0.01$). Interestingly, compared to GOLD I-II, LFs from GOLD III-IV COPD patients had much higher expression of HLAs involved in autoimmune responses to self-antigens and adaptive immune evasion, such *HLA-DRA*, *HLA-DRB1*, *HLA-DPA1, HLA-DPB1*, *HLA-DQA1*, *HLA-DQB1*, *HLA-E* and *HLA-B* ($p<0.0001$).

Conclusions: We show for the first time that LFs from patients with severe COPD are characterized by expression of HLAs associated with immune evasion and autoimmune responses, whereas LFs in milder stages of COPD are characterized by induction of immune responses controlled by tolerance mechanisms.

Keywords: autoimmunity, COPD, HLA, lymphoid follicles, immune checkpoints.

Funding Source: RO1 HL 149744-04/06

Poster 15

Epigenetic Targeting of PRC2 Complexes Upregulates MHC Antigen Presentation Components in Gastrointestinal Cancer Cells

Tovar Perez JE[1,2], Kapoor S[1,2], Muhsin A[1,2], Dashwood WM[1,2], Rajendran P[1,2], Kobayashi K[3], and Dashwood RH[1,2]

1. Center for Epigenetics & Disease Prevention, Texas A&M Health, Houston, TX.
2. Dept. Translational Medical Sciences, Texas A&M College of Medicine, Houston, TX.
3. Dept. Immunology, School of Medicine, Hokkaido University, Sapporo, Japan.

Corresponding author: Jorge Enrique Tovar Perez, Center for Epigenetics & Disease Prevention, Texas A&M Institute of Biosciences & Technology, 2121 W Holcombe Blvd, Houston, TX. E-mail: jtovar@tamu.edu

Background: Low tumor immunogenicity is associated with immune escape, immunotherapy resistance, and poor patient survival [1-3]. Major histocompatibility complex (MHC) antigen presentation pathways (APPs) play a crucial role in promoting tumor T-cell recognition and initiating antitumoral immune responses. However, epigenetic silencing of APPs is a common mechanism in various cancers, including gastrointestinal malignancies [3,4].

Hypothesis/Goals: In the current investigation, mouse colon cancer (MC38/OVA), human colon and duodenal cancer (HCT116 and HUTU80, respectively), and normal colonic epithelial (CCD841) cell lines were treated with epigenetic drug candidates. Additionally, human familial adenomatous polyposis (FAP) organoids and Pirc rat colon adenoma primary cell lines were also treated with epigenetic drug candidates to assess possible immunomodulatory effects in pre-cancer and cancer models, such as induction of APP machinery.

Methods: Immunoblotting and RT-qPCR assays were performed to measure MHC expression, while cell membrane and cytosolic fractions were isolated to assess MHC expression in the surface of cells through immunoblotting. T-cell activation was determined by IL-2 secretion measured by enzyme-linked immunosorbent assay (ELISA), after co-culturing for 20 hours MC38/OVA cells with B3Z $CD8^+$ T-cell hybridomas capable of detecting OVA when presented in the cell surface through MHC-I complexes.

Results: As reported [5], a decrease in histone H3K27 methylation marks via polycomb repressive complex 2 (PRC2) inhibition increased the expression of APP components, based on immunoblotting and RT-qPCR experiments. Normal colonic epithelial cells showed resistance to the treatments, indicating cancer cell-specific effects of the test agents. In MC38/OVA cells, cell fractionation and ELISA assays corroborated that PRC2 inhibition increased cell surface occupancy of MHC-I complexes and increased CD8+ T-cell activation.

Conclusions: These findings have implications for the clinical application of next-generation epigenetic agents [6,7], targeted towards increased tumor immunogenicity and enhanced efficacy of new immunoepigenetic strategies in both preventive and therapeutic scenarios.

Acknowledgements
Supported in part by NCI grant CA122959, by the John S. Dunn Foundation, and by a Chancellor's Research Initiative.

References
1. J Galon, D Bruni. *Nat Rev Drug Discov* 2019;18:197-218.
2. S Yoshihama *et al*., *Sci Rep* 2021;11:3258.
3. S Yoshihama *et al*., *Proc Natl Acad Sci USA* 2016;113:5999-6004.
4. K Suzuki, Y Luo. *Adv Protein Chem Struct Biol* 2017;106:71-111.

5. ML Burr *et al*., *Cancer Cell* 2019;36:385-401.
6. P Rajendran *et al*., *Cancer Res* 2019;79:918-927.
7. S Kapoor *et al*., *Cancers (Basel)* 2021;13:1438.

Poster 16

Diverse Immune Responses of Fecal Microbiota Transplantation Suggest Differences in Enterotype of Microbiota

Verma R[1], Yalcinkaya N[1], Herath M[1], Savidge T[1]

1. TCH Pathology, Baylor College of Medicine (BCM)

Corresponding author: Ravi Verma, TCH Pathology, Baylor College of medicine, 1102 Bates Ave, Feigin Tower, Houston, Texas 77030, E-mail: ravi.verma@bcm.edu

Abstract

Background: The intestinal microbiota play a critical role in the modulation of human health. Dysregulation of the commensal flora, in both diversity and composition, is intimately linked to functional changes of the immune system and subsequently contributes to development of immune disorders. The gut microbiota not only shape the immune system to strengthen health but also to maintain homeostasis.

Hypothesis/Goals: To restore homeostasis of the gut microbiota and immune system, fecal microbiota transplantation (FMT) is considered due to prophylactic or therapeutic modalities. However, efficacy of FMT is genus and species specific and shows great variation within the healthy donors as they may have different enterotypes.

Methods: To identify immune responses induced by FMT, we have tested human healthy donors fecal samples (donor 1,2,3) and mouse donor fecal samples in germ free (GF) mice. We analyzed the immune cells and their cytokine from Liver, mLN, spleen and colon by flow cytometry.

Results: All donor samples including mouse FMT induce RORγt^{+} iTreg cells. Among them, human donor 3 and mouse donor FMT show inducing capabilities the Th17 with RORγt expression suggest that both share some common enterotypes. On the other hand, donor 2 can induce Th1 and Th2 responses by expression of T-bet and GATA3 expression suggest these two donor have different enterotype. Total Foxp3^{+} Treg cells elevation was only observed in mouse FMT group and completely lacked in the human donor group. Further, CD4^{+}Foxp3^{+} Helios^{low} Treg (iTreg) cells induction greatly represented by mice FMT but human donor group exhibited marginal differences.

Conclusions: Our study suggest that different donor microbiota can be differ and it reflect in the form of immune response even though human donor can be different from mice as well. These findings provide new insights into the human donor FMT consideration as each healthy donor represents different immune signatures and they are also different from mouse donor FMT.

Acknowledgements: We thank to CCM animal facility from BCM, TCH Flow cytometry, NIH PO1 for funding the project and all my lab members for their support.

Poster 17

Eosinophil Orchestrates Tissue Repair After Hepatic Ischemia Reperfusion Injury

Yang Y[1], Xu L[1], Atkins CL[1], Wen Y[1], Jeong J-M[1], Kuhlman L[1], Moreno NF[1], Jacobsen EA[1], Ju C[1] *

1. Department of Anesthesiology, McGovern Medical School, University of Texas Health Science Center at Houston

Corresponding author: Cynthia Ju, Department of Anesthesiology, McGovern Medical School, University of Texas Health Science Center at Houston, 6431 Fannin Street, MSB 6.246; Houston, Texas 77030, Tel: 713-500-7424, Changqing.ju@uth.tmc.edu

Background: Hepatic ischemia reperfusion (IR) injury is an inevitable process during liver transplantation surgery, hemorrhagic shock and trauma. Liver injury from IR is a major risk factor not only for early organ dysfunction and failure after liver transplantation but also for acute and chronic rejection and exacerbates the worldwide shortage of transplantable organs. Therefore, research aimed at discovering effective preventive and therapeutic strategies are needed.

Hypothesis: We have previously shown that eosinophils are rapidly recruited to liver after IR surgery in mice and exert a profound hepato-protective function. Interestingly, our examination of the kinetics of eosinophil recruitment revealed that the peak of eosinophil accumulation in the liver was on day 3 after IR injury, coinciding with the critical time point of liver repair and regeneration after injury. The data suggested to us that eosinophils may contribute to liver repair.

Methods and Result: We used an inducible eosinophil-deficient mouse model to deplete eosinophils after the occurrence of hepatic IR injury and observed a marked delay in liver repair compared to eosinophil-intact mice. In contrast, adoptive transfer of bone marrow-derived eosinophils to eosinophil-deficient mice normalized liver repair to a similar extent as in the wild-type mice. Mechanistic studies making use of eosinophil-specific IL-4/IL-13-deleted mice and neutralizing antibodies demonstrated that eosinophil-derived IL4, but not IL-13, is critically involved in liver repair after IR injury. Experiments using hepatocyte-specific and macrophage-specific IL-4Rα knockout mice demonstrated that IL-4 signaling through liver macrophages, but not hepatocytes, plays an essential role in tissue repair after hepatic IR injury. Furthermore, we found that heparin-binding epidermal growth factor-like growth factor (HBEGF) was produced by hepatic macrophages in response to IL-4 release from eosinophils. Moreover, mice lacking liver macrophages-derived HBEGF exhibited impaired tissue repair after IR injury.

Conclusion: Our studies demonstrate that in hepatic IR mouse model, eosinophils persisted in the liver beyond the injury phase and play an essential role in promoting liver repair. Mechanistic studies elucidate that the cross-talk between eosinophils and hepatic macrophage through IL-4/HB-EGF signaling, facilitates hepatocyte proliferation. These findings support further exploration of eosinophils and IL-4/HB-EGF signaling as potential therapeutic targets to improve the outcomes of liver transplantation surgery.

Funding sources: This work was supported by the NIH DK121330, DK122708, DK122796, DK109574 and the University of Texas System Translational STARs award to Cynthia Ju.