LSU System Multi-COBRE Colloquium

FEBRUARY 9 - 10, 2026

Center for Medical Education

LSUHS Shreveport Campus

PROGRAM

Schedule of Events:

MONDAY, FEB 9

8:30 AM **Continental Breakfast** (Center for Medical Education 1st floor)

9:00 AM **Welcome / Introductions** (Assembly Room #2)

Oral Presentations Morning Session 1 (Assembly Room #2)

9:05 – 9:35 AM MBD Presentation #1 – Dr. Jackie Stephens, LSU Department of Biological Sciences & Adipocyte Biology PBRC- *Uncoupling adipose tissue mass and metabolic health*

9:35 – 10:05 AM MBD Presentation #2 –Dr. Timothy Allerton, Vascular Metabolism PBRC- *Role of hydrogen sulfide in skeletal muscle dysfunction and exercise intolerance in HFpEF*

10:05 –10:40 AM **Colloquium Attendees Group Photo (CME stair well) and Network Break**

10:45 –11:15 AM CRBCD Presentation #1 - Dr. Tarek Magdy, Department of Pathology & Translational Pathobiology, LSUHS- *Multi-Omics Profiling of hiPSC-derived Cardiomyocytes Identifies Novel Molecular Drivers and Therapeutic Targets of Sepsis-Induced Cardiomyopathy*

11:15 –11:45 AM CRBCD Presentation #2- Dr. Gopi Kolluru, Department of Pathology & Translational Pathobiology, LSUHS- *CSE and reactive sulfur species regulation in aging vasculature*

11:45 –12:00 PM CRBCD Presentation #3- Dr. Hugh Nam, Department of Pharmacology, Toxicology & Neurosciences, LSUHS- *The role of hydrogen sulfide in heavy alcohol consumption in both humans and mice*

12:00 –12:15 PM CRBCD Presentation #4- Dr. Nobel Bhuiyan, Department of Medicine, LSUHS- *AI, machine learning and cardiovascular disease and future*

12:15 – 1:15 PM **LUNCH (Center for Medical Education- CRAVE Café and outdoors)**

1:20 – 2:00 PM Keynote Talk 1 - Dr. Chris Kevil, *History and Impact of Redox Biology and Cardiovascular Disease COBRE*

Schedule of Events:

MONDAY, FEB 9

Oral Presentations Afternoon Session 1 (Assembly Room #2)

2:00 – 2:30 PM CLBD Presentation #1- Dr. Basel Abuaita, Department of Pathobiological Sciences, LSU Vet Med- *Myeloid IRE1a activation impairs host defense mechanisms against acute respiratory infections*

2:30 – 3:00 PM CLBD Presentation #2- Dr. Sadiya Parveen-Nesson, Department of Microbiology & Immunology, LSUHS- *Targeting host glutaminase as a host-directed therapy for tuberculosis*

3:00 – 3:15 PM CLBD Presentation #3- Dr. Naohiro Kato, Department of Biological Sciences, LSU- *Call for collaboration: fucoxanthinol- a Louisiana-produced natural compoundd with antioxidant, anti-inflammatory, and metabolic activities*

3:15 – 3:30 PM CLBD Presentation #4- Dr. Sarah Voth, Department of Cell Biology and Physiology, VCOM-LA- *When sentinels become saboteurs: the amyloid paradox in ARDS*

3:30 – 3:40 PM **Break (10 minutes)**

3:40 – 4:10 PM Louisiana Training Platform (LTP) Presentation- Mr. Ojasvi Dutta, Program Manager, LBRN Program, Department of Pathobiological Sciences, LSU Vet Med

4:10 – 4:40 PM CPcCR Presentation #1- Dr. Shang Su, Department of Comparative Biomedical Sciences, LSU Vet Med- *Deciphering prostate cancer dormancy for potential therapies against lethal bone metastases*

4:40 – 4:55 PM CPcCR Presentation #2- Dr. Brent Stanfield, Department of Pathobiological Sciences, LSU Vet Med- *The guinea pig model of KSHV infection*

4:55 – 5:10 PM CPcCR Presentation #3- Dr. Weishan Huang, Department of Pathobiological Sciences, LSU Vet Med- *Modulation of antigen receptor signalling for sustainable CAR-T cell therapy*

5:15 PM **Poster Session (Center for Medical Education Gym)** Enjoy passed hors d'oeuvres during the session)

6:15 PM **Dinner Service (Center for Medical Education Gym)**

8:00 PM **Adjourn 1st day**

Schedule of Events:

TUESDAY, FEB 10

8:30 AM Continental Breakfast (Center for Medical Education 1st floor)

9:00 AM **Trainee Awards** (Assembly Room #2)

9:15 – 10:30 AM Campus COBRE Infrastructure Overview (Rasberry Auditorium – 2nd Floor, Room #2315)

10:30 – 11:10 AM Keynote Talk 2 - Dr. Andrew Yurochko, *History and Impact of Immunology and Infectious Disease COBRE* (CME Rasberry Auditorium – Room #2315)

11:15 – 12:00 PM **LUNCH** (Center for Medical Education CRAVE Café and outdoors)

Oral Presentations Afternoon Session 2 (Assembly Room #2)

12:00 – 12:30 PM CAIPP Presentation #1- Dr. Rohit Jangra, Department of Microbiology & Immunology, LSUHS- *From platform to insight: a versatile new system dissects the functions of hantavirus entry glycoproteins*

12:30 – 1:00 PM CAIPP Presentation #2- Dr. Hongyan Guo, Department of Microbiology & Immunology, LSUHS- *ZBP1 in Action: Shielding Against Viruses While Fueling Inflammation*

1:00 – 1:15 PM CAIPP Presentation #3- Dr. Jason Comer, Department of Microbiology & Immunology, LSUHS- *Entry of North American Arenaviruses into Human Cells*

1:15 – 1:30 PM CAIPP Presentation #4- Dr. Stephanie Ander, Department of Microbiology & Immunology, LSUHS- *Defining the Specificity of EEEV Interactions with Heparan Sulfate*

1:30 – 1:40 PM **Break (10 minutes)**

1:40 – 2:10 PM CTVO Presentation #1- Dr. Omeed Moaven, Department of Surgery, LSUHSC-NO- *Reprogramming the Pancreatic Tumor Microenvironment with a Bioengineered Oncolytic Virus Enhances Antitumor Immunity and Treatment Response in Preclinical Models*

2:10 – 2:40 PM CTVO Presentation #2- Dr. Monika Rak, Department of Interdisciplinary Oncology, LSUHSC-NO- *Human endogenous retroviruses (HERVs) associated with glioblastoma prognosis*

2:40 – 2:55 PM CTVO Presentation #3- Dr. Dicle Yalcin, Department of Interdisciplinary Oncology, LSUHSC-NO- *Immune and Inflammatory Determinants of Disease Progression and Therapeutic Response in Kaposi Sarcoma*

2:55 – 3:10 PM CTVO Presentation #4- Dr. Giulia Monticone, Department of Genetics, LSUHSC-NO- *Designing Multifunctional Immunotherapeutics for Viral-Driven Cancers*

3:15 PM **Closing Remarks & Adjourn**

LIST OF POSTERS

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Abstracts

Poster 1

Deciphering The Role of the Genome in MASLD Using Human Induced Pluripotent Stem Cell-Derived Hepatocytes.

Tasneem Abdulsattar, Hilansi Rawat, Tarek Magdy.
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Metabolic dysfunction-associated steatotic liver disease (MASLD) affects ~ 100 million individuals in the US, with a subset progressing to MASH (metabolic-associated steatohepatitis), a major risk factor for hepatocellular carcinoma and liver failure. Genome-wide association studies (GWAS) have identified over 370 single-nucleotide polymorphisms (SNPs) associated with MASLD predisposition and progression; however, the mechanistic role of these SNPs in MASLD remains unknown, primarily due to the lack of a suitable model. To address this, we utilized human-induced pluripotent stem cells (hiPSCs), which capture the human genetic makeup, to develop a highly reproducible and cost-effective 20-day protocol for differentiating hiPSCs into functional hepatocytes (hiPSC-Heps). This innovative approach utilizes an optimized in-house–formulated chemically defined differentiation medium, substantially reducing costs from ~$500/L to $150/L. Our hiPSC-Heps robustly express key hepatic markers, including HNF4, ALB, and ASGR1, and demonstrate hallmark hepatic functions, including albumin secretion, lipid accumulation in response to lipid loading, glycogen storage, urea production, and metabolism of indocyanine green. We then employed our hiPSC-Heps to establish a human-derived in vitro MASH model by treating hiPSC-Heps with 400 μM palmitic acid plus 400 μM oleic acid for three days, which induced MASH hallmark phenotypes: significant lipid accumulation, ALT and AST secretion, dysfunctional mitochondrial respiration, ROS production, and expression of key inflammation markers (CCL2, CCL5, IL-6, IL-8, TNF-α, and more). To dissect the genetic contribution to MASH, we performed in-silico functional annotation of over 370 GWAS-identified MASH-associated SNPs to prioritize putative deleterious SNPs. Integrating these GWAS loci with differentially expressed genes (DEGs) in MASH-induced hiPSC-Heps identified 51 candidate genes that harbor SNPs and are transcriptionally dysregulated during MASH. To prioritize functionally relevant genes, we will perform genome-wide pooled CRISPR screening in our hiPSC-Heps MASH model. This will pinpoint causal variants and genes that modulate MASLD, enabling the discovery of predictive biomarkers and personalized therapeutic targets.

Sources of Support: NIGMS Center of Biomedical Research Excellence (COBRE, 2P20GM121307-06) and NSF Center of Research Excellence in Science and Technology (CREST, 2537597).

Poster 2

CMGC-Mediated Phosphorylation Licenses Human ZBP1 Signaling during HSV-1 Infection.

Oluwamuyiwa T. Amusan, Shuqi Wang, Ebubechukwu H. Nkadi, Jason Bodily, Rona Scott, and Hongyan Guo.
Department of Microbiology and Immunology, LSU Health Shreveport.

Z-form nucleic acid–binding protein 1 (ZBP1) is an interferon-inducible cytosolic sensor that detects double-stranded DNA (dsDNA) and RNA (dsRNA) in the left-handed Z-conformation (Z-DNA and Z-RNA) and orchestrates cell death and inflammatory responses to viral infection. Although ZBP1 signaling is well appreciated, the mechanisms underlying its activation in human cells during viral infection remain poorly understood. Here, using herpes simplex virus type 1 (HSV-1)—a dsDNA virus that infects over 50% of the human population worldwide—as a trigger for ZBP1 activation, we identify serine 309 (S309) of ZBP1 as a primate-specific phosphorylation site by mass spectrometry. We hypothesized that this phosphorylation is important for ZBP1-driven functions. Indeed, through cell death assays, molecular analyses, and immunoassays coupled with genetic manipulation, we show that phosphorylation of ZBP1 at S309 is essential for mediating necroptosis and proinflammatory signaling. We further demonstrate that HSV-1 infection activates multiple CMGC family kinases, including p38/MAPK, DYRK, and CDKs, which cooperatively phosphorylate ZBP1 at S309. Accordingly, pharmacological inhibition of p38/MAPK and DYRK, or pan-CDK blockade, abrogates S309 phosphorylation, suppresses necroptosis, and reduces tissue damage in a human skin organotypic raft model. Together, these findings define a previously unrecognized virus-activated signaling axis linking host CMGC kinases to a pathogen recognition receptor and uncover a species-specific post-translational regulatory mechanism for ZBP1. This work advances our understanding of ZBP1 regulation in primates and highlights potential kinase targets for therapeutic modulation of ZBP1-driven inflammation and tissue pathology.

This work is supported by the NIH R21 R21AI175590 and NIH COBRE P20GM134974 Grant to Hongyan Guo, and an intramural Ike Muslow Predoctoral grant to Oluwamuyiwa T. Amusan.

Poster 3

Immunoprecipitation-Based Mass Spectrometry Identification of Lipin-1 Interactors in Activated Macrophages.

Andrii Andriichuk, Oluwakemi O. Igiehon, Palmer Cora, Martin Zachariah, Nion Javier, Matthew D. Woolard.
Department of Microbiology and Immunology, LSU Health Sciences Center at Shreveport.

Biochemical reactions occur in a crowded, heterogeneous milieu favoring proteins acting in complexes; thus, elucidating protein–protein

interactions offers deeper insight into how they coordinate cellular function. Lipin-1, a phosphatidic acid phosphatase with transcriptional coregulatory activity, is known to contribute to macrophage pro-inflammatory and pro-resolution responses, however, the mechanism by which Lipin-1 mediates these functions remains unknown. Lipin-1 has been shown to localize to mitochondrial membranes; thus, we speculated that it might form mitochondrial protein complexes relevant to macrophages, in that it aligns mitochondrial metabolism with macrophage function. We propose that this interaction is crucial for regulating mitochondrial function and, consequently, macrophage phenotypic responses.

Considering the above, we hypothesize that Lipin-1 binds to mitochondrial proteins, promoting mitochondrial metabolism that enables proper macrophage function in response to both pro-inflammatory and pro-resolution stimuli. To begin testing this hypothesis, we aim to identify proteins with which Lipin-1 interacts in macrophages under both pro-inflammatory and pro-resolving conditions.

IL-4–treated, LPS-treated, and untreated bone marrow–derived macrophages (BMDMs) were lysed, and lysates were subjected to immunoprecipitation of lipin-1, followed by Western blotting, silver staining, and mass spectrometry.

Five proteins were identified exclusively or at significantly higher levels in samples treated with monoclonal antibodies compared to IgG control samples. These protein candidates are involved in key cellular processes, including intracellular vesicle transport, post-transcriptional RNA regulation, molecular chaperone–mediated protein folding, mitotic chromosome segregation, and cellular metabolic pathways.

These candidate interactors lay the groundwork for targeted functional validation of Lipin-1's role in mitochondrial metabolism during macrophage polarization.

Poster 4

A mechanistic understanding of the enhanced pseudotyping efficiency of Rift Valley fever virus.

Ridwan Arinola[1,2,3], Upendra P Lambe1,2,3, Sushma Bharrhan[1,2], Stephanie R. Monticelli[4,5], Thomas G. Batchelor[4,5], Andrew S. Herbert[4] and Rohit K. Jangra[1,2,3].

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Rift Valley fever virus (RVFV) is an emerging mosquito-borne RNA virus that causes hemorrhagic fever, encephalitis, and oculitis in humans, as well as abortion storms in domestic animals. Currently, there are no FDA-approved therapeutics or vaccines for RVFV in humans. RVFV is a BSL3 pathogen considered a Select Agent by the United States Centers for Disease Control and Prevention (CDC). The RVFV genome encodes a glycoprotein complex (GPC) that is further processed to generate Gn/Gc glycoproteins, which are incorporated into viral particles to mediate cellular entry during infection. To study RVFV entry in a BSL-2 setting, our lab developed a recombinant vesicular stomatitis virus (rVSV-RVFV) expressing the GPC as its entry glycoproteins. The generation of rVSV-RVFV required the acquisition of two adaptive mutations, M1 and M2, in GPC, which synergistically enhanced viral titers. Our preliminary data show that M2 enhances pseudotyping efficiency by increasing the incorporation of Gn/Gc proteins into rVSV particles. Unlike M2, M1 does not enhance Gn/Gc cellular expression, cell-surface localization, or virion incorporation. M1 is a substitution of arginine with glutamine in Gn. Our structural analysis of the RVFV Gn head domain reveals that the arginine residue is surface-exposed and is located near the apex of the RVFV Gn hexamer ring, which might be involved in interaction with the RVFV entry receptor Lrp1. Moreover, this arginine forms a salt bridge with two neighboring glutamic acid residues, and mutation of the arginine to glutamine (M1) is predicted to disrupt this salt bridge. We hypothesize that the M1 mutation enhances pseudotyping efficiency by disrupting the salt bridge, which may also improve the Gn: Lrp1 binding. We test this hypothesis using assays such as receptor-binding ELISA, virus infection assays, and western blot. Our data indicate that M1 does not enhance Gn/Gc's binding to Lrp1, but point mutations of glutamic acid residues largely phenocopied M1, suggesting that disruption of the salt bridge is the driving force behind M1's enhanced pseudotyping efficiency. Overall, our data suggest that M1 and M2 mutations facilitate the development of rVSV-RVFV via distinct mechanisms.

LSUHS Seed Fund, CEVT-Grant-in-aid, NIGMS (P20GM134974) and NIAID (U19AI17403).

Poster 5

Machine Learning–Based Detection of Pancreatic Ductal Adenocarcinoma Using Protein and Peptide Biomarkers in Blood.

Lily Bodily, Xinggui Shen.

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Pancreatic Ductal Adenocarcinoma (PDAC) is the most common form of exocrine pancreatic cancer and is associated with an exceptionally poor prognosis. Despite ranking only 11th in incidence, PDAC is the 3rd leading cause of cancer-related death, underscoring the urgent need for improved diagnoses and treatments. Because PDAC is usually asymptomatic

until metastasis, most patients are diagnosed at advanced, unresectable stages of the disease. The only current PDAC blood test measures the CA19-9 protein, which is not sensitive or specific enough for screening. A non-invasive and highly accurate diagnostic tool could enable earlier detection and significantly improve outcomes. In this project, we developed machine learning models to detect PDAC using protein and peptide abundance from blood samples. Five algorithms were evaluated: neural network, support vector machine, logistic regression, XGBoost, and random forest. Models were trained using five-fold cross-validation. Biomarker selection was performed using the Least Absolute Shrinkage and Selection Operator (LASSO) within each fold and models were trained on the optimal number of features. The logistic regression model achieved an accuracy of 96% when trained on only the five top-ranked biomarkers. This model has a 15% better sensitivity and about 10% better specificity than the CA19-9 test, showing potential for the application of blood-based protein and peptide assays in PDAC diagnosis.

Poster 6

The B domain of VEEV E2 glycoprotein determines viral clearance in a reductionist viremia model.

Paulina A. Borysewicz, Trinity Saul, Stephanie E. Ander.
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Introduction: Viremia development, the presence of virus in the blood, is an essential step in vertebrate-to-invertebrate transmission of arthropod-borne viruses (arboviruses). Moreover, the magnitude and duration of vertebrate viremia also factor into arboviral disease severity and geographic spread—yet mechanisms modulating arboviral viremia levels are poorly defined. Members of the Venezuelan equine encephalitis virus (VEEV) complex are mosquito-transmitted, positive-strand RNA viruses endemic in the Americas and causative agents of recurrent outbreaks of febrile and encephalitic disease in equines and humans. VEEV subtypes are classified as epizootic (high equine viremia) or enzootic (low equine viremia). Historically, VEEV epidemics were associated with epizootic variants, however recent VEEV epidemics and outbreaks have been increasingly associated with re-emergence of enzootic VEEV.
Objectives: To investigate viral determinants of VEEV virion interactions with the host vasculature.
Methods: Reverse genetics systems were generated of a representative panel of attenuated, BSL-2 safe, chimeric Sindbis/VEEV both epizootic and enzootic viruses. The viruses generated were employed in an in vivo reductionist viremia model. Viral burden of animal sera (mice, cotton rats and chicks) harvested up to 3 hpi was determined by RT-qPCR. Phylogenic analysis was performed on VEEV protein-coding sequences.
Results: We find VEEV susceptibility to murine vascular clearance falls along viral phylogenetic lines of E2 of the viral spike. Vascular resolution phenotypes of enzootic (IV) and epizootic (IAB) are conserved across diverse animal models. Mutational studies of the E2 glycoproteins indicate the B-domain is a viral determinant of persistence or clearance in our reductionist viremia model.
Conclusions: Our data suggest enzootic strains of VEEV can be divided into 2 phylogenetically supported subgroups based on viral clearance phenotypes in a reductionist viremia model. Vascular clearance phenotypes were dependent on the B-domain of the E2 glycoprotein – a recognized hot-spot for viral determinants of VEEV emergence in equines. Our results suggest the E2 glycoprotein may be a key viral determinant of viremia resolution. In future studies, we will aim to define both specific molecular features of the E2 glycoprotein required for VEEV vascular clearance and its cognate host ligand.
Sources of support: NIH-NIAID F32 AI161866; LSUHS start-up funds; CAIPP pilot funding.

Poster 7

Lymphocyte Subpopulation–Specific Adhesive Interactions with Red Blood Cells and Platelets in Sickle Cell Disease

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Sickle cell disease (SCD) is characterized by chronic hemolysis, inflammation, and aberrant adhesive interactions between red blood cells (RBCs), platelets, and leukocytes that contribute to vascular dysfunction. While RBC interactions with myeloid cells have been widely studied in vitro, far less is known about RBC–lymphocyte and platelet–lymphocyte interactions in vivo, particularly within distinct lymphocyte subpopulations. Using a novel no-lysis, 15-color, flow cytometry protocol, we characterized lymphocyte composition and heterotypic aggregate formation in non-sickle (AA) and sickle (SS) mice. SS mice exhibited a redistribution of circulating lymphocytes, with an increased proportion of Non-T/B lymphocytes at the expense of B cells, while overall T cell, including cytotoxic and helper T cell, proportions were largely preserved. Total circulating RBC–lymphocyte aggregates (RLyAs) were increased in SS mice; however, in both AA and SS mice, RLyA composition largely reflected underlying lymphocyte distributions, with a modest enrichment of B cell representation in both groups. In AA mice, both RBC–lymphocyte (RLyAs) and platelet–lymphocyte aggregates were predominantly B cell–driven. In SS mice, RBC-containing aggregates remained B cell–enriched, whereas platelet-containing aggregates were largely composed of Non-T/B lymphocytes, suggesting disease-specific selectivity in aggregate formation. Assessment of activation status revealed that SS mice exhibited increased CD44 and decreased CD62L

expression on individual lymphocytes and RBC–lymphocyte aggregates versus AA counterparts, consistent with a more activated phenotype, while platelet–lymphocyte aggregates displayed heightened CD44 with similar CD62L expression to AA, indicating distinct signaling or trafficking potential. These findings highlight lymphocyte subpopulations as underappreciated contributors to SCD vaso-occlusive pathophysiology and suggest that differential aggregate composition may influence inflammatory and vascular responses.

Funding: Fellowship to M. Butler (T32HL155022, NIH NHLBI to Orr & Stokes), 5R01HL134959 (NIH NHLBI to Stokes), 1P206M134974-01A1 (NIGMS for the COBRE Center for Applied Immunology and Pathological Processes to Woolard), Fellowship to M. Butler from The Center for Post-Transcriptional Regulation (supported by the National Science Foundation under Award Number (FAIN) 2537597). We'd like to thank the Flow Cytometry Core of the Research Core Facility.

Poster 8

Eosinophils Promote Systemic Dissemination and Cardiac Pathology during Bordetella spp. Infection in Hypereosinophilic Hosts

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Eosinophils are a type 2 immune cell classically associated with asthma, allergies, and immune responses to parasites. However, growing literature is revealing the critical role for eosinophils during pathologies including bacterial infections. Interestingly growing literature also indicates that the function of eosinophils during heart pathologies remain unclear and while eosinophils can be beneficial for tissue repairing following heart injury, they have also been shown to exacerbate cardiovascular diseases. Understanding the contribution of eosinophils to the improvement or worsening of cardiorespiratory pathologies is imperative due to the ramping increase of eosinophilic associated pathologies.

Here, we investigated the impact of hypereosinophilia on susceptibility to Bordetella spp. infection. Using a murine model of wildtype (Balb/c genetic background) and hypereosinophilia (homozygous TgCD2-IL5 mice). We demonstrate that eosinophils facilitate infection by Bordetella bronchiseptica and B. pertussis, requiring lower infectious doses and developing more severe disease, including bacterial persistence, systemic dissemination, and increased mortality. We found that elevated circulatory eosinophils numbers correlate with the isolation of Bordetella spp. within spleen eosinophils, potentially aiding bacterial dissemination. Infected TgCD2-IL5 mice displayed decrease cardiorespiratory function and enhanced Th2/Th17/Th1 responses, resulting in pronounced lung and cardiac fibrosis, and progressive cardiac pathology, which worsened upon reinfection. Interestingly our data reveal that increase in eosinophil numbers dysregulate inflammatory responses suppressing the ability of the immune system to maintain immune homeostasis and decrease inflammation post day 28 post-infection. Furthermore, increased IL4/IL13 serum signatures were observed in mice with elevated eosinophils suggesting a role for these cytokines to activate STAT6 pathway promoting fibroblast activation and explaining the exacerbated pathology observed.

This work serves as foundation to mechanistically investigate eosinophils contribution as key immunomodulators and drivers of post-infection cardiorespiratory immunopathology.

Poster 9

Fucoxanthinol Delivered from Microalgae to Prevent Cell Death in Lung Epithelial Cells After Exposure to Copper Oxide.

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Microalgae are a great source of natural compounds beneficial for human health. One such compound is fucoxanthin, a carotenoid pigment with anti-inflammatory properties. Fucoxanthin can be further enzymatically hydrolyzed to form fucoxanthinol, which is the bioactive form in the human body. However, fucoxanthinol is currently rarely available for researchers due to high cost. We have developed an efficient method for extracting, hydrolyzing, and purifying fucoxanthinol from cultured microalgae. Our method yields about 2 mg of pharmacological grade (purity > 95%) fucoxanthinol from 10 g of dried microalgal biomass. Here, we present an overall method for producing fucoxanthinol and its application in anti-inflammatory research using a Human Bronchial Epithelial Cell Line (BEAS-2B). Future experiments will be conducted to determine the efficacy of fucoxanthinol in preventing inflammation.

Poster 10

Sex-Related Differences in the Correlation of Plasma Redox Pathway Proteins and Cognitive Impairment in Alzheimer's Disease and Related Dementias.

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Introduction: Alzheimer's disease and related dementias (ADRD) are the most common forms of dementia and the 6th leading cause of death worldwide. Women are 2-3 times more likely to develop ADRD, although it remains unclear if biomarkers reflect these differences or the underlying mechanisms. Redox imbalance has been implicated as an early change in ADRD. We hypothesized that plasma oxidative stress markers would be elevated in ADRD and correlate with cognitive impairment, and that females would exhibit greater oxidative stress than males.

Methods: Plasma samples were isolated from blood drawn from control and ADRD participants. ADRD was defined as having an Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-cog) score >17. Dot blot analyses were performed, and probed for antioxidant enzymes (superoxide dismutase 3 (SOD3), catalase (CAT), glutathione peroxidase (GPx), transcription factor Nuclear factor erythroid 2-related factor 2 (Nrf2)), and a subunit of the superoxide-generating enzyme NADPH oxidase (NOX2).

Results: NOX2, SOD3, CAT, and Nrf2 were significantly higher in ADRD plasma versus controls, and positively correlated with ADAS-cog scores. When separated by sex, the same proteins were elevated in females whereas only NOX2 and SOD3 were elevated in males. In males, SOD3 correlated with ADAS-cog score, whereas plasma NOX2, SOD3 and Nrf2 levels positively correlated with ADAS-cog scores in females. There was a significant difference in the association of Nrf2 levels with ADAS-cog in males vs. females.

Conclusion: Measurements in plasma of ADRD patients revealed increased NOX2 and antioxidant enzyme levels, with the latter potentially being a compensatory response to oxidative stress. While the direction and magnitude of change for most proteins were similar between males and females, the correlation between the redox proteins and ADAS-cog was stronger in females than in males, suggesting females experience stronger oxidative stress that requires more robust antioxidant defenses, and is more tightly associated with the cognitive impairment. Whether this is directly related to the mechanisms underlying the higher prevalence of ADRD in females remains to be determined.

Funding: R25HL147665 (Stokes), T32HL155022 - NIH NHLBI (Esmond, to Orr & Stokes); Malcolm Feist pre doctoral fellowship from the CCDS (Esmond), 3P2012130701A1S1 and HL149264-01A1 NIGMS NIH (Kevil).

Poster 11

Investigating the role of Mycobacterium tuberculosis Glutamine Synthetase as a Host Immune Modulator.

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Tuberculosis (TB) remains the leading infectious cause of death worldwide, emphasizing the critical need to identify new therapeutic targets in Mycobacterium tuberculosis (Mtb). Glutamine is a conditionally essential amino acid for Mtb and serves as a key nitrogen donor and carbon source for both the pathogen and host immune cells. In Mtb, glutamine is synthesized primarily by glutamine synthetase (GS), and among its four GS-encoding genes (glnA1, glnA2, glnA3, glnA4), glnA1 is the predominant and essential isoform required for bacterial survival. Our preliminary observations suggest that pharmacologic inhibition of host glutamine metabolism using JHU083 limits Mtb growth, promotes early T-cell recruitment, reduces immune-suppressive cell populations, improves lung pathology, and extends survival of infected mice. These findings raise the possibility that Mtb glutamine metabolism, particularly GlnA1 activity, may influence host immune function during infection. However, GlnA1 is essential for Mtb growth in vitro and in vivo, making it challenging to decipher the function of GlnA1 in the host. To overcome this, we have isolated Mtb strain carrying a point mutation in GlnA1 (Y186C) that is resistant to L-methionine-SR-sulfoximine (MSOR). The point mutant is viable though exhibits conditional glutamine auxotrophy, and reduced fitness in ex-vivo macrophage infection model. In order to compare the enzyme activity of WT and MSOR GlnA1 proteins, we cloned WT and MSOR glnA1 in a pET-24(+) system and purified the proteins from E. coli BL21(DE3) using Ni-NTA affinity chromatography. We are currently performing GS activity assay to compare the enzymatic activity of WT and MSOR GlnA1 proteins. We will then assess the effect of WT and MSOR GlnA1 proteins upon the macrophage physiology including cytokine profiling, phagocytosis assay, and metabolomic profiling. Together, these studies will define how Mtb GlnA1 activity shapes macrophage physiology and may reveal new immunometabolic strategies to restrict TB pathogenesis.

Sources of support: CoBRE CAIPP startup Fund and Departmental Seed package.

Poster 12

HCMV-Induced Signaling Regulates Syntaxin 6 Translation to Promote Viral Nuclear Translocation in Primary Human Monocytes.

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Introduction: Human cytomegalovirus (HCMV) is the leading infectious cause of congenital birth defects and significantly increases morbidity and mortality in immunocompromised patients. HCMV dissemination and establishment of life-long persistence within the host is facilitated by infection of peripheral blood monocytes. Viral entry and nuclear translocation in monocytes relies on virus-induced signaling via the binding of viral glycoproteins gB and gL/gH/UL128-131 (pentamer) to EGFR and integrins, respectively. Syntaxin 6 (Stx6) is a vital regulator of HCMV transport from early endosomes to the trans-Golgi network (TGN), a requisite for viral nuclear translocation. In this study, we examine how HCMV-induced signaling regulates Stx6 at the protein and transcript level during infection in primary monocytes.
Hypothesis: HCMV-induced signaling upregulates the translation of Stx6 to promote viral trafficking to and through the TGN.
Methods: Human monocytes were isolated from whole donor blood via dual density centrifugation. Cells were synchronously infected with HCMV TB40E, BADR (pentamer-pos), and BADWT (pentamer-null). Protein lysates were immunoblotted. Cellular RNA was harvested, reversed transcribed, and transcripts were amplified via quantitative PCR. Immunofluorescence microscopy was performed utilizing a Nikon N-SIM E Super Resolution microscope system. Phosphoproteomic and transcriptomic data of HCMV-infected monocytes was also re-analyzed.
Results: HCMV infection decreases Stx6 transcripts in monocytes but rapidly increases Stx6 protein. Stx6 transcripts and protein are associated with P-bodies. HCMV infection increases phosphorylation of p70S6K, and translation inhibition blocks Stx6 protein upregulation. Infection with pentamer-null HCMV abrogates Stx6 protein upregulation. Further, we observe increased phosphorylation of syntaxin family and translational regulators, CaMKII and CK2, during infection.
Conclusion: Our current data suggests that HCMV infection upregulates Stx6 protein by inducing the translation of P-body-associated Stx6 transcripts, resulting in transcript deterioration. Additionally, the translational event is dependent on HCMV pentamer-integrin signaling. Further, we documented that HCMV infection causes increased phosphorylation of syntaxin family and translational regulators, CK2 and CaMKII, which lie downstream of both integrin and EGFR signaling. In summary, the results argue that HCMV-induced signaling events regulate Stx6 protein and transcripts to facilitate viral trafficking and nuclear translocation in monocytes.

Sources of Support: NIH P01 Grants AI127335, P20GM134974, AI159672, and FWCC Carroll Feist Predoctoral Fellowship.

Poster 13

Laguna Negra virus and Black Creek Canal virus Gn/Gc interact with PCDH1 to mediate their entry.

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Hantaviruses are a diverse group of emerging zoonotic viruses carried by small mammals. Rodent-borne hantaviruses cause hantavirus cardiopulmonary syndrome (HCPS) in the New World and hemorrhagic fever with renal syndrome (HFRS) in the Old World. Despite extensive research, there are no approved vaccines or therapeutics for hantavirus-caused illness. There are 48 ICTV-recognized species of mammalian hantaviruses; for most of which there are no virus isolates, and their pathogenic potential and entry pathways remain unknown. Protocadherin-1 (PCDH1) was identified as the entry receptor for 5 Hantavirus species, including the New World rodent-born Andes virus and Sin Nombre virus. We generated self-replicating recombinant vesicular stomatitis viruses (rVSVs) carrying the sole hantavirus surface Gn/Gc glycoproteins of six hantaviruses of diverse geographic and host origin to evaluate their ability to mediate entry and receptor usage in human cells. These are: New World rodent-borne Laguna Negra virus (LANV) and Black Creek Canal virus (BCCV); Old World rodent-borne Dabieshan virus (DBSV) and Tigray virus (TIGV); and shrew-borne Seewis virus (SWSV) and Cao Bang virus (CBNV). Infection of human cells genetically knocked out for PCDH1 showed that the genetic ablation of PCDH1 resulted in a reduction in infection by LANV and BCCV. However, the infection of DBSV, CBNV, TIGV, and SWSV was not affected by the knockout of PCDH1. ELISA experiments using soluble PCDH1 demonstrated that the Gn/Gc glycoproteins of LANV and BCCV bind to PCDH1 in a dose-dependent manner; however, LANV Gn/Gc showed more efficient binding to PCDH1 than BCCV. Follow-up experiments demonstrated that these differences were explained by lower affinity and lower Gn/Gc incorporation of BCCV into the rVSV particles. The infection of both LANV and BCCV was reduced in a dose-dependent manner when the interaction of their Gn/Gc with PCDH1 on cells was blocked by an anti-PCDH1 monoclonal antibody or a soluble form of PCDH1. Finally, a broadly protective human mAb (ADI-42898) targeting a highly conserved region of the hantavirus Gn/Gc recognized Gn/Gc from all six hantaviruses included in this study and neutralized their infection to varying degrees. Thus, we have

identified entry pathways and intervention strategies against six hantavirus species.
Sources of support: LSU Health Seed Funds, NIH R21 and NIGMS CAIPP CoBRE (P20 GM134974).

Poster 14

Lipin-1 promotes mitochondrial respiration to facilitate macrophage pro-resolving responses.

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Introduction: Atherosclerosis, the leading cause of death worldwide, is a chronic inflammatory disease driven by defective efferocytosis. Pro-resolving macrophages drive inflammation resolution and atherosclerosis regression by engulfing apoptotic cells through efferocytosis. Mitochondrial respiration supports macrophage efferocytosis and pro-resolving responses. However, the regulatory pathways that govern macrophage mitochondrial metabolism during resolution responses have yet to be clearly elucidated. Lipin-1 is a phosphohydrolase and a transcriptional co-regulator that regulates mitochondrial metabolism. We previously demonstrated that macrophage lipin-1 attenuates atherosclerosis and promotes inflammation resolution by enhancing mitochondrial oxidative phosphorylation (OXPHOS) and efferocytosis. However, the mechanism by which lipin-1 enhances OXPHOS and efferocytosis in pro-resolving macrophages remains unclear. In cardiac muscles, lipin-1 maintains the levels of cardiolipin, a mitochondria-exclusive phospholipid that stabilizes electron transport chain complexes to improve OXPHOS capacity. Cardiolipin abundance is largely dependent on mitochondria-ER contacts (MERCs), which enable the transfer of ER-derived lipid precursors essential for cardiolipin synthesis to the mitochondria. Notably, hippocampal lipin-1 supports MERCs formation.
Hypothesis: Macrophage lipin-1 augments efferocytosis by facilitating MERCs formation to enhance cardiolipin synthesis, which in turn promotes mitochondrial respiration.
Methods: We employed flow cytometry, fluorescence microscopy, mass spectrometry, and RNA interference to assess cardiolipin abundance and its impact on efferocytosis in lipin-1 knockout (lipin-1 KO) and wildtype (WT) bone marrow-derived macrophages (BMDMs). In addition, we used transmission electron microscopy to investigate macrophage lipin-1-dependent MERCs formation.
Results: Macrophage lipin-1 increased cardiolipin levels and knockdown of PTPMT1, a key cardiolipin synthesis enzyme, impaired efferocytosis in WT BMDMs. Also, electron microscopy revealed that lipin-1 drives MERCs formation.
Conclusions: Our findings suggest that lipin-1 facilitates MERCs formation and cardiolipin synthesis to support macrophage OXPHOS for improved efferocytosis and pro-resolving responses. These advance our understanding of the cellular and molecular mechanisms driving inflammation resolution and may inform future studies on metabolic regulation of immune responses in chronic inflammatory diseases.
Funding Sources: AHA predoctoral fellowship under grant number 25PRE1373728; NIH under grant number R01HL163106 and 1P20GM134974-01A1; CCDS under grant number CCDS000013.

Poster 15

Dysregulation of Mitochondrial Fatty Acid Metabolism Driving Desminopathy.

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Background: Desmin, a muscle-specific intermediate filament protein, plays a key role in maintaining the structural integrity and contractile apparatus of cardiomyocytes. Mutations in human DES gene have been linked to various cardiomyopathies, often characterized by arrhythmias, heart failure, and sudden cardiac death. Despite extensive characterization of desmin mutations, the molecular mechanisms driving disease pathogenesis remain poorly understood.
Hypothesis: Myocardial fatty acid metabolism fuels the high-energy demand of the heart primarily through the mitochondrial β-oxidation of long-chain fatty acids. However, mitochondrial spatial organization and function are markedly altered in desminopathy. We hypothesize that perturbations in fatty acid metabolism drive mitochondrial dysfunction, ultimately leading to cardiomyopathy.
Methods and Results: We utilized a mouse model of desminopathy generated by cardiomyocyte-specific overexpression of mutated desmin (7 AA deletion R172-E178 in the desmin gene: D7Des Tg). The D7Des Tg mice provide a clinically relevant mouse model of desminopathy that recapitulates the human phenotype, including electron-dense aggregate accumulation, myofibrillar degeneration, and impaired cardiac contractility. We performed transcriptomic and untargeted proteomic analyses on D7Des Tg hearts to uncover novel mechanisms underlying desminopathy. The D7Des Tg hearts demonstrated markedly distinct transcriptomic and proteomic profiles compared with control hearts. Interestingly, multiple metabolic pathways were significantly enriched with several genes and enzymes involved in fatty acid metabolism, showing substantial alterations. Among the significantly altered metabolic targets, we observed significant downregulation of carnitine palmitoyltransferase 2 (CPT2) at both the

transcriptomic and proteomic levels. CPT2 is an enzyme essential for transporting long-chain fatty acids into mitochondria for β-oxidation. We also confirmed the CPT2 downregulation by immunoblot and qPCR analysis. Moreover, our integrated multi-omics analysis indicated that altered PPAR signalling may regulate CPT expression.
Conclusion: Collectively, we identified CPT2 as a key contributor to the metabolic dysfunction contributing to the pathophysiology of desminopathy, with important implications for mitochondrial function and cardiac metabolic health.
Funding: This work was supported by National Institutes of Health grants: R01HL172970, R01HL145753, R01HL145753-01S1, R01HL145753-03S1, and R00 HL122354, LSUHSC-S CCDS Grant-in-Aid, Chancellor's high aim, and Pathway Research Award to M.S.B.; AHA pre-doctoral fellowship (26PRE1561609) and LSUHSC-S Malcolm Feist pre-doctoral fellowship from the Center for Cardiovascular Diseases and Sciences to T.I.

Poster 16

Multifunctional nucleoside analogs stimulate antitumor and antiviral immune responses through the adenosine pathway.

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Introduction: Adenosine signaling has been identified as a key immunosuppressive pathway that is overactivated in both infections and tumors. Our previous work has shown that adenosine-mediated activation of the Adenosine A2A receptor (A2AR) blocks Notch1 signaling in T-cells, leading to suppression of T-cell mediated immunity. Whereas A2AR blockade restimulates antitumor and antiviral T-cell responses.
Objective: While ganciclovir has been tested against viral-driven cancers, including Epston-Bar Virus (EBV), This study aims to evaluate its unrecognized immunomodulatory functions as an A2AR receptor antagonist.
Methods: CGS21680 (CGS) A2AR agonist, ZM241385 (ZM) A2AR antagonist, and ganciclovir, were used alone and in combination for investigation of their immunomodulatory effects. Molecular docking was performed to predict binding between the compounds and A2AR and validated using cyclic adenosine monophosphate (cAMP) assay, the second mediator of A2AR, assay. Compounds alone and in combination were administered via intraperitoneal injections in immunocompetent mice for a week. Splenocytes and peripheral blood were subjected to flow cytometry at the end of the study to characterize the effect of the compounds on immune cell function. Antitumor and antiviral effects of compounds were assessed in spheroids generated using EBV positive cells SNU-719 using the IncuCyte system.
Results: Computational docking revealed that ganciclovir shares A2AR binding sites with ZM. cAMP assay confirmed that ganciclovir competes functionally with CGS, like ZM, suggesting A2AR antagonist activity. Ganciclovir restored CD8+ T-cell proliferation and increased activation and cytotoxic markers, including CD69 and Interferon-gamma (IFN-γ), in immunocompetent mice under immunosuppression.
In 3D spheroids, ZM and ZM + CGS treatment strongly inhibited spheroid growth reflecting potential role of A2AR receptor activation in both antitumor and antiviral effects. Combination of ganciclovir and CGS also inhibited spheroid growth to an extent suggesting that ganciclovir is endowed with a dual antiviral and antitumor function via A2AR antagonism.
Conclusions: This study identifies ganciclovir as a compound with multiple functions that target EBV directly, modulates A2AR signaling, and enhances antiviral and antitumor T-cell immunity, thus suppressing tumor growth associated with EBV. This study provides new insights on targeting adenosine signaling pathway by immuno-antiviral drugs as a novel immunotherapeutic approach for viral oncogenesis.
Sources of Support: NIH-NIGMS (COBRE) P20GM121288.

Poster 17

Call for Collaboration: Fucoxanthinol—A Louisiana-Produced Natural Compound with Antioxidant, Anti-Inflammatory, and Metabolic Activities

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Our ongoing project addresses three globally significant and locally urgent challenges—saltwater intrusion into agricultural land, increasing prevalence of chronic inflammatory diseases, and plastic pollution—through a regionally adaptable microalgal innovation platform. In coastal Louisiana, saltwater intrusion has rendered many rice paddies unsuitable for conventional agriculture. We repurpose these abandoned lands as cultivation sites for salt-tolerant microalgae. From these microalgae, we extract fucoxanthin, a bioactive carotenoid with well-documented antioxidant, anti-inflammatory, anticancer, and antidiabetic properties. To enhance its therapeutic utility, fucoxanthin is converted to fucoxanthinol, a more bioavailable metabolite suitable for pharmaceutical development. Residual algal biomass is further utilized to produce biodegradable plastics—most notably sustainable Mardi Gras beads—demonstrating an integrated, circular model that links environmental restoration, public health innovation, and sustainable materials production.
This presentation will highlight recent advances in fucoxanthinol production and propose a working

hypothesis that fucoxanthin acts at the plasma membrane by interfering with the assembly of receptor–ligand complexes, thereby modulating downstream signaling pathways. Biomedical-grade fucoxanthinol (>97% purity) is available for research use, and collaborations with interested investigators are welcome.

Poster 18

A novel BSL2 system for comprehensive analysis of hantavirus entry glycoproteins.

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Hantaviruses cause severe hantavirus cardiopulmonary syndrome (HCPS) in North and South America, including the United States, with case fatality rates reaching 40%. There are no FDA-approved vaccines or treatments for these viruses, and progress is slowed by the need for BSL-3 containment to study pathogenic hantaviruses. The virion surface proteins, Gn/Gc, are essential and sufficient for cellular entry and major targets for protective immune responses. Therefore, pseudotyped viruses carrying Gn/Gc proteins serve as excellent models for studying hantavirus entry at BSL-2. However, current pseudotyping systems do not support high-throughput analysis of the molecular determinants of Gn/Gc's role in entry and antigenicity. To overcome these limitations, we developed a self-replicating BSL-2 system called Sem-HantaVirus (SHV), a Semliki Forest virus (SFV) replicon that expresses Gn/Gc proteins from an HCPS-causing Andes virus (ANDV). By serial passaging in cell culture, we identified twelve adaptive mutations—six in Gn-Head, two in Gn-Tail, and four in the SFV nonstructural proteins (nsP)—that enabled robust SHV replication. Paradoxically, these mutations reduced the amount of Gn/Gc incorporated into SHV particles. Mechanistic experiments indicate that Gn-Head and Gn-Tail mutations enhance pseudotyping efficiency via distinct mechanisms, and that nsP mutations downregulate SFV's subgenomic promoter activity by delaying nsP proteolytic cleavage. Interestingly, ANDV Gn adaptive mutations identified in SHVs facilitated the generation of SHVs for another closely related hantavirus, Maporal virus, indicating their broad applicability across hantaviruses. Syrian hamsters immunized twice, 21 days apart, via intramuscular or intraperitoneal routes, developed neutralizing antibodies and were protected against a lethal challenge with Andes hantavirus, indicating SHV's potential to display Gn/Gc in their native conformation and serve as a candidate hantavirus vaccine. Finally, we generated a single-site saturation variant library encoding all 20 amino acids at 110 positions in the Gn-Tail. Generation of SHV variants and serial passaging revealed highly conserved sites in the Gn-Tail under negative selection and identified multiple variants that further increased titers by 100-fold. Notably, some fast-growing variants overlapped with the aforementioned Gn-Tail mutations, underscoring their role in SHV replication and Gn/Gc functionality.

Sources of Support: LSU Health Seed Funds, NIGMS CAIPP CoBRE (P20GM134974), NIH R56 (AI175292).

Poster 19

Forodesine has anticancer immunomodulatory properties through the adenosine pathway.

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Introduction: Adenosine is an immunosuppressive metabolite that is overproduced in the tumor microenvironment and a major player in tumor-induced immunosuppression. Work from our group has contributed to show that adenosine binding to the Adenosine A2A Receptor (A2AR) suppresses CD8 T cell function and activation in the tumor microenvironment, whereas blocking A2AR restimulates anticancer CD8 T cell responses.
Objectives: In this study, we aimed to identify novel therapeutics that can effectively block A2AR signaling, thus restoring CD8 T cell anticancer function.
Methods: We used molecular docking modeling to screen drugs for the biding to A2AR. We tested the screened compounds in primary CD8 T-cells against an adenosine agonist and measured functional markers associated with T-cell activation and A2AR signaling using flow cytometry. We also did in vivo studies in immunocompetent mice to test the immunomodulatory effects of selected drugs.
Results: Using molecular docking modeling, we have found that the nucleoside analog forodesine is predicted to bind to A2AR with a similar ΔG and similar binding residues as adenosine, suggesting it may act on A2AR signaling. We confirmed that forodesine antagonizes A2AR and counteracts adenosine-mediated immunosuppression, as we observed restimulation of T-cell function in primary CD8 T-cells treated with forodesine. We also tested forodesine in highly immunosuppressive Triple-Negative Breast Cancer (TNBC) mouse models and found that the treatment reduces tumor growth via stimulation of CD8 T-cell responses, indicating that the A2AR antagonist properties of forodesine result in restimulation of antitumor immunity.
Conclusions: Based on our findings, nucleoside analogs, like forodesine, could be investigated as novel immunotherapeutics to successfully stimulate T-cell responses against cancer.

Sources of support: Carolyn L. Kuckein Student Research Fellowship; COBRE grant: NIH-NIGMS (COBRE) P20GM121288.

Poster 20

HPV16 transport vesicles selectively target PML isoform II to promote early viral transcription.

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Promyelocytic leukemia nuclear bodies (PML NBs) play a critical role in intrinsic immunity and their interactions with viral infections are complex, as viruses can both evade and exploit PML NB functions. PML NBs are dynamic, membrane-less subnuclear structures in mammalian cells, formed by self-assembly of specific PML isoforms I-VI. DNA viruses such as human papillomavirus (HPV) have evolved mechanisms to manipulate PML NBs for their genome delivery and transcription at the early stage of infection. It is well established that incoming HPV virions associate with PML NBs. However, the mechanism through which HPV targets PML NBs to facilitate early transcription and replication, including the requirement of specific PML isoforms, remains unclear.
We have recently demonstrated that HPV virions are delivered into the nucleus inside a membrane-bound vesicle during mitosis and associate with PML protein prior to the release of the viral genome from the transport vesicle. Herein, we demonstrated that the PML II isoform is selectively recruited to incoming HPV harbouring transport vesicles. Interestingly, all PML isoforms associated with the overexpressed capsid L2 protein in HeLa cells to a similar extent. Since PML II has been known to associate with lipid droplets in the nucleus, we conclude that recruitment of PML II is mediated via its interaction with lipids of the HPV harbouring, membrane-bound vesicles rather than with the L2 protein. Moreover, we observed that the association of PML NBs with the HPV16 viral genome is transient and lost over time. We also observed that the PML II isoform is preferentially recruited to incoming transport vesicles and, together with PML V, modulates PML NBs dynamics to facilitate early transcription and establishment of infection. Importantly, our findings further confirm the importance of PML proteins in HPV infection and demonstrate that the incoming viral genome resides within the transport vesicle. These insights reveal promising therapeutic targets and highlight the molecular complexity of virus-host interactions.

Poster 21

A self-replicating BSL2 system for studying Rift Valley Fever Virus entry.

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Rift Valley fever virus (RVFV) is an emerging mosquito-borne RNA virus that causes severe disease, including large-scale abortion events in livestock and hemorrhagic fever in humans. No FDA-approved vaccines or therapeutics are currently available for human use. RVFV research requires BSL3 containment, and the virus is classified as a Select Agent. To enable investigation of RVFV entry and antigenicity under BSL-2 conditions, we engineered a recombinant vesicular stomatitis virus (rVSV) in which the native VSV-G glycoprotein gene was replaced with a human codon-optimized RVFV glycoprotein precursor (GPC). The WT GPC sequence did not support rVSV-RVFV generation. After blind passaging, we identified an adaptive mutation (m-1) in the RVFV Gn protein that enabled efficient rVSV replication, a phenotype confirmed by subsequent functional analyses. Continued passaging led to a second mutation (m-2) in the GPC. Together, these two mutations synergistically enhanced rVSV growth. As with authentic RVFV, rVSV entry into target cells required endosomal acidification. Knockout of LRP1, the host receptor for RVFV, in human cells specifically reduced rVSV-RVFV infection, and this reduction was restored by complementation of knockout cells with cluster IV of LRP1 (LRP1-CLiv). Moreover, soluble LRP1-CLiv specifically bound to rVSV-RVFV and blocked its infection. In addition, rVSV-RVFV was recognized, and its infection was neutralized by RVFV Gn-specific antibodies. Taken together, these results demonstrate that rVSV-RVFV mimics RVFV's major entry mechanisms and antigenic properties. To assess its safety and immunogenicity, mice were immunized twice with rVSV-RVFV, 21 days apart, via either the intramuscular or intraperitoneal route and observed for morbidity. Immunized animals showed no signs of morbidity or weight loss. Antisera collected from immunized mice contained RVFV Gn- and Gc-specific antibodies and neutralized authentic RVFV and rVSV-RVFV. Upon challenge with a lethal dose of RVFV on day 42, immunized animals demonstrated 100% protection. Thus, we have developed a high-titer, self-replicating rVSV to study RVFV entry and antigenicity, which can serve as a useful tool for developing medical interventions against this deadly virus.
Funding: LSUHS Seed Funds, CEVT-Grant-in-aid, NIGMS (P20GM134974)

Poster 22

AKT-Dependent Arachidonic Acid Metabolic Reprogramming Drives Pro-Inflammatory Monocyte Differentiation during HCMV Infection

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Human cytomegalovirus (HCMV) is associated with severe disease in immunocompromised individuals

and with chronic inflammatory conditions in otherwise healthy populations, including atherosclerosis and transplant vasculopathy. In this study, we used an integrated omics-based approach in primary human monocytes to investigate how HCMV reprograms arachidonic acid (AA) metabolism. Our analyses identified cyclooxygenase-2 (COX-2/PTGS2) as a central regulator of AA metabolic pathways during HCMV infection. COX-2 expression and activity were controlled by EGFR-PI3K-AKT and integrin-c-Src signaling cascades. Functional studies demonstrated that AKT activation is required for COX-2 induction and drives monocyte-to-macrophage differentiation and M1 polarization through IL-12 and NF-κB signaling. Consistent with this role, AKT knockdown impaired monocyte differentiation, migration, and pro-inflammatory responses. Together, these findings reveal a key signaling axis by which HCMV reshapes monocyte AA metabolism to promote inflammatory macrophage phenotypes, providing mechanistic insight into HCMV-associated inflammation and its contribution to vascular disease.

Poster 23

Designing Multifunctional Immunotherapeutics for Viral-Driven Cancers

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Introduction: Oncoviruses account for approximately 15–20% of human cancers worldwide, yet therapeutic options targeting viral-driven malignancies remain limited. Conventional antivirals are primarily designed to inhibit viral entry or replication, but are often insufficient to clear infection without a robust immune response. Further, in virus-associated cancers, viral replication is rarely the main driver of tumor maintenance, rendering antivirals alone ineffective at inducing tumor regression. These challenges, compounded by limitations in preclinical modeling, hinder the development of effective therapies against viral oncogenesis.
Objectives: We propose a systematic, computational-assisted strategy for the design of multifunctional therapeutics against viral neoplasia. This approach aims to identify compounds with a trivalent activity: (i) direct antiviral effect, (ii) immunomodulatory antiviral activity, and (iii) immunomodulatory anticancer properties.
Methods: Computational molecular docking coupled with Artificial Intelligence (AI)-assisted modeling was used to screen existing antiviral drugs for immunomodulatory activity. High-throughput and functional assays in primary cells, 3D culture models and mouse models of infection and cancer were used to validate and dissect the predicted immunomodulatory and direct antiviral activity of the screened drugs.
Results: Using computational molecular docking, we found that certain nucleoside analogs have both intrinsic antiviral activity, through inhibition of viral replication, and the ability to stimulate effective anticancer and antiviral CD8+ T-cell responses via antagonism of the Adenosine A2A Receptor (A2AR) pathway. These compounds have demonstrated stimulation of antiviral immune responses in infection mouse models, leading to viral clearance and disease resolution, as well as anticancer immune responses that promote tumor regression in cancer models. Based on these findings we generated and validated an AI-assisted model that can predict whether a compound has both direct and immunomodulatory functions. We validated the model by screening existing antivirals drugs that were predicted to have immunomodulatory functions through A2AR. We found that these compounds can antagonize A2AR and restore antiviral and antitumor immune responses in 3D culture models.
Conclusions: Our findings indicate that it is possible to design multifunctional drugs endowed with both direct and immunomodulatory properties and these are promising therapies that could effectively target viral-driven cancers. This research paves the way for new strategies in viral oncogenesis therapy, shifting from traditional antivirals to integrated immunomodulatory approaches that promote immune protection against viral oncogenesis.
Sources of Support: NIH-NIGMS (COBRE) P20GM121288; US Department of Defense (DOD) Discovery Award grant W81XWH-21-1-0078

Poster 24

The Role of Hydrogen Sulfide in Heavy Alcohol Consumption in both Humans and Mice.

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Chronic alcohol consumption induces biological tolerance and can progress to alcohol use disorder (AUD), which affects approximately 11.2% of adults in the United States. AUD is associated with numerous clinical and pathological conditions, including liver failure, cognitive impairment, and increased cardiovascular risk. Hydrogen sulfide (H_2S) is an endogenously produced gasotransmitter that regulates diverse physiological processes, such as antioxidant defense, inflammation, and neurotransmission. Our clinical data demonstrate that individuals with AUD exhibit significantly elevated plasma H_2S levels, accompanied by altered cystathionine γ-lyase (CSE) expression. However, the molecular mechanisms underlying increased H_2S production in AUD remain unknown. Endogenous H_2S is primarily synthesized by CSE, which is highly expressed in the liver and

endothelial cells. We hypothesize that chronic heavy alcohol consumption elevates systemic H_2S production, thereby contributing to alcohol-induced brain damage. To validate our clinical observations, we employed mouse models of AUD to examine alcohol-induced alterations in CSE expression and H_2S levels. Specifically, we assessed whether chronic alcohol exposure via oral gavage or chronic intermittent ethanol (CIE) vapor exposure modifies CSE and H_2S expression in the liver, lung, and blood. In addition, untargeted metabolomics was used to characterize alcohol-induced alterations in transsulfuration metabolism and to compare metabolic changes between the oral gavage and CIE models. Collectively, these findings provide new insights into how chronic alcohol exposure disrupts systemic H_2S homeostasis and suggest a previously unrecognized mechanism contributing to alcohol-induced brain damage.

Poster 25

Lipin-1 Regulates Cardiolipin Homeostasis and Mitochondrial Function in Macrophages.

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Introduction: We previously demonstrated that Lipin-1 is required for proper mitochondrial oxidative phosphorylation in macrophages responding to both pro-inflammatory and pro-resolving stimuli. However, the mechanisms by which Lipin-1 promotes oxidative phosphorylation remain unclear. Cardiolipin (CL), a mitochondrial inner membrane phospholipid, is essential for cristae structure and electron transport chain stability.
Objective: Here, we investigated whether Lipin-1 regulates CL abundance and whether CL synthesis contributes to macrophage function.
Methods: Bone marrow–derived macrophages (BMDMs) from wild-type (WT) and Lipin-1 knockout (KO) mice were analyzed under basal conditions and following LPS or IL-4 stimulation. CL abundance was assessed using nonyl acridine orange (NAO) staining and confocal microscopy, and validated with targeted lipidomics to quantify total CL and profile molecular species. To determine the contribution of CL synthesis to macrophage function, we performed siRNA knockdown of CL biosynthetic enzymes and measured efferocytosis.
Results: Lipin-1 KO BMDMs showed a consistent reduction in cardiolipin signal compared with WT across basal and stimulated conditions.
Targeted lipidomics confirmed decreased total CL and revealed altered CL molecular species. siRNA-mediated silencing of cardiolipin biosynthetic enzymes impaired efferocytosis, reproducing features of the Lipin-1 KO phenotype.
Conclusions: These data identify Lipin-1 as a regulator of cardiolipin homeostasis in macrophages. Loss of Lipin-1 reduces total CL and alters CL species distribution, while disruption of CL synthesis phenocopies Lipin-1 deficiency. This work provides mechanistic insight into how Lipin-1–dependent lipid metabolism supports mitochondrial function and resolution of inflammation.

Poster 26

Dysregulated E2F activity negatively regulates the transcription of EBV immediate early genes BRLF1 and BZLF1.

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Co-infections with human papillomavirus (HPV) and Epstein–Barr virus (EBV) have been identified in a subset of oral squamous cell carcinomas, raising the key question of whether EBV acts as a cofactor in these tumors. HPV's carcinogenic activity is largely driven by its E6 and E7 oncoproteins, which inactivate the tumor suppressors p53 and pRb, respectively. In contrast, EBV promotes oncogenesis through the expression of latency-associated oncogenes as well as lytic factors. Using a 3D organotypic raft culture model, which mirrors the differentiation and stratification required for both viral lifecycles, we observed a disruption of EBV lytic replication and a shift towards latency in HPV-immortalized epithelium. This Inhibition of EBV lytic replication was due to HPV16 E7-facilitated pRb degradation and dysregulated E2F activity. The block in EBV replication correlated with impaired immediate early (IE) gene expression, BRLF1 and BZLF1. Evidence from the literature also shows that E2F1 binds to and inhibits transcription from the BZLF1 promoter. To mechanistically delineate the requirement of pRb in EBV IE gene expression, we generated an HPV/EBV co-positive epithelial cell line. Similarly, EBV reactivation from latency was blocked in monolayer cultures, and an abortive type infection was observed in 3D organotypic raft cultures. Overexpression of both EBV IE proteins, but not individually, rescued EBV reactivation in HPV/EBV co-positive cells. With these findings, we hypothesize that the dysregulated E2F activity in HPV-immortalized tissues restricts EBV immediate early gene transcription to inhibit lytic replication.
This work is supported and funded by the Chancellor's Pathway Research Award to Dr. Rona Scott, the Ike Muslow Pre-doctoral Fellowship to Ebubechukwu Nkadi, and the CAIPP COBRE - P20GM134974.

Poster 27

Serum Starvation Reveals an Adhesion-Dependent Permissive State for Early HCMV Gene Expression in Monocytes.

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Human cytomegalovirus (HCMV) is a ubiquitous β-herpesvirus infecting the majority of the global population and remains a leading viral cause of congenital disease and a major source of morbidity in immunocompromised individuals, including transplant recipients. Following primary infection, HCMV establishes lifelong persistence within the myeloid lineage, using circulating monocytes for dissemination and differentiated macrophages as sites of productive replication. Monocytes are classically considered non-permissive for viral gene expression; however, prior work has demonstrated that viral gene expression emerges only weeks after infection and, even then, productive replication is restricted to a subset of cells, with the majority remaining non-productive. The host determinants that govern these divergent infection outcomes remain poorly understood. Here, we investigated whether microenvironmental cues could be leveraged to reveal and experimentally manipulate distinct infection states in monocytes. We found that serum starvation induced viral gene expression as early as one day post-infection, in contrast to the delayed expression observed under serum-rich conditions. Importantly, serum starvation promoted a highly adherent monocyte phenotype independent of HCMV infection, characterized by strong substrate attachment and resistance to standard enzymatic detachment. To directly test whether adhesion was required for this early permissive state, serum-starved monocytes were cultured on non–tissue culture–treated suspension plates that prevent adhesion. Under these conditions, viral gene expression was completely inhibited despite serum starvation, demonstrating that adhesion-dependent signaling is necessary for permissiveness. These findings indicate that serum starvation alone is insufficient to drive viral gene expression and instead induces a host cellular state characterized by adhesion. Collectively, this work establishes serum starvation as a tractable experimental framework for studying heterogeneous infection outcomes in monocytes, distinguishing permissive from non-permissive cellular states prior to macrophage differentiation. By identifying adhesion as a critical host determinant of early viral gene expression, this study provides new insight into how microenvironmental conditions shape productive versus non-productive HCMV infection outcomes and contribute to a broader understanding of the mechanisms underlying HCMV persistence, latency, and reactivation.

This work is supported by National Institute of Health Grants AI127335, P20GM134674, and AI159672.

Poster 28

Validation of a Tamoxifen-Inducible LysM-CreERT2 Model for Studying Lipin-1 in Myeloid Cells.

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Lipin-1 is a key regulator of cellular physiology, integrating lipid metabolism with mitochondrial respiration to support immune cell function. In macrophages, this coordination is essential for efferocytosis, the clearance of apoptotic cells that drives inflammation resolution, wound repair, and protection from chronic disease, such as atherosclerosis. Our laboratory has demonstrated that lipin-1 is atheroprotective, enhances wound closure, and promotes inflammation resolution by enabling mitochondrial metabolism to meet the energetic demands of efferocytosis. Using the constitutive LysM-Cre model, we previously deleted lipin-1 in myeloid cells and uncovered profound defects in lipid handling, mitochondrial respiration, and efferocytosis. In vivo, these impairments contributed to increased atherosclerotic plaque burden, impaired wound healing, and reduced resolution of inflammation. However, because lipin-1 is deleted prior to disease initiation in this system, it is not possible to determine how changes in lipin-1 expression impact disease regression alone. To address this limitation, we generated a tamoxifen-inducible LysM-CreERT2 model that allows temporal control of lipin-1 deletion in myeloid cells, enabling direct investigation of lipin-1 function during ongoing disease processes during atherosclerosis resolution. We validated the LysM-CreERT2 model by confirming efficient lipin-1 deletion in vitro and in vivo. Functional assays, including Seahorse metabolic profiling and efferocytosis assays, demonstrated that the inducible model recapitulates the metabolic and efferocytic defects observed in the constitutive knockout. These findings establish LysM-CreERT2 as a reliable system for inducible gene deletion in macrophages, providing a strong foundation for future studies defining lipin-1's role in inflammation resolution and atherosclerosis regression.

Poster 29

Host glutamine metabolism inhibition improves phagocytic activity of macrophages.

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Introduction: Tuberculosis caused by Mycobacterium tuberculosis (Mtb) remains the leading infectious disease threat worldwide. Mtb primarily infects and replicates within host macrophages, driving upregulation of glutamine (Gln) metabolism, potentially promoting immune tolerance and suppressing antimicrobial responses. We recently demonstrated that JHU083-mediated pharmacologic inhibition of Gln metabolism increases the recruitment of interstitial macrophages to infected lungs and reduces Mtb burden in vivo.

Hypothesis: Inhibition of host glutamine metabolism improves antimycobacterial activity of macrophages.

Methods: To evaluate the impact of host glutamine metabolism on macrophage antimycobacterial activity, we performed: (1) single-cell RNA sequencing of Mtb-infected lungs following JHU083 treatment; (2) untargeted metabolomics of JHU083-treated, Mtb-infected macrophages; and (3) phagocytosis assays using fluorescent Escherichia coli as a probe.
Results: Single cell RNA sequencing analysis revealed that these macrophages exhibit a more inflammatory and less immunosuppressive transcriptional profile. In silico and untargeted metabolomics indicated that these macrophages rely predominantly on amino acids and complex lipids for energy. Reduced levels of reactive oxygen species, together with the accumulation of antioxidant metabolites, suggest an overall decrease in cellular oxidative stress. Additionally, JHU083-treated macrophages exhibited significantly increased phagocytic activity compared to controls. Ongoing isotope tracing studies aim to define the metabolic pathways responsible for this phenotype.
Conclusion: Together, these findings indicate that JHU083, a pleiotropic inhibitor of glutamine metabolism, reprograms macrophage metabolism to enhance phagocytic function and reduce intracellular Mtb burden, revealing a novel metabolic target for host-directed TB therapy.
Source of Funding: LSU-HSC Departmental Seed Package; JHU-TRAC Developmental Award; COBRE CAIPP Startup Funds & Pilot Award; and COBRE CBLD RPL Award.

Poster 30

Bordetella bronchiseptica suppress gd T cell enhancement to prevent iBALT formation and clearance of infection in the lung.

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Bordetella spp., causative agent of whooping cough, are very successful at suppressing host immune responses allowing for colonization and transmission. We have previously discovered BtrS, a Bordetella spp. σ factor that regulates immunosuppressive pathways. While murine challenge with wildtype B. bronchiseptica, RB50, results in chronic infection that mimics the human pertussis disease; infection with the DbtrS strain results in rapid clearance and robust immune response yielding long-term protection. Upon infection with the DbtrS strain, formation of induced bronchus-associated lymphoid tissue (iBALT) takes place and drives the effective adaptive immune response. Protective immunity and rapid clearance of DbtrS require eosinophils. Thus, we hypothesized that Bordetella spp., via BtrS, suppress eosinophil-mediated activation of T cell responses.
Bulk and scRNA sequencing of the lungs of wildtype and eosinophil deficient mice infected with RB50 or DbtrS was performed to investigate transcriptomic signatures that correlate with better immune responses.
Our results revealed that challenge with the DbtrS strain promotes an increase in BCR/TCR unique variables, including an enhancement in gdTCR unique variables, correlated with increased numbers of gdT cells found in the lungs of DbtrS infected mice. We observed that gdT cell activation/proliferation is eosinophil dependent. It was observed that a specific subset of gdT cells was enhanced during DbtrS infection. This enhanced gdT cells showed a higher production of IL-17 and IFNg. Our results also revealed that this enhancement of IL-17 served as seed for iBALT formation, indicating that cross-communication of eosinophil and gdT cells can orchestrate iBALT and adaptive immune responses. Overall, we propose a new mechanism to drive adaptive protective immune responses against bacterial infections with gd T cells as mediators of germinal centers.

Poster 31

Caveolin-1 Orchestrates stemness and chemosensitivity through FAK/c-Myc in TNBC.

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Triple-negative breast cancer (TNBC) is characterized by early metastasis, limited targeted treatment options, and frequent chemotherapy resistance. Cancer stem-like cells (CSCs) contribute to recurrence and drug tolerance in TNBC. Caveolin-1 (Cav-1), a caveolae-associated membrane scaffolding protein, is linked to poor outcomes in TNBC, and immunoblot analyses of patient-derived xenograft (PDX) tumors show substantial inter-tumor variability in Cav-1 expression, supporting dysregulated Cav-1 as a contributor to TNBC progression.
We previously demonstrated that Cav-1 knockout (KO) reduces lung metastasis in a syngeneic 4T1 TNBC model, partly through integrin α3–dependent mechanisms. Because focal adhesion kinase (FAK) is a central integrin-proximal signaling node and regulates stemness-associated programs, we investigated whether Cav-1 promotes CSC-like traits through a FAK/c-Myc axis. Cav-1 depletion in murine 4T1 and human SUM159PT cells reduced pluripotency/stemness markers, including SOX2, OCT4, and NANOG. Cav-1 loss also altered pY397-FAK and c-Myc levels, consistent with attenuation of a FAK-dependent stemness program.

Cav-1 KO increased paclitaxel (PTX) sensitivity compared with control 4T1 cells (48 h PTX IC50: 24.51 nM vs 30.82 nM). Enhanced drug response was associated with reduced expression of ABC drug-efflux transporters, including MRP1 (ABCC1) and P-glycoprotein (ABCB1). Supporting relevance to acquired resistance, Cav-1 expression was higher in PTX-resistant human Pac200 cells compared with parental SUM159PT cells.
Collectively, these findings support a model in which Cav-1 promotes TNBC stemness and multidrug resistance through integrin-associated signaling that modulates a FAK/c-Myc–dependent stemness program and ABC transporter–mediated drug efflux. Targeting the Cav-1FAK signaling axis may suppress CSC-like traits and improve chemotherapy efficacy in metastatic TNBC. Given limited conventional drug pockets of Cav-1, targeted protein degradation approaches such as Cav-1 directed PROTACs may represent a promising therapeutic strategy.
Key Words: Triple Negative Breast Cancer, caveolin-1, cancer stem-like cells, chemosensitivity, and PROTAC.

Poster 32

Human endogenous retroviruses (HERVs) associated with glioblastoma prognosis.

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Introduction: Glioblastoma (GB) is the most aggressive primary brain tumor in adults, with a 5-year overall survival of just over 5%. Progress toward improving patient outcomes has been hindered by limited therapeutic options, few effective clinical trials, and a lack of robust prognostic biomarkers. Although overall prognosis remains poor (median survival of approximately 15 months), individual survival times vary substantially. This variability highlights the need for reliable biomarkers capable of stratifying patients into groups with distinctly longer or shorter survival to better inform clinical decision-making and optimize clinical trial design. Human endogenous retroviruses (HERVs), which comprise approximately 8% of the human genome, have recently been implicated in GB biology and correlated with patient survival. However, despite these emerging associations, the prognostic utility of HERV expression remains largely unexplored.
Objective: Assess the prognostic potential of HERVs as biomarkers in GB.
Methods: Secondary analysis of RNA-Seq datasets from The Cancer Genome Atlas (TCGA), including Telescope (a computational software tool providing locus specific estimation of HERV expression), Principal Component Analysis (PCA), Genomic Regions Enrichment of Annotations Tool (GREAT), Pathway Analysis, Kaplan-Meier analysis.
Results summary: Applying in silico analyses to the datasets from TCGA, we determined a locus-specific HERV expression for glioma that identified 211 HERVs significantly dysregulated between GB and normal brain (NB), GB and low-grade glioma (LGG), as well as LGG and NB. Based on this analysis we developed a HERV-based scoring algorithm that segregated GB, LGG, and NB. Functional prediction analysis linked the 211 HERV loci with 18 voltage-gated potassium channel genes. Moreover, we have developed a risk score (RS-13) based on the RNA expression of 13 HERV loci, which stratifies GB patients into four distinct survival groups, outperforming conventional gene-based classifiers. The stratification approach detects a 12.5 times difference in the risk of death between GB patients with low and high RS-13 scores.
Conclusions: Our data provides a strong framework for the development of HERV-based biomarkers for GB, expanding new opportunities for prognostic tools and potentially supporting therapeutic approaches.
Sources of support: NIH NIGMS COBRE grant #P20GM121288 (LSUHSC New Orleans Center for Translational Viral Oncology - CTVO).

Poster 33

The Power of Reprograming: Human Induced Pluripotent Stem Cells (hiPSCs)- Derived Endothelial Cells for Vascular Disease Modeling.

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Vascular endothelial cells (ECs) are a single layer of cells that line the inner surface of blood vessels, extending from large vessels to the microvasculature of various organs. Vascular injury and endothelial dysfunction (ED) are central to the pathogenesis of many cardiovascular and inflammatory diseases, including thrombosis, atherosclerosis, sepsis, and ischemia-reperfusion injury. In 2019, an estimated 17.9 million people died from CVDs, representing 32% of all global deaths. Over the years, in vitro modelling of the ED has been conducted on primary ECs. Despite their usefulness, they are limited by donor availability, donor-to-donor variability, their phenotypic drift and patient derived cells. By contrast, induced pluripotent stem cells (iPSCs) are easily obtained and undergo unlimited self-renewal, overcoming primary cell concerns. hiPSCs provide a powerful and renewable source of patient-specific endothelial cells that retain the genetic background, while enabling standardized differentiation. hiPSC-derived ECs offer a unique platform to recapitulate key aspects of vascular biology, including barrier function, inflammatory activation, and thrombogenic responses. In this study, hiPSCs were generated and validated from peripheral

blood mononuclear cells (PBMCs). hiPSCs were subsequently differentiated into endothelial cells and comprehensively characterized. To evaluate the cells as a vascular disease model, endothelial cells were treated with lipopolysaccharide (LPS), resulting in reduced cellular viability, increased pro-inflammatory cytokine expression, and induction of apoptotic responses. In this study, our hiPSCs model expressed the core pluripotency markers, including OCT4, SOX2, SSEA-4 and TRA-1. Also, on differentiating them endothelial cells, they expressed lineage specific markers, CD31 and VE-cadherin. Upon treating them with lipopolysaccharide (LPS), cellular viability studies showed significant reduction in the viability after 24 h of treatment. Also, low dose of LPS for 24 h, showed reduced cell confluence and significant increase in the activity of the executer caspases 3 and 7. Furthermore, treatment with LPS for 6 h upregulated the pro-inflammatory cytokines IL-1β, NF-κB, TNF-α, IL-6 and IL-8. These findings indicated that hiPSC-derived endothelial cells recapitulate the key aspects of LPS-induced cell damage and provided a reliable patient specific platform for mechanistic and genetic studies. This iPSC-derived model offers a more physiologically relevant alternative to immortalized cell lines and may serve as a valuable model for studying vascular diseases genetics and pathogenesis, and testing candidate therapeutic interventions.

Funding sources: National Institutes of Health (P20GM121307); NSF (24-575).

Poster 34

Human-induced Pluripotent Stem Cell-Derived Cardiomyocytes recapitulate Functional, Transcriptional, and Epigenetic Perturbations Associated with Septic Cardiomyopathy.

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Background: Sepsis is a life-threatening organ dysfunction and the leading cause of death in hospitals and accounts for >$24 billion of annual total U.S. hospital costs. Sepsis cardiomyopathy is a fatal acute ventricular dysfunction unrelated to myocardial ischemia that occurs in up to 40% of patients with sepsis and is associated with a significant increase in the mortality rate of up to 70-90%. Cardiomyocyte damage represents a primary contributor to multi-organ failure and poor outcomes after sepsis. Besides, sepsis survivors who undergo myocardial remission after similar cardiomyopathies are at higher risk of developing severe cardiovascular morbidities in the future. Although factors such as male sex, age, hemoglobin level, and diabetes are risk factors for sepsis cardiomyopathy the mechanism of sepsis cardiomyopathy remains an unsolved puzzle. This is because sepsis in vivo models do not fully recapitulate the response of patients' cardiomyocytes to sepsis. Human cardiac response to sepsis should ideally be studied in the heart tissues of sepsis patients; however, human cardiac tissue is essentially unavailable for such analysis. Hypothesis: Sepsis cardiomyopathy patients show dysregulated and exaggerated immune response, which is unique and regulated by patient specific regulatory response that alters the cardiac gene expression.

Objective and Methods: Here, we investigated the utility of patient-specific induced pluripotent stem cells (iPSC)-derived cardiomyocytes to model sepsis cardiomyopathy and whether they recapitulate cardiac perturbations known to occur in sepsis cardiomyopathy patients.

Conclusion: Human iPSC-cardiomyocytes successfully model the phenotype of sepsis- induced cardiomyopathy (SIC), replicating key cellular and functional characteristics. This in vitro model offers a robust platform for investigating the molecular and cellular mechanisms underlying sepsis cardiomyopathy, facilitating the identification of potential therapeutic targets and biomarkers and accelerate the development of novel treatment strategies.

Acknowledgements: This project is supported in part by the Grant in Aid Award by Center for Cardiovascular Diseases and Sciences LSUHS, supported by the center for Redox Biology and Cardiovascular Disease Center of Biomedical Research Excellence, supported by the National Institute of General Medical Sciences IDeA program of the National Institutes of Health under award P20GM121307 and by the IDeA Center of Biomedical Research Excellence grant P20GM103424.

Poster 35

Human papillomavirus (HPV) genome tethering to mitotic chromosomes regulates viral genome levels in basal keratinocytes.

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Human papillomaviruses (HPV) are small DNA viruses that infect mucosal and cutaneous epithelia. High-risk HPVs are the leading cause of cervical cancer and are associated with other types of cancers, including anogenital and head and neck cancers.

Persistence of HPV infection is strongly associated with carcinogenesis and occurs in proliferative basal keratinocytes, where the HPV genome copy number is maintained during subsequent cell divisions. We recently reported that this maintenance is achieved by

robust replication of the viral genome in S/G2 cell phases, followed by a failure of most of the viral episomes to tether to host chromosomes during mitosis and their subsequent degradation in the cytoplasm throughout interphase; thus resetting the nuclear viral genome copy number to the levels observed at the beginning of S phase.
Using highly sensitive in situ hybridization (DNAscope) and confocal microscopy to study the localization of viral DNA during mitosis, we find a progressive loss of chromosomal association of viral genomes, from early (41%) to late mitosis (14% of viral genomes per cell). Furthermore, colocalization analyses between viral genomes and previously reported tethering factors – TOPBP1 and Brd4, which are reported to anchor viral genomes to mitotic chromatin through interaction with the viral protein E2 – reveal that only a limited subset of viral genomes associated with host chromosomes (around 15%) directly colocalize with these tethering factors. Consistent with this, inhibition or knockdown of TOPBP1 or Brd4 leads to a modest reduction in viral genome association with mitotic chromatin.
Our findings highlight mitotic tethering as a main regulator of HPV genome copy number in basal keratinocytes. Future research will aim to identify the critical viral and host determinants of HPV genome persistence and nuclear retention, including the identification of alternative tethering factors for the viral genome.

Poster 36

Investigating Madariaga virus as a non-select agent model to study eastern equine encephalitis virus interactions with heparan sulfate.

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Introduction: Arthropod-borne viruses (arboviruses) Madariaga virus (MADV) and eastern equine encephalitis virus (EEEV) are members of EEEV complex within the Togaviridae family that circulate in Central/South America and North America, respectively. Unlike many other arboviruses, natural isolates of EEEV are highly virulent despite enhanced interactions with heparan sulfate (HS), a polysaccharide ubiquitously expressed at cell surfaces and functions as a viral attachment factor.
Objective: We hypothesize EEEV interactions with HS can be modeled with MADV, the only non-select agent member of the EEEV complex, and support future studies on how these virion-HS interactions affect viral pathogenesis.
Methods: Our present studies utilize attenuated, BSL-2 Sindbis/EEEV chimeric viruses expressing the structural proteins of EEEV to study virion-HS interactions. For our initial feasibility studies with MADV, we are generating a chimeric Sindbis virus encoding the structural genes of MADV which will be applied to animal models of viral dissemination and viremia to investigate the specificity of virion-HS interactions.
Results: In mice, we found early dispersal of subcutaneously inoculated EEEV virions to the draining lymph node is independent of their capacity to engage with HS. However, vascular HS associated with blood-filtering phagocytes restricts further lymphohematogenous dispersal. Interestingly, we observed enzymatic depletion of high- but not low-sulfated vascular HS inhibited viral clearance from murine circulation. We also observed host species-specificity in these interactions, as EEEV viremia is modulated by murine but not avian vascular HS. Our analysis of the MADV E2 glycoprotein amino acid sequence and predicted structure show conservation of the two basic patches required for Sindbis/EEEV interactions with vascular HS.
Conclusions: Our published data with Sindbis/EEEV suggests that EEEV-HS interactions occur within host-, tissue-, and cell-specific contexts. Follow-up experiments indicate that EEEV specifically interacts with highly sulfated HS in the murine vasculature. Our computational analyses of the MADV E2 glycoprotein show complete conservation of basic patches required for EEEV-HS interactions. Once we generate the chimeric Sindbis/MADV, we intend to investigate the putative interactions of the MADV virion with heparan sulfate as a foundation for future viral pathogenesis studies with authentic MADV in our BSL-3 laboratory.
Support: CAIPP pilot project and LSUHS start-up package.

Poster 37

Engineered Oncolytic HSV-1 Restrains Tumor Dissemination in a Metastatic Pancreatic Cancer Model.

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Pancreatic ductal adenocarcinoma (PDAC) is marked by early metastatic spread and limited responsiveness to cytotoxic chemotherapy, making durable disease control difficult to achieve. As a result, there is a critical need for treatment strategies that address not only primary tumor growth but also metastatic progression. Oncolytic virotherapy represents a promising approach because it combines direct tumor cell killing with immune stimulation, potentially complementing standard chemotherapy. In this study, we investigated the anti-tumor and anti-metastatic effects of a genetically engineered herpes simplex virus-1, HSV-1(VC2) expressing murine GM-CSF, both as a monotherapy and in combination with gemcitabine. In vitro experiments using murine KRASG12D, TP53R172H, Cre (KPC) cells revealed a strong synergistic interaction between oncolytic virotherapy and gemcitabine, supported by ZIP synergy modeling.

Transcriptional analyses showed that gemcitabine treatment increased expression of EMT-associated and pro-survival genes, including TGF-β, fibronectin, TAZ, CAV1, AKT, and PI3K, whereas oncolytic virotherapy primarily activated STING-associated innate immune signaling pathways. When combined, the treatments suppressed gemcitabine-induced EMT and proliferative signaling while maintaining antiviral and immunostimulatory gene expression, suggesting coordinated transcriptional effects consistent with enhanced cytotoxic activity. To determine whether these findings translated in vivo, we employed an optimized immunocompetent orthotopic PDAC model generated by pancreatic implantation of KPC cells into C57BL/6 mice. Refinement of this model resulted in consistent liver metastasis in untreated tumor-bearing animals, providing a rigorous baseline for therapeutic evaluation. Under these conditions, oncolytic virotherapy alone reduced primary tumor burden and markedly limited liver metastasis in most treated mice, while untreated controls uniformly developed metastatic disease. Combination therapy with gemcitabine led to further reductions in primary tumor size. Similar patterns of tumor growth control and metastatic limitation were also observed in a Panc-1 xenograft model of human PDAC. Ongoing studies using flow cytometry, targeted transcriptomics, and proteomic analyses are focused on defining the immune and molecular mechanisms underlying the differences observed between treatment groups. Together, these results highlight the capacity of HSV-1(VC2) GM-CSF to constrain metastatic progression in PDAC and support its continued development as a rational partner for chemotherapy.

Keywords: Pancreatic ductal adenocarcinoma, oncolytic virotherapy, gemcitabine, metastasis, synergy

Poster 38

Cumulative environmental exposures and metabolic syndrome: A study of heavy metals and volatile organic compounds.

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Background: Metabolic Syndrome (MetS), a condition affecting over one-third of the U.S. population, heightens the risk of cardiovascular disease, Type 2 diabetes, and premature mortality. While individual links between heavy metals (HM), volatile organic compounds (VOC), and MetS have been established, the impact when these environmental toxins are combined remains unclear and unexplored. This study investigates how simultaneous exposure to HMs and VOCs influences the risk of MetS.

Methods: Weighted Quantile Sum regression and Bayesian kernel Machine Regression were performed on data from 6603 participants in the National Health and Nutrition Examination Survey (2011–2020) to determine the impact of HMs and VOCs detected in urine on MetS. Further analyses were performed for individuals placed in subgroups based on age, sex, race/ethnicity, and monthly poverty level index.

Results: The analyses reveal that combined exposure to HMs and VOCs is associated with an increased risk of MetS; in particular, exposure to cadmium, tin, N-acetyl-S-(N-methyl carbamoyl)-Lcysteine, and N-acetyl-S-(2-carboxyethyl)-L-cysteine significantly elevates the risk of developing MetS. Younger adults (18–50 years), men, Hispanics and non-Hispanic whites, and those with a monthly poverty index > 1.3 (higher socioeconomic status) emerged as the most vulnerable groups.

Conclusion: These findings emphasize an urgent need to address and tackle the cumulative impact of environmental toxins through a shift in public health efforts to go beyond investigating isolated exposures to address real-world chemical exposures. By understanding these cumulative risks, we can begin to mitigate them and pave the way for more effective interventions, especially for at-risk populations.

Poster 39

Proteomics-Driven Function Discovery and FDA-Approved Drug Repurposing in Pancreatic Cancer.

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Pancreatic cancer is the third leading cause of cancer-related deaths in the United States, primarily due to late-stage diagnoses resulting from its asymptomatic progression. In this study, label-free quantitative (LFQ) proteomics–driven bioinformatics were applied to identify biomarkers for diagnosis, to enable potential drug development via drug repurposing, and to enable targeted drug scoring and ranking. Twelve pancreatic tissue samples were analyzed using liquid chromatography-mass spectrometry (LC-MS). Formalin-fixed paraffin-embedded (FFPE) pancreatic tissues underwent deparaffinization and protein extraction, followed by trypsin digestion into peptides for LFQ proteomics analysis. Differential expression analysis was performed using false discovery rate (FDR)–adjusted criteria to identify statistically significant protein signatures. Significant proteins were then subjected to functional enrichment analysis via g:Profiler. To further translate these significant proteins

into clinical opportunities, they were queried against DrugBank, DrugCentral, and DGIdb to identify potential drug development. Furthermore, a ranking system for the candidate drug in the market was established based on target multiplicity and pathway relevance. This project accelerates the development of precision treatments and early diagnosis, providing a data-driven foundation for identifying biomarker and therapeutic targets for pancreatic patients.

Poster 40

Host Glutaminase-1 Inhibition Enhances Phagocytic Activity of Macrophages.

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Introduction: Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), remains the leading cause of death from a single infectious agent worldwide, underscoring the urgent need for new host-directed therapeutic strategies. Macrophages are the primary host cells for Mtb, internalizing bacteria, and serving as a permissive niche for intracellular survival and replication. During infection, Mtb actively rewires host metabolic pathways, including glutamine metabolism, to support bacterial persistence and immune evasion. Consistent with this, infected macrophages upregulate genes involved in glutamine uptake and utilization. Our previous studies demonstrated that pharmacologic inhibition of glutamine metabolism using the pleiotropic inhibitor JHU083 significantly reduces bacillary burden in Mtb-infected macrophages ex vivo and in vivo. However, the specific mechanism driving this protective effect remains understudied. In this study, we investigated the role of glutaminolysis in tuberculosis pathogenesis by targeting glutaminase-1 (GLS1), a key enzyme that catalyzes the conversion of glutamine to glutamate.
Hypothesis: Host glutaminolysis promotes bacillary survival in macrophages and that selective GLS1 inhibition will enhance antimycobacterial activity of macrophages.
Methods: We treated bone marrow–derived macrophages (BMDMs) with GLS1 specific inhibitors (CB-839 and BPTES) and assessed the impact of GLS1 inhibition upon (1) phagocytic activity using Abcam Green E. coli Phagocytosis Kit; (2) cell viability using Promega LDH-Glo assay; (3) intracellular glutamine/glutamate levels using the Promega Glutamine/Glutamate-Glo assay, and (4) intracellular reactive oxygen species (ROS) levels using Promega ROS-Glo assay.
Results: Both CB-839 and BPTES significantly enhanced macrophage phagocytic capacity without inducing cytotoxicity. GLS1 inhibition resulted in a significant reduction in intracellular glutamate levels, confirming effective suppression of glutaminolysis. In parallel, intracellular ROS levels were significantly decreased upon GLS-1 inhibition. Together, these data indicate that glutaminolysis inhibition enhances phagocytic activity of macrophages by altering macrophage metabolic and redox states.
Conclusions: Our findings identify GLS1 as a critical metabolic regulator of macrophage phagocytic function and a promising target for the development of novel host-directed therapy for TB. Our future studies will evaluate the effect of GLS1 inhibition upon Mtb clearance in murine models of TB infection.
Sources of support: CoBRE CBLD RPL Award, CoBRE CAIPP startup & Pilot Award and Departmental Seed package.

Poster 41

The Guinea Pig Model of Kaposi Sarcoma Associated Herpesvirus Infection.

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Background: KSHV causes three malignancies in immunocompromised populations, yet therapeutic development is limited by inadequate preclinical models. Mouse models use murine gammaherpesvirus with low KSHV homology, while non-human primate models are prohibitively expensive. Guinea Pig Herpes-Like Virus shares 84% homology with KSHV and encodes homologues of critical oncogenes (vBCL2, vPK, viral cyclin, LANA, vGPCR), prompting investigation of guinea pigs as a host for KSHV infection.
Methods: In vitro: Guinea pig fibroblasts JH4 and 104C1 were infected with KSHV.219 (MOI=1), selected with puromycin, and reactivated with sodium butyrate. In vivo: BC-3 cells produced cell-free virus concentrated to 1E10 genomic equivalents/mL. Twenty-eight female Hartley guinea pigs received: dexamethasone (dex) + UV-inactivated virus (n=2), dex + 1E9 genomic equivalents IP (n=6), dex + intraoral infection (n=6), or identical treatments without dex. Viremia was measured by qPCR targeting ORF50. KSHV antibodies were assessed using a 37-protein Luminex panel.
Results: Both cell lines demonstrated efficient KSHV infection and reactivation. All animals showed viremia at 2 weeks, decreasing to undetectable by day 28. Daily dex extended viremia to 28 days in orally infected animals. Orally infected animals developed sporadic gingival inflammation; 2/28 developed symmetrical dermal ear inflammation at 80 days. Serological analysis identified structural (SCP, MCP, ORF19, K8.1) and nonstructural (K10.5, LANA) proteins as antibody targets.
Conclusions: Guinea pigs provide a physiologically relevant, scalable KSHV infection model with translational relevance through conserved immune responses consistent with human data. This model enables cost-effective evaluation of prophylactic and therapeutic interventions, addressing critical gaps in KSHV research for diseases affecting vulnerable

populations worldwide.
Sources of support: Research reported in this abstract was supported by an Institutional Development Award (IDeA) from the National Institute of General Medical Sciences of the National Institutes of Health under grant number P2O GM135000-02.

Poster 42

Loss of Adipocyte KAT8 Results in Lipoatrophy and Oxidative Stress in Adipose Tissue in Mice.

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KAT8 (lysine acetyltransferase 8), also known as MOF or MYST1, plays cell-specific roles in processes such as cell proliferation, differentiation, and survival/death by acetylating various protein substrates, including histones. Although KAT8 is expressed in adipose tissue (AT) and its gene contains single-nucleotide polymorphisms (SNPs) linked to body mass, its function in adipocytes had not been previously studied. To investigate this, we created a novel mouse model with KAT8 depleted specifically from adiponectin-expressing cells (KAT8AKO) and measured body weight, body composition, and insulin tolerance. We also examined gene and protein expression of antioxidant and mitochondrial targets in white AT (WAT), assessed mitochondrial copy number, and measured cellular and mitochondrial redox poise in AT explants and isolated mitochondria using electron paramagnetic resonance (EPR) combined with spin trapping and simultaneous respirometry/fluorometry.
KAT8AKO mice developed lipoatrophy and insulin resistance, with reduced expression of antioxidant genes and mitochondrial oxidative phosphorylation protein complexes as well as decreased mitochondrial copy number. Gonadal WAT (gWAT) explants from both female and male KAT8AKO mice released more superoxide compared to controls, and isolated mitochondria from KAT8AKO gWAT showed impaired succinate oxidation and increased hydrogen peroxide production.
These findings suggest that adipocyte KAT8 is crucial for maintaining AT integrity and function, potentially through regulating oxidative stress and mitochondrial metabolism. The observed increase in reactive oxygen species (ROS) and defects in mitochondrial respiratory capacity in AT of KAT8AKO mice contribute to a deeper understanding of KAT8's role in AT biology and its implications for metabolic disorders associated with adipocyte dysfunction.

Poster 43

An ethanolic extract of Artemisia scoparia (SCO) inhibits lipolysis in vivo and has anti-lipolytic effects on murine adipocytes in vitro.

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Introduction: An ethanolic extract of Artemisia scoparia (SCO) has metabolically favorable effects on adipocyte development and function in vitro and in vivo and improves measures of insulin sensitivity in a mouse model of diet-induced obesity.
Objectives: To investigate SCO's effects on lipolysis in vivo and in vitro.
Methods: Lipolysis was assessed by measuring free fatty acids (NEFA) and glycerol in the serum C57BL/6 mice fed a high-fat diet with or without supplementation with SCO. In vitro, we measured NEFA and glycerol released by 3T3-L1 adipocytes in response to TNFα treatment, with or without SCO pretreatment. Levels of genes or proteins involved in lipolysis were determined by qPCR or immunoblotting, respectively.
Results: SCO reduced circulating NEFA and glycerol levels in an in vivo diet-induced obesity (DIO) model and inhibited TNFα-induced NEFA and glycerol release in cultured adipocytes. Although SCO did not reverse TNFα-induced expression of lipolytic genes, it induced anti-lipolytic changes in the phosphorylation of hormone-sensitive lipase (HSL) and perilipin.
Conclusions: Metabolically favorable effects of SCO in DIO mice are likely to involve the regulation of inflammation-induced lipolysis in adipocytes through modulation of phosphorylation sites in proteins such as HSL and perilipin known to activate or suppress lipolysis.
Sources of Support: This work was supported by National Center for Complementary and Integrative Health and the Office of Dietary Supplements of the National Institutes of Health (Award Number P50AT002776). Gene expression analysis employed Genomics Core facilities supported in part by COBRE (NIH 8 P20 GM103258) and NORC (NIH 2P30DK072476).

Poster 44

Uncovering functional networks of glycosylation using parallel CRISPR screens.

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*** Our lab is looking for a postdoc! Please email Kimberly.tsui@lsuhs.edu for more information.**

All cell surfaces are decorated by a diverse array of glycan structures that vary between cell types and cellular states. These glycans are synthesized in a

stepwise, non-template manner through the activity of hundreds of glycosyltransferases and glycosidases. However, a cell's glycome is determined not just by the activity and localization of these biosynthetic enzymes, but also by the availability of sugar nucleotides, intracellular trafficking, and ER and Golgi function. This complex functional network together regulates the glycome both during homeostasis and in response to perturbations such as cellular stress. While decades of studies have deepened our understanding of how known glycogenes regulate the synthesis of distinct glycan structures, our knowledge of how genes beyond biosynthetic enzymes contribute to shaping the glycome remains limited.

To address the identity and organization of this regulatory network of glycosylation, we performed a dozen genome-wide CRISPR screens in K562 cells to identify genetic regulators of high-mannose, biantennary, and highly branched N-glycans, bisecting GlcNAc, core fucose, LacNAc, α2,3- and α2,6-sialic acid epitopes. This enabled us to measure the effects of knocking down every gene in the genome on the cell surface expression of these glycan epitopes. These screens have not only revealed a large number of novel regulators of glycosylation but also allowed us to uncover functionally linked gene modules that control the cell surface glycocalyx at a systems level. Using hierarchical clustering of glycosylation phenotypes, we identified many groups of functionally related genes that control specific glycan epitopes. These include a group of Golgi regulators that only impact the levels of high-mannose but no other glycan epitopes, as well as two distinct subsets of mitochondrial genes that regulate highly branched N-glycans and core fucose, respectively. Ongoing work is focused on understanding how these gene modules interact to modulate the glycome and on how these regulatory networks change in response to different cellular stress states in various cell types.

Together, these comprehensive genetic regulatory networks, constructed using functional genomics and systems biology approaches, will provide important insights into relationships between glycan biosynthetic enzymes, the Golgi, and intracellular trafficking regulators, as well as predict the function of previously uncharacterized genes that have similar glycosylation phenotypes to known genes. This work will accelerate our understanding of how different cell types regulate glycosylation in normal and stressed conditions.

Poster 45

Trends in Mortality Related to Atrial Fibrillation/Flutter and Disparities in Race, Sex, and Ethnicity from 1999–2020.

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Introduction: Atrial fibrillation (AFib) is the most common persistent arrhythmia, and it is associated with morbidity from stroke and systemic embolism. Atrial flutter (AF) is another supraventricular tachycardia with similar morbidity and mortality associations grouped under the same diagnostic code (ICD-10 = I48). Despite significant advances in strategies for applying both anticoagulation and rhythm control application, demographic and regional trends on AFib/AF-related mortality remain to be fully appreciated.

Hypothesis: AFib/AF-related AAMRs will differ among the demographics measured.

Methods: The data analyzed came from the Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiological Research (CDC WONDER). From 1999 to 2020, age-adjusted mortality rates (AAMRs) per 100,000 people were calculated for AFib/AF-related mortality. Trends in AAMR were analyzed with joinpoint regression stratified by sex, race and ethnicity.

Results: Of all groups, NH White individuals had the highest AFib/AF mortality burden. In this group, AAMRs were higher in females until 2017 when males surpassed them. Overall APC values for AAMRs in NH substrata (Q1) ranged from 3.58% to 4.73%, with differences between groups not reaching statistical significance. Overall APCs in White substrata (Q2) were similar; group differences were not statistically significant. However, this finding shows that AAMRs significantly increased across all groups (except AIAN persons, for whom APC calculations could not find a significant effect, likely due to low representation). For most groups, joinpoint analysis found a segment change in the period from 2015 to 2017 which caused the average APC to decrease. This finding did not occur in some groups in Q1 modeling (NH Black/White females and AIAN groups). This finding was statistically significant in White males regardless of Hispanic origin, and in NH Black males.

Conclusions: AFib/AF-related mortality in the United States has increased over the past two decades. These findings underscore the growing public health burden of supraventricular arrhythmias and contrast with improving outcomes observed for some other cardiovascular conditions. Targeted interventions addressing disparities in access to anticoagulation, rhythm management, and longitudinal cardiovascular care are needed to reduce AFib/AF–related mortality.

Sources of Support: IDeA from NIGMS (NIH grant P20GM121307), Ike Muslow Endowed Chair of Healthcare Informatics.

Poster 46

Therapeutic Advancement in GBM: Integrating Oncolytic HSV-1(VC2) GM-CSF with Existing Therapies.

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Oncolytic virotherapy (OVT) represents a promising therapeutic strategy in cancer, especially in the case of

glioblastoma (GBM). GBM is one of the most common and malignant brain tumors in adults, and its poor prognosis leads to only 5-10% of the patient population surviving more than 5 years post-diagnosis. OVT is a novel and innovative treatment alternative that uses genetically modified viruses to target cancer cells. Their dual mechanism of action, comprising the cytolytic and immunogenic activity, provides an advantage in the treatment of GBM. Previous studies using the in-house HSV-1(VC2) GM-CSF showed increased infiltration of immune cells and reduced breast cancer (BC) metastasis to lungs in a 4T1 Balb/c model of BC. Based on this, we investigated the effect of HSV-1(VC2) GM-CSF in the treatment of GBM. In our preliminary studies, we observed a significant dose-dependent cytopathic effect (CPE) early in the treatment at 6-12 hours in both human LN229 and U-87; and - mouse GL261 GBM cell lines starting at a dose of 0.1 MOI; however, there was no oncolytic effect until 24 hours. To further evaluate the OV effect in vivo, we established an orthotopic murine C57BL/6 model by stereotactic implantation of ~50,000 GL261_luc tagged cells into predetermined coordinates in the frontal lobe. Following the tumor implantation, HSV-1(VC2) GM-CSF was administered at 105 & 106 pfu/ml at 7-10 days at the same stereotactic coordinates to ensure targeting of the tumor mass. Upon immunoblot analysis, there was a significant upregulation of eIF4A1 and HMGB1 in the tumor control, suggesting an aggressive proinflammatory tumor microenvironment (TME). A marked increase in SPP1 and Iba1 was also observed in the brain tumor tissues, reflecting enhanced activation of tumor-associated macrophages/microglia (TAMs). Whilst the molecular analysis to delineate the effect of HSV-1(VC2) GM-CSF treatment on the regulation of these markers is underway, the treatment significantly improved the overall survival (OS) from 35-40 days to 45 days as compared to the tumor control group. Importantly, IHC analysis of (VC2) GM-CSF-treated brain tissues showed a notable increase in CD8+ T-cell infiltration, suggesting an anti-tumor immune response. Additionally, we would like to evaluate the synergistic effect of the virus in combination with the standard GBM therapy, including temozolomide. In the future, we aim to investigate the effect of (VC2) GM-CSF on the transcriptome of GBM by RNA -seq analysis.

We acknowledge the Louisiana Biomedical Research Network (LBRN) for research support provided through NIH-NIGMS grant 2P20GM103424, which made this study possible.

Poster 47

Protocadherin-1 is required for the entry of Necocli, Tula, and Nova hantaviruses

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Hantaviruses are zoonotic RNA viruses that infect endothelial cells, causing hantavirus cardiopulmonary syndrome (HCPS) in the New World and hemorrhagic fever with renal syndrome (HFRS) in the Old World. No FDA-approved vaccines or therapeutics exist against these deadly viruses, and the entry mechanisms of most hantaviruses remain poorly characterized. Here, we developed a panel of recombinant vesicular stomatitis viruses (rVSVs) expressing Gn/Gc glycoproteins from seven hantaviruses with unknown receptor usage: shrew-borne Thottapalayam virus (TPMV) & Kenkeme virus (KKMV); mole-borne Nova virus (NVAV) & Oxbow virus (OXBV); vole-borne Tula virus (TULV), African rodent-borne Sangassou virus (SANGV); & New World rodent-borne Necocli virus (NECV). The Gn/Gc proteins of all these hantaviruses, except KKMV, didn't require adaptive mutations to mediate entry into human cells. KKMV Gn/Gc harbored one mutation, but its relevance to rVSV production and/or cellular entry is unclear. We hypothesized that TULV and NECV use New World hantavirus receptor, protocadherin-1 (PCDH1), as they are phylogenetically related to PCDH1-using viruses. We evaluated receptor usage of these rVSVs in human cells lacking PCDH1. Human osteosarcoma U2OS and endothelial TIME cell experiments indicate that infection with rVSV-NECV and -TULV Gn/Gc, but not those of the others, is significantly reduced in PCDH1 knockout cells, and that their infection was neutralized by PCDH1-targeting interventions. Consistent with this, NECV and TULV Gn/Gc proteins bind to human PCDH1 in ELISAs. Authentic hantavirus experiments with TULV and NVAV corroborated these findings. Interestingly, rVSV carrying NVAV Gn/Gc proteins, a virus distantly related to PCDH1-using viruses, demonstrated weak binding to and dependence on PCDH1 for infection. Finally, we evaluated the neutralizing activity of a broadly neutralizing human monoclonal antibody (ADI-42898) against these seven hantaviruses. Our results show that all viruses, except TPMV, can be effectively neutralized, with differences in neutralization effectiveness correlating with variations in epitope sequences and antibody binding to Gn/Gc. Taken together, our data indicate that there are no barriers to the entry of these diverse hantaviruses into human cells, delineate receptor usage, and demonstrate the antiviral activity of a broadly neutralizing antibody against these viruses.

Funding: LSU Health Seed Funds, NIAID R21 (AI156482), NIGMS CAIPP CoBRE (P20GM134974).

Poster 48

Epigenetic clocks capture residual mortality risk beyond clinical risk factors.

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Background: Current cardiovascular risk prediction models (e.g., PREVENT) rely on clinical risk factors

derived from population averages. However, significant heterogeneity in mortality risk remains among individuals with similar clinical profiles.
Hypothesis: We hypothesized that a composite DNA methylation (DNAm) risk score could capture biological risk and improve mortality risk prediction beyond standard clinical models.
Methods: We analyzed NHANES 1999–2002 participants (n=2301) with available DNAm epigenetic biomarkers and mortality linkage. We constructed a composite DNAm mortality score (DNAmScore) using elastic-net regularization on a panel of epigenetic clocks; hyperparameters were selected using repeated, nested cross-validation to reduce overfitting. We fit three Cox proportional hazards models on a single common complete-case set: (1) DNAmScore alone, (2) a PREVENT-like clinical model (age, sex, BMI, systolic blood pressure, total cholesterol, HDL, eGFR, diabetes, and smoking), and (3) the combined model (clinical + DNAmScore). We assessed discrimination at 10 years using inverse probability of censoring–weighted (IPCW) time-dependent ROC/AUC.
Results: In the combined model, DNAmScore remained strongly associated with mortality (HR=2.30 per 1 SD increase in DNAmScore, 95% CI 1.93-2.75, p<0.001), indicating that epigenetic clocks capture risk unmeasured by clinical covariates. Kaplan-Meier demonstrated strong risk stratification, with significant separation between high and low DNAmScore tertiles (log-rank p<0.001). Ten-year discrimination was AUC = 0.796 for PREVENT-like model, 0.795 for DNAmScore alone, and 0.809 for the combined model, indicating modest incremental discrimination when adding DNAmScore to PREVENT.
Conclusions: A DNA methylation–derived score captures biological mortality risk that is independent of standard clinical factors. By quantifying the biological deviation from expected clinical trajectories, DNAm biomarkers offer a pathway toward precision risk stratification and may help identify high-risk individuals missed by conventional population-based scores.
Funding: This work was supported by an Institutional Development Award (IDeA) from the National Institutes of General Medical Sciences of the NIH under grant number P20GM121307 to MANB. This project is also partially supported by the Ike Muslow, MD Endowed Chair in Healthcare Informatics of LSU Health Sciences Center Shreveport.

Poster 49

Study of North American Arenavirus Entry Using rVSV Pseudotyped Virus.

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Introduction: North American arenaviruses are members of clade D of the New World arenaviruses within the family Arenaviridae. These bi-segmented, negative-sense RNA viruses are maintained primarily in rodent reservoirs and have zoonotic potential yet remain understudied due to limited experimental tools for investigating early viral entry under standard biosafety conditions. Whitewater Arroyo virus (WWAV), first isolated in New Mexico, has been associated with severe human disease, but the molecular determinants governing its cellular entry are poorly characterized. New World Arenavirus entry is mediated by interactions between the viral glycoprotein complex (GPC) and host cell factors, including transferrin receptor 1 (TfR1). Recombinant vesicular stomatitis virus (rVSV) expressing the arenavirus GPC provides a BSL-2–compatible platform to study GPC-mediated entry independently of downstream replication events.
Objectives: To generate a rVSV expressing WWAV GPC and characterize time-dependent viral entry across multiple cell lines.
Methods: The WWAV GPC was cloned into rVSV(ΔG) backbone expressing monomeric NeonGreen (mNG). The rVSV-WW_GPC was rescued by transfecting rVSV helper plasmids and genomic plasmid into 293 FT cells and confirmed by fluorescence microscopy following infection of permissive cells. Growth kinetics was studied in five cell lines (A549, BHK-21, Huh7.5.1, HEK-293T, and Vero) based on reporter expression and $TCID_{50}$ estimation from culture supernatants at defined post-infection time points.
Results: The rVSV-WW_GPC successfully infected all tested cell lines, demonstrating functional incorporation of the glycoprotein and efficient viral entry. Fluorescent reporter expression was first detectable by 12 hours post-infection in all cell lines. A549 cells supported limited early infection, with restricted foci that failed to expand over time. In contrast, BHK-21, Huh7.5.1, HEK-293T, and Vero cells exhibited progressive infection and increasing infectious titers through 60 hours post-infection.
Conclusions: Our findings indicate that WWAV GPC mediates entry into multiple cell types, including human cells, and that early post-entry events are cell type-dependent. The observed cell type-dependent infection kinetics suggest the presence of host-specific barriers acting after initial viral entry. This system provides a scientific tool for future studies to identify viral and host determinants that regulate entry and infection.
Sources of Support: P20 GM134974 NIH COBRE Pilot Grant and LSUHS Start-up Funding

CORES

Poster 50

Empowering Research: The Evolution of the Bioinformatics and Modeling Core in the COBRE Center for Applied Immunology and Pathological Processes.

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The COBRE Center for Applied Immunology and Pathological Processes (CAIPP) established a fee-for-service Bioinformatics and Modeling core to support research, training and education in various aspects of bioinformatics and data science. The Core has rapidly expanded to meet research needs and is now capable of analyzing any annotated species, from microbes to humans. Over 117 projects have been supported, encompassing bulk and single-cell transcriptomics, spatial transcriptomics, weighted correlation gene network analysis (WGCNA), variant calling, ChIP-seq, ATAC-seq, AlphaFold protein structure prediction, proteomics, Hi-C, Deep Mutation Scanning, TCR and BCR assembly from RNA-seq data, and metabolomics. To extract biological knowledge from these datasets, many profiling approaches rely on the exploration of shared functions among genes . For this purpose, we employ clusterProfiler and 3PodR to evaluate ontological classification and enrichment utilizing multiple biological databases (GO, KEGG, REACTOME, and NIH LINCS). While clusterProfiler offers visualization capabilities for gene classification and enrichment analyses, 3PodR integrates GSEA, targeted gene pathway analysis, and perturbagen analysis into an automated pipeline. Comparison of input gene profiles to perturbagen signatures in the LINCS database identifies regulators that mimic or reverse the effects of the input treatment. Additionally, our core provides hands-on training opportunities for undergraduate and master's students to build infrastructure that assists with FAIR data practices. Our trainees have created databases and user interfaces for project tracking and antibody inventory systems, and have conducted research to develop DeathScope: a high-throughput, YOLO-powered system for cell death detection in Incucyte phase-contrast imaging. Through such short-term internships, the CAIPP Bioinformatics and Modeling Core continues to build essential infrastructure to support research at LSU Health Shreveport.

Funded by NIH NIGMS P20 GM134974.

Poster 51

Creating a Cost-Efficient Immunophenotyping Core Supported by COBRE to Streamline Technology Adoption and Training

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In 2021, we established the COBRE Center for Applied Immunology and Pathological Processes (CAIPP) Immunophenotyping core at Louisiana State University Health-Shreveport (LSUHS). This Shared Resource Laboratory provides COBRE investigators with access to state-of-the-art immunophenotyping technology. We collaborate with investigators to optimize flow cytometry experimental design, develop protocols, conduct experiments, and analyze data. So far, we have worked with 15 laboratories, including COBRE and non-COBRE investigators at LSUHS. We have completed 18 projects (involving panel designing, staining, and data analysis), and five projects are ongoing. Additionally, we improved the single-cell isolation from complex tissues for downstream analysis by encouraging investigators to use the gentleMACS dissociators at our core. Acquiring a spectral flow sorter has advanced our campus's flow cytometric capabilities. However, this led to a challenge: upfront costs for antibodies and reagents deterred investigators interested in spectral flow. To address this, our core purchased generalized antibody panels. Investigators can now acquire smaller antibody aliquots to test hypotheses. Through discussions with faculty, we have identified key panels for purchase. We have initiated the availability of these panels on campus, providing researchers with the option to begin spectral flow cytometry experiments. In addition, we recently procured a Curiox laminar wash system, eliminating the need to centrifuge the samples during the staining steps. We have had great success with Curiox as it provides better cellular viability, debris removal, and signal-noise ratio in our flow cytometry experiments with different kinds of tumors and fragile cell lines.

Funded by NIH NIGMS P20 GM134974.

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Pulmonary Immunopathology Core

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This instrument core was established under the Center for Lung Biology and Disease to facilitate research projects of our COBRE-funded laboratories and any research lab in the Louisiana scientific community. The PIP Core houses a variety of equipment for live cell imaging, fluorescent cell and tissue imaging, multiplex cytokine quantification, cell metabolic analysis, multicolor flow cytometry sorting, and lung function testing for live animals. This core offers consultation

and training by staff in instrument operation and data analysis.
Funded by NIH NIGMS P20GM130555.

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Inhalation and Infection Core – COBRE Center for Lung Biology and Disease

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Exacerbation of respiratory infections and lung diseases by environmental exposures are a leading cause of morbidity and mortality worldwide. Every year, exposures to particulate matter air pollution are responsible for the premature deaths of 200,000 Americans. In addition, tobacco kills over 8 million people globally, while approximately 1.3 million non-smokers dye from exposure to secondhand smoke. There has also been an exponential increase in the prevalence of e-cig use in the US, with > 8 million adults and 2 million middle and high school students using e-cig devices daily. Infectious agents also represent a major public health concern. Lower respiratory infections are a leading cause of death worldwide, resulting in approximately 2.5 million to 2.7 million deaths annually. The highest number of deaths are from pneumonia, often caused by Streptococcus pneumoniae, Klebsiella pneumoniae, and Staphylococcus aureus. In addition, seasonal influenza contributes an added 290,000 to 650,000 respiratory deaths per year. Over 1.5 million deaths from respiratory infections annually are attributable to environmental factors, such as indoor and outdoor air pollution. Since outdoor and indoor air pollutants can induce and/or exacerbate respiratory infections and diseases, there is an urgent research need for co-exposure models of inhaled pollutant plus infectious agents to develop strategies to avoid these fatalities. The new Inhalation and Infection Core (IIC) of the LSU Lung COBRE was created to support the research needs of COBRE Promising Junior Investigators (PJIs) and NIH-funded scientists in their endeavors to study the combination effects of pulmonary infectious plus non-infectious agents within a single model. The IIC is poised to address mechanisms of respiratory diseases under real-life environmental exposure scenarios.
Funded by NIH NIGMS P20GM130555.

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Advancing Biomedical Research Through Collaborative Networks: The Role of the Louisiana Biomedical Research Network (LBRN)

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The Louisiana Biomedical Research Network (LBRN) plays a pivotal role in enhancing biomedical research capacity across the state. Supported by the National Institutes of Health (NIH) Institutional Development Award (IDeA) program, LBRN fosters interdisciplinary research collaborations, provides access to cutting-edge facilities in collaboration with two COBRE programs administered by the Division of Biotechnology and Molecular Medicine (BioMMED) at the LSU School of Veterinary Medicine, and offers comprehensive training programs for all IDeA students, early-career scientists, and faculty at participating institutions.

At the heart of LBRN's mission is the development of infrastructure and expertise in biomedical research across primarily undergraduate institutions (PUIs), research universities, and medical schools in Louisiana. Through its support of diverse research areas—ranging from cancer biology, infectious diseases, and neurobiology to bioinformatics and data science LBRN facilitates the growth of an inclusive scientific community dedicated to improving health outcomes both regionally and nationally.

This presentation will highlight key LBRN initiatives, including its support for research projects, mentoring programs, and the development of a robust network for sharing resources and expertise. Special attention will be given to the outcomes of LBRN-supported projects that have advanced scientific research, supported workforce development, and prepared underrepresented students for biomedical careers.

As LBRN continues to expand its impact, it remains committed to strengthening Louisiana’s position as a leader in biomedical research and innovation. This poster aims to showcase LBRN’s contributions to scientific knowledge, capacity building, and collaboration at the LSU System Multi-COBRE Colloquium. This information will be useful to all IDeA programs.

Keywords: Louisiana Biomedical Research Network, biomedical research, collaboration, NIH IDeA, workforce development, research capacity.
Funded by NIH NIGMS P20GM103424.