The 3rd Annual
Physician-Scientist Symposium
and Dr. Nancy C. Andrews Lecture

Abstract Book

Wednesday, January 22, 2020
12:00 p.m. to 5 p.m.
Trent Semans Center
Great Hall
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WELCOME TO THE 3RD ANNUAL PHYSICIAN-SCIENTIST SYMPOSIUM AND DR. NANCY C. ANDREWS LECTURE

On behalf of the organizing committee, it is a great pleasure to welcome you to the 2020 Duke Physician-Scientist Symposium and Dr. Nancy C. Andrews Lecture. The symposium has been organized to bring together physician-scientists from across Duke’s campus to celebrate the accomplishments of our students, trainees and junior faculty; to facilitate conversation and collaborations; and to engage physician-scientists in the mission of the Office of Physician-Scientist Development (OPSD). We are honored to welcome guest speaker Dr. P. Kay Lund from the National Institutes of Health and keynote speaker, Dr. Elizabeth McNally from Northwestern University.

We hope you enjoy the symposium!

Organizing Committee:
We would like to thank our organizing committee members for their time and insight.

Christopher Holley, MD, PhD, Committee Chair
Assistant Professor of Medicine
Assistant Research Professor of Molecular Genetics and Microbiology

Sallie Permar, MD, PhD
Associate Dean for Physician-Scientist Development
Professor of Pediatrics
Professor of Immunology
Professor of Molecular Genetics and Microbiology

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Professor of Pediatrics
Professor of Medicine

Gerry Blobe, MD, PhD
Professor of Medicine
Professor of Pharmacology and Cancer Biology
Director, Lefkowitz Society

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Professor of Medicine
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Assistant Professor in Obstetrics and Gynecology
Co-Director, Community of Scholars

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Medical Scientist Training Program

Allison McElvaine, PhD
Administrative Director, Office of Physician-Scientist Development

Ashton Spicer
Program Coordinator, Department of Medicine
Communications Specialist, Office of Physician-Scientist Development
OPSD was established in 2018 by Dean Mary E. Klotman to promote scientific engagement among physicians, trainees, and medical students. It is led by Associate Dean of Physician-Scientist Development, Sallie Permar MD, PhD, and Faculty Director, Rasheed Gbadegesin, MD, MBBS.

With support from the Duke University School of Medicine, the Burroughs Wellcome Fund, and the National Institutes of Health, our mission is empowering physician-scientists to launch successful research careers.

OPSD programs include:

The [OPSD Scholars Concierge Mentoring Program](#) supports residents, fellows, and junior faculty seeking career mentorship. OPSD Scholars are connected to a Master Mentor who provides a wealth of knowledge to support individualized physician-scientist career development. OPSD also offers mentor consultation services for Medical Students.

OPSD [funding opportunities](#) support medical student research, provide partial salary support for research technicians, and support early development of research programs by junior faculty physician-scientists.

The [Research Careers Ahead!](#) seminar series provides skills needed for students, trainees and junior faculty to develop a robust research program. Featured speakers include Dr. Mitchell Heflin, Professor of Medicine in Geriatrics and Dr. Sally Kornbluth, Provost of Duke University and Jo Rae Wright University Distinguished Professor.

A Basic Science Research Track for the Duke Master of Health Sciences (MHSc) degree program, scheduled to launch in Fall 2020, will serve physician-scientists and trainees seeking the skills required to perform rigorous basic science, manage, analyze and present data; run a laboratory; and compete for research funding. Medical students intending to pursue a second third year experience, fellows working in basic science laboratories, early stage faculty and potential K award applicants are especially encouraged to apply.

**DR. NANCY C. ANDREWS LECTURE**

Nancy C. Andrews, MD, PhD served as Dean of the Duke School of Medicine for 10 years and emphasized interdisciplinary collaboration both within the School of Medicine and across the university. She established a host of new research and education programs, including the opening of five new departments and establishment of a satellite campus in the Durham Innovation district. An alumna of Yale (BS, MS), MIT (PhD), and Harvard (MD), Dr. Andrews trained in pediatric hematology/oncology and served in faculty and leadership roles at Harvard before moving to Duke in 2007. Internationally recognized for discoveries in iron biology, she was an HHMI investigator and has been elected to the National Academy of Medicine, the National Academy of Sciences and the American Academy of Arts and Sciences.

The Andrews Lectureship was developed to honor Dr. Andrews’ service to the development of physician-scientists and leadership at Duke.

**Historical Dr. Nancy C. Andrews Keynote Speakers:**

### 2018:

**Svati Shah, MD, MHS**
Professor of Medicine  
Associate Dean of Genomics  
Director of Precision Genomics Collaboratory  
Director, Duke Adult Cardiovascular Genetics Clinic  
Co-Director, Translational Research, Duke Molecular Physiology Institute  
Vice-Chief, Translational Research, Division of Cardiology

**Kafui Dzirasa, MD, PhD**
Associate Professor of Psychiatry & Behavioral Sciences  
K. Ranga Rama Krishnan Associate Professor  
Assistant Professor of Biomedical Engineering  
Associate Professor in Neurobiology  
Assistant Professor in Neurosurgery  
Investigator in the Duke Institute for Brain Sciences

### 2019:

**Rodger Liddle, MD**  
Professor of Medicine
GENERAL ANNOUNCEMENTS

Oral Presentations
Each platform session is scheduled to last 40 minutes in total with 4 speakers at each session. This includes 5 minutes for the presentation followed by 5 minutes for discussion.

Posters
All posters will be displayed for the entirety of the symposium. Posters are numbered according to the abstract portion of this program book.

Awards
Poster awards will be announced at the conclusion of the symposium.

Evaluations
Evaluations will be sent to all participants via email after the conference. These evaluations provide important feedback and help the organizers improve future meetings.

Acknowledgements
We are very grateful for all of the people who have worked diligently behind the scenes to make this meeting success. We also thank our keynote speaker, Dr. Elizabeth McNally and our guest speaker, Dr. P. Kay Lund.
SPONSORS:
The Office of Physician-Scientist Development would like to thank our symposium sponsors.

The 2020 Physician-Scientist Symposium and Dr. Nancy C. Andrews Lecture is funded in part by Burroughs Wellcome Fund under Award Number 1018899. The content of this conference is solely the responsibility of the organizers and does not necessarily represent the official view of the Burroughs Wellcome Fund.

**The Robert J. Lefkowitz Society** provides a home for MD and MD/PhD post-graduate trainees who are in the Duke University School of Medicine, including the Department of Medicine Internal Medicine Residency and Fellowship programs, and who are pursuing careers with a primary focus on basic and translational research as physician-investigators. Through formal and informal mentoring relationships, the Lefkowitz Society provides promising post-graduate trainees with a greater understanding of how to develop successful academic careers.

**Physician-Scientist Strong Start Awards Program** is intentionally designed to integrate and complement Duke initiatives that train physician-scientists at even earlier points in their career, such as the Medical Scientist Training Program (MD-PhD students) and the R38 Stimulating Access to Research during Residency Program (StARR, clinical residents). In this way, the “Strong Start” Award Program will ensure that Duke University School of Medicine remains a leader in the training of outstanding physician-scientists, a group uniquely committed to the advancement of the medical sciences in our own community and in the nation.

**Duke Pediatric Research Scholars Program** is a Physician-Scientist Training Program (PSTP) dedicated to preparing burgeoning physician-scientists for careers in academic medicine. The program focuses on the period from the completion of the MD, DO, MD/PhD, or DO/PhD degree through residency and fellowship training, with the goal of achieving a full-time academic appointment as an investigator. DPRS combines the intensive clinical training environment of Duke Children’s with the rigorous scientific training of the world-renowned laboratories at Duke University.

PARTNER PROGRAMS:
For more information on our partner programs, please visit the host tables located by the posters.

**Research Navigators** helps investigators identify relevant resources, connect with experts, and understand processes and best practices for performing research at Duke.

**My Research Home** recognizes making advances in research is central to Duke's mission, and giving our community the tools to do it is key. The myRESEARCHhome portal, funded by Duke's CTSA, puts relevant applications, resources, and information specific to you and your projects at your fingertips. Your portal's content is personalized based on your researcher profile, showing you content you want and need to see, saving you time and effort.

**Community of Scholars** connects scholars with resources, opportunities, and each other to build a robust and diverse support network, creates synergy and improve efficiency by strengthening connections among career development programs at Duke, shares best practices and resources for program leadership, mentors, and scholars, and coordinates efforts to facilitate and increase diversity among scholars, mentors, and programs.

**Advancing Scientific Integrity, Services and Training (ASIST)** supports the Duke research community by promoting a culture of scientific integrity, improving data management practices, developing educational materials, organizing outreach activities, and providing individual consultations.

**Duke Clinical Translational Science Institute (CTSI)**, with support from the NIH Clinical and Translational Science Award and Duke Health, CTSI accelerates real-world translational research at Duke with funding, innovative resources, and nationwide collaborations.

**Clinical Research Training Program (CRTP):** provides Duke and National Institutes of Health (NIH) physicians, investigators and other healthcare professionals with the academic training needed to stand out in today’s dynamic clinical research environment.
Symposium Agenda

12:00 – 12:30pm    Check In and Lunch

12:30 - 12:35pm    Welcome and Opening Remarks
                   Chris Holley, MD, PhD
                   Assistant Professor of Medicine, Cardiology
                   Assistant Research Professor of Molecular Genetics and Microbiology

12:35 - 12:45pm    State of the Program Address
                   Sallie Robey Permar, MD, PhD
                   Associate Dean for Physician-Scientist Development
                   Professor of Pediatrics, Molecular Genetics & Microbiology, and Immunology

12:50 – 1:30pm     Speakers:
                   Vivian Lei, MS3 (Dermatology)
                   OPSD Burroughs Wellcome Fund Medical Student Scholarship Recipient
                   Noelle Young, MD
                   Assistant Professor of Pediatrics
                   Strong Start Award Recipient
                   Megan Kelly, GS4 (Biochemistry)
                   Medical Scientist Training Program
                   Jordan Pomeroy, MD, PhD (Fellow, Department of Medicine)
                   OPSD Technician Support Award Recipient

1:30 – 2:00        Strategies to Recruit and Retain Physicians in the NIH Funded Physician-Scientist Workforce
                   P. Kay Lund, PhD
                   Director, Division of Biomedical Research Workforce
                   Office of Extramural Research (OER)
                   Office of the Director (OD)
                   National Institutes of Health (NIH)

2:00 – 2:10        BREAK

2:10 – 2:50pm      Speakers:
                   Mark Draelos, MS4 (Biomedical Engineering)
                   Medical Scientist Training Program
                   Anna Williams, MD (Resident, Department of Pediatrics)
                   R38 Scholar
                   Muath Bishawi, MD (Resident, Department of Surgery)
                   R38 Scholar
                   Nellie Farrow, MD (Resident, Department of Surgery)
Symposium Agenda (Continued)

2:50 – 3:45pm  Poster Session and Reception

3:45 – 4:00pm  Introduction of Nancy C. Andrews Physician-Scientist Lecture
Mary Klotman, MD
Dean, School of Medicine
R.J. Reynolds Professor of Medicine
Professor in Molecular Genetics and Microbiology
Professor of Pathology

4:00 – 5:00pm  Nancy C. Andrews Physician-Scientist Lecture
Complexity of Single Gene Disorders
Elizabeth McNally, MD, PhD
Elizabeth Ward Professor Director of the Center for Genetic Medicine
Northwestern University, Feinberg School of Medicine

5:00pm  Presentation of Poster Awards
Gerry Blobe, MD, PhD
Professor of Medicine, Pharmacology and Cancer Biology
Lefkowitz Society Director

Closing Remarks
Chris Holley, MD, PhD
SPEAKERS

Keynote Speaker

Elizabeth McNally, MD, PhD

Dr. Elizabeth McNally directs the Center for Genetic Medicine at Northwestern University’s Feinberg School of Medicine. As the Elizabeth J. Ward Professor of Genetic Medicine, Dr. McNally is a cardiologist with expertise in genetics. Her work focuses on understanding genetic mechanisms of cardiovascular disease and using genetic signals to drive therapy development. She has a special interest in neuromuscular genetic diseases like muscular dystrophy and identifying genetic modifiers. Her translational work has been recognized by an award from the Burroughs Wellcome Fund and a Distinguished Clinical Scientist Award from the Doris Duke Charitable Foundation. She serves on the Advisory Boards for the Muscular Dystrophy Association, Parent Project Muscular Dystrophy, and is the Vice Chair for the Council on Basic Cardiovascular Sciences of the American Heart Association. She is a past president of American Society for Clinical Investigation and a member of the Association of American Physicians.

Guest Speaker

P. Kay Lund, PhD

As Director of the Division of Biomedical Research Workforce (DBRW), Dr. P. Kay Lund provides leadership for development, implementation, policy and evaluation of extramural programs related to research training, career development and diversity of the biomedical research workforce, including institutional training grants, individual pre- and postdoctoral fellowships and Career Development (K) awards. Recent emphasis has been on innovative strategies to recruit, retain and accelerate independence for early stage physician/clinician scientists, including new Institutional Research in Residency programs with opportunities for Transitional Scholar K awards during fellowship (Academic Medicine. 2017, 92:1382)

Dr. Lund joined NIH from a career in academia including appointments at the Massachusetts General Hospital and Harvard, and the University of North Carolina at Chapel Hill where she held a Sarah Graham Kenan Distinguished Professorship. Throughout her career, she partnered with clinician investigators. Her research and publications focused on glucagon-like peptides (GLPs) and insulin-like growth factors (IGFs) including basic molecular biology, gene structure and regulation and roles in intestinal epithelial renewal, regeneration, inflammatory bowel diseases and early stage cancer.

Dr. Lund mentored many undergraduates, graduate students, postdocs and early stage faculty, both Ph.D. and clinician scientists, a majority of whom are succeeding as independent researchers. She has received many awards (Award for the Advancement of Women, the Davenport award from American Physiological Society and the 2016 Distinguished Mentor Award from the American Gastroenterology Association).
Non-Linearities Between Spinal Cord Stimulation Rate and Response Frequency Propagated Along Dorsal Column Aβ Fibers

Andreas Seas*, Nathan Titus, Warren Grill

1Department of Biomedical Engineering, Duke University

Chronic pain is a widespread and challenging problem affecting thousands of persons in the United States and abroad. Spinal cord stimulation (SCS) is a well-established surgically implanted device therapy for chronic pain, and there is an opportunity to improve the efficacy of SCS through understanding the underlying mechanisms of action. Computational modeling and simulation is a powerful tool to analyze mechanisms and design therapeutic innovations. However, previous models of SCS assumed that stimulation pulse repetition rate and axonal firing rates within the dorsal columns are equivalent. In this study, we quantified the relationship between stimulation rate and axon firing rate in a simplified model of SCS. A model of monopolar, monophasic stimulation was built in NEURON and the average rates, spikes per pulse, and interspike interval of the model axons response were calculated in MATLAB across various stimulation rates (25 - 1200 Hz), amplitudes (25 - 1500 uA), as well as model axon distances (1000 - 2000 µm) and diameters (5, 8, 12 µm). Near threshold, model Aβ axon firing rates responded linearly with SCS frequencies up to ~800 Hz. Model axons responded to further increases in the frequency of stimulation by transitioning to a response rate of 1/2 the stimulation rate. At higher amplitudes we saw an additional transition in the larger fibers to desynchronized firing and transient activation. Notably, transition frequencies varied with stimulation amplitude, as well as axonal diameter and distance. The nonlinear relationship between stimulation rate and Aβ fiber response indicates the need to constrain current models of SCS to reflect the true nature of signals reaching dorsal horn circuits. The simulations were performed in a simplified model of SCS, and more complex models reflective of current clinical applications need to be developed and tested.

References

Supported by NIH Grant U18 EB029257.

POSTER 2:

The endogenous anti-inflammatory Annexin A1 augments recovery following bladder outlet de-obstruction

Brent D. Nosé*, Shelby Harper, Francis M. Hughes Jr., Todd J. Purves

1Division of Urology, Department of Surgery, Duke University Medical Center

Introduction: Due to inflammation during bladder outlet obstruction, bladder dysfunction persists in many patients following de-obstruction surgery. Our lab has extensively studied the mechanisms that trigger this inflammatory response, but the role of endogenous anti-inflammatories in the bladder, notably Annexin A1, has never been explored. In this study, we tested the ability of Annexin A1 to expedite the resolution of inflammation following de-obstruction and improve bladder function recovery.

Methods: Sprague Dawley rats underwent bladder outlet obstruction via urethral ligation around a 1 mm (o.d.) catheter. De-obstruction was performed after 12 days and rats were randomized to treatment with 1 mg/kg/day of AC2-26 (the
active N-terminal peptide of Annexin A1) in PBS or vehicle for two days. For inflammation assays, 25 mg/kg of Evans blue dye was injected IV one hour prior to sacrifice. Bladders were then weighed, and Evans blue concentrations measured spectrophotometrically. For functional assays, suprapubic tubes were placed at the time of obstruction and cystometry performed two days after de-obstruction. Functional assays included a sham surgery group while inflammation assays included a no-treatment group to establish controls. The sham cohort underwent loose urethral ligature placement and subsequent removal after 12 days.

Results: Inflammation measured by Evans blue extravasation decreased following de-obstruction from 27.8 ng EB/mg to 21.88 ng EB/mg after two days; AC2-26 further decreased this to 15.5 ng EB/mg which was significantly less than the obstructed baseline. Functionally, 83% of rats that received AC2-26 had a return of normal micturition after 2 days as compared to 50% who received vehicle only and 100% of sham operated rats.

Conclusion: We demonstrated that the resolution of inflammation following de-obstruction is augmented significantly when treated with AC2-26. Furthermore, the addition of AC2-26 results in improved return of micturition cycles even when controlled for the effects of surgery. Overall these results demonstrate that Annexin A1 can enhance the resolution of inflammation following bladder de-obstruction and this correlates with improved bladder function.

POSTER 3:

Clostridium immunis: a human commensal bacteria with therapeutic immunomodulatory effects

Chin Yee Tan2,4, Neil Surana1,2,3*

1Department of Pediatrics, Duke University School of Medicine, 2Department of Molecular Genetics and Microbiology, Duke University School of Medicine, 3Department of Immunology, Duke University School of Medicine, 4Duke-NUS Medical School, Singapore

The modulation of the human microbiome is an attractive method to promote health and abrogate disease. Members of the host microbiota regulate host immunity, illuminating an attractive entry point for the treatment of autoimmune disease. Utilizing microbe-phenotype triangulation coupled with directed culture techniques, we have identified a new species of human gut commensal bacteria, Clostridium immunis. C. immunis causally protects mice against colitis and autoimmune encephalitis, two distinct animal models of human autoimmune disease. Spatiotemporal characterization of C. immunis reveals that a) its colonic localization likely allows for direct local effects to ameliorate colitis, and b) its short-term kinetics upon oral administration indicates that prolonged colonization is not required for disease protection. Preliminary mechanistic studies show that C. immunis downregulates colonic group 3 innate lymphoid cells, a cell population interestingly implicated in both colitis and autoimmune encephalitis. Current efforts are directed at identifying the bacterial product(s) responsible for its disease modifying effect by using a combination of comparative genomics and biochemical approaches.

References

POSTER 4

Biased Agonism at CXCR3 Drives Differential Phosphoproteomic and Transcriptomic Profiles and Cellular Outputs

Dylan S Eiger, BS1, Jeffrey S Smith, MD, PhD2, Chia-Feng Tsai, PhD3, Jon M Jacobs, PhD3, Tujin Shi, PhD3, and Sudarshan Rajagopal, MD, PhD1,*

1Duke University, Durham, NC; 2Providence Portland Medical Center, Portland, OR; 3Pacific Northwest National Laboratory, Richland, WA.
**Background:** G-Protein Coupled Receptors (GPCRs) are the largest family of receptors and the target of ~30% of approved small molecule drugs. GPCRs signal through many downstream effectors like G proteins and β-arrestins. Some ligands activate G protein over β-arrestin signaling, or vice versa - a phenomenon known as biased agonism. To investigate the mechanisms and implications of biased agonism, we studied CXCR3, a chemokine receptor on T cells, which binds three endogenous ligands, CXCL9, CXCL10, and CXCL11. Despite its role in cancer, atherosclerosis, and other inflammatory disorders, no drugs target CXCR3.

**Methods:** Using mass spectrometry and RNA-seq, we assessed changes in the phosphoproteome and transcriptome of CXCR3 overexpressing HEK293 cells and activated CD8+ human T-cells, respectively, following stimulation with the aforementioned ligands.

**Results:** Our phosphoproteomic analyses identified 19349 phosphorylation sites (phosphosites) on 5519 different proteins, of which 1532 phosphosites were differentially regulated between treatment groups. Similarly, our transcriptomic analyses identified 48162 transcripts from 12405 genes, of which 887 transcripts were differentially regulated between treatment groups. These data also demonstrate that the profiles of CXCL9 and CXCL10 differ greatly from that of CXCL11 which is concordant with published data demonstrating that CXCL9 and CXCL10 activate G protein and β-arrestin signaling equally whereas CXCL11 is β-arrestin biased. Further analyses of these data demonstrate biased regulation of endocytosis, the cortical cytoskeleton, cell-cell adhesion, cell division/cycle, ubiquitination, and the Jak-STAT and MAPK signaling pathways.

**Conclusions:** We show that the endogenous ligands of CXCR3 change the phosphoproteome and transcriptome in a biased manner. Although these ligands signal through the same receptor, they are not redundant in function. Further exploration of these chemokines and CXCR3 may highlight the therapeutic promise of developing specific biased agonists to treat a variety of inflammatory disorders.

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**POSTER 5:**

**Neutrophil Dectin-1 signaling negatively regulates T cell proliferation**

Emre D. Cardakli¹, M. Elizabeth Deerhake¹, Mari L. Shinohara¹,²

¹Department of Immunology, Duke University School of Medicine, Durham, NC ²Department of Molecular Genetics and Microbiology, Duke University School of Medicine, Durham, NC

Dectin-1 is a C-type lectin receptor that recognizes β-glucans, the principal component of fungal cell walls, and promotes inflammation and the production of reactive oxygen species (ROS). While the antifungal functions of Dectin-1 signaling in macrophages are well-studied, it remains largely unknown how Dectin-1 signaling in neutrophils functions and whether Dectin-1 signaling modulates neutrophil – T cell interactions. In this study, we demonstrate that Dectin-1 signaling in neutrophils promotes an antigen presenting cell-like (APC-like) phenotype and upregulates expression of T-cell checkpoint molecules, including programmed death ligand 1 (PD-L1). Moreover, we found that neutrophil Dectin-1 signaling is able to suppress CD4+ T cell proliferation in vitro in a partially ROS-dependent manner. We are currently evaluating whether neutrophil Dectin-1 signaling may suppress T cell proliferation in a checkpoint molecule dependent manner as well. We also sought to test whether Dectin-1 signaling in neutrophils can suppress CD4+ T cell mediated autoimmunity in vivo. Remarkably, we found that systemic administration of a Dectin-1 agonist lessens the severity of experimental autoimmune encephalomyelitis (EAE), a model of multiple sclerosis. Also, we found that CNS-infiltrated neutrophils in EAE express checkpoint molecules PD-L1, DC-HIL, and ILT3, and a subpopulation of CNS-infiltrated neutrophils express MHC-II, possibly presenting antigens to T cells. We hypothesize that this unconventional neutrophil population may be able to suppress proliferation of T cells in a potentially antigen-dependent manner. Together, our data suggests that neutrophil Dectin-1 signaling can suppress T cell proliferation and may have a protective role at least in the context of EAE.

References

POSTER 6:

**Protective role of CD11c+CX3CR1+ macrophages in experimental septic AKI**

Jamie R. Privratsky\(^1\), Jiafa Ren\(^2\), Benjamin T. Morris\(^1\), Steven D. Crowley*\(^{2,3}\)

Departments of \(^1\)Anesthesiology and \(^2\)Medicine, Duke University Medical Center, Durham, NC 27710; \(^3\)Durham VA Medical Center, Durham, NC 27710

Acute kidney injury (AKI) is one of the most frequent forms of organ dysfunction and is seen in up to 70% of critically ill patients. The most common cause of AKI in critically ill patients is sepsis. Despite its high incidence and associated morbidity, there are currently no treatment options for septic AKI as the pathophysiology of septic AKI remains poorly understood. We performed unbiased profiling of inflammatory cells infiltrating the kidney following cecal ligation and puncture (CLP)-induced sepsis, and found substantial infiltration of CD11c+CX3CR1+ macrophages. Based on these findings, we hypothesized that depletion of CD11c+CX3CR1+ macrophages would ameliorate CLP-induced septic AKI. To explore their effect on septic AKI, we selectively depleted CD11c+CX3CR1+ macrophages via diphtheria toxin (DT) administration to mice in which the diphtheria toxin receptor (DTR) is expressed downstream of the CX3CR1 promoter in CD11c+ cells (CD11cCre(+)/CX3CR1\(^{dtr/wt}\)) and subjected these mice to CLP. Contrary to our hypothesis, compared to CD11cCre(-)/CX3CR1\(^{dtr/wt}\) mice, CD11cCre(+)/CX3CR1\(^{dtr/wt}\) mice demonstrated more severe kidney injury as measured by serum creatinine (0.22 mg/dl vs 0.40 mg/dl, p=0.02) and BUN (99 mg/dl vs 113 mg/dl, p=0.02) and heightened systemic and intra-renal inflammation as measured by Luminex bead cytokine arrays. CD11cCre(+)/CX3CR1\(^{dtr/wt}\) and CD11cCre(-)/CX3CR1\(^{dtr/wt}\) mice had similar mortality following lethal CLP sepsis (p=0.99) indicating results were not solely due to differences in survival. We are currently investigating mechanisms through which CD11c+CX3CR1+ macrophages afford protection from septic AKI as CX3CR1+ myeloid cells have also been shown impact development of AKI in human sepsis. In conclusion, we believe that modulation of infiltrating CD11c+CX3CR1+ macrophages warrants further consideration as a therapeutic modality to dampen intra-renal inflammation and thereby attenuate septic AKI.

Funding sources:
- NIH R01 DK087893 and RO1 HL128355 to SDC
- NIH K08 GM132689, IARS Mentored Research Award, and Duke Anesthesiology Dream Innovation Grant to JRP

POSTER 7:

**Dectin-1 regulates CNS autoimmunity through a non-canonical pathway**

Deerhake ME\(^1\), Inoue M \(^2\), Danzaki K\(^1\), Cardakli E\(^1\), Nonaka T\(^1\), Shinohara ML\(^{1,3,*}\)

\(^1\)Department of Immunology, Duke University School of Medicine, \(^2\)Neuroscience Program, University of Illinois at Urbana-Champaign, \(^3\)Department of Molecular Genetics and Microbiology, Duke University School of Medicine

Innate immunity mediates both damage and repair of the central nervous system (CNS) in neurologic disorders. Although pathologic roles for innate immunity are well-described in multiple sclerosis (MS) and its animal model, experimental autoimmune encephalomyelitis (EAE), protective aspects of the immune response are less understood. We found that dectin-1, a C-type lectin receptor (CLR), limited neuroinflammation in EAE while its canonical signaling mediator, Card9, promoted disease. Myeloid cells from the bone-marrow mediated the regulatory function of dectin-1 in EAE and upregulated expression of Oncostatin M (Osm), a neuroprotective cytokine, through a non-canonical Card9-independent Dectin-1 signaling pathway. We found that the Osm receptor (OsmR) functioned specifically in astrocytes to reduce EAE severity. RNA-seq profiling of the Card9-independent Dectin-1 transcriptional program identified multiple targets with neuroprotective functions, including Osm, which were regulated by NFAT signaling. Furthermore, we found that galectin-9, a recently described endogenous dectin-1 ligand, was upregulated in the CNS during EAE and limited disease in a dectin-1 dependent manner. Our data describe a new mechanism of neuroprotective myeloid-astrocyte crosstalk regulated by a non-canonical dectin-1 pathway.
POSTER 8:

Identification of Allosteric Nanobodies for the Carvedilol bound β-2 Adrenergic Receptor

Shashank Vege¹, Biswaranjan Pani, Ph.D.¹, Robert J. Lefkowitz, M.D.¹

¹Howard Hughes Medical Institute, Duke University, Department of Medicine

G-protein coupled receptors (GPCRs) are a major class of trans-membrane proteins. GPCRs mediate cellular signaling by binding of ligands to their canonical orthosteric site as well as, topographically distinct, allosteric sites. Carvedilol is a prototypical orthosteric blocker of the β-adrenergic receptors (β-ARs) which has been FDA approved for treating cardiovascular ailments. The mechanism(s) by which this β-blocker elicits cardioprotective effects remains unclear. We posit, gaining structural insight into receptor-drug interactions would advance our understanding of carvedilol function, and facilitate in developing potentially more efficacious therapeutics. While allosteric drugs are emerging as a new therapeutic paradigm, regulation of carvedillos’ pharmacological profile by allosteric β2-AR ligands remains unexplored.

We show that compound-6 (cmpd-6), the first small-molecule positive allosteric modulator of the β2-AR, significantly augments the affinity of carvedilol for the β2-AR. Cmpd-6 displays a strong positive cooperativity with carvedilol but no other β-blockers tested. To discern the structural mechanisms that underlie this unique positive cooperativity, we aim to develop conformational nanobodies to stabilize β2-AR simultaneously bound to carvedilol (at the orthosteric site) and cmpd-6 (at an allosteric site). We present an outline summarizing our approach to screen phage display nanobody libraries and a detailed biochemical characterization of the β2-AR target.

POSTER 9:

Calcium Pyrophosphate and Monosodium Urate Activate the NLRP3 Inflammasome within Bladder Urothelium via Reactive Oxygen Species and Thioredoxin Interacting Protein

Shelby N. Harper¹, Patrick D. Leidig¹, Francis M. Hughes Jr.¹*, Huixia Jin¹, J. Todd Purves¹²

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Introduction/Objectives: Urinary stones provoke inflammation within the urinary tract and this can result in pain, fibrosis, and scarring of the tissue. In this study, we investigated the mechanism by which stone-forming components activate the NLRP3 inflammasome within urothelium to promote pro-inflammatory mediator production. Specifically, we aimed to describe the contributions of reactive oxygen species (ROS) and thioredoxin interacting protein (TXNIP), an important structural component of the inflammasome, to this activation.

Methods: Urothelial cells were harvested and incubated overnight. For agonist studies, cells were treated with varying concentrations of calcium pyrophosphate and monosodium urate. For inhibitor studies, cells were treated with either N-acetylcysteine (1 hour) or Verapamil (4 hours) prior to incubation with either calcium pyrophosphate (62.5 ug/mL) or monosodium urate (1.25 ug/mL) for 24 hours. Untreated controls were incubated with ATP (1.25 mM) for 1 hour to maximally stimulate NLRP3 inflammasome activity (measured as caspase-1 cleavage of the fluorogenic substrate Ac-YVAD-AFC). Results are reported as a percentage of maximum ATP response.

Results: Calcium pyrophosphate and monosodium urate activate caspase-1, the functional component of NLRP3, in urothelial cells in a dose-dependent manner, reaching ~50% and ~25% of the ATP response, respectively. Pre-treatment with the ROS scavenger N-acetylcysteine reduces this activation in a dose-dependent manner. Additionally, activation was suppressed through treatment with Verapamil, a previously described downregulator of TXNIP expression.

Conclusions: The stone components calcium pyrophosphate and monosodium urate activate NLRP3 in a ROS and TXNIP-dependent manner in urothelium. These findings demonstrate the importance of ROS and TXNIP and suggest that targeting either may be a way to decrease inflammation in the urinary tract that results from stone formation.
POSTER 10

Pain and Functional Outcomes in Single-Dose versus Fractionated Stereotactic Body Radiation Therapy for Spinal Metastases

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Introduction: Spinal stereotactic body radiation therapy (SBRT) offers an efficient, non-invasive treatment modality for the control of spinal neoplasms. This study aims to examine whether 3-fraction SBRT improves pain and functional outcomes compared to single-fraction SBRT.

Methods: A single-institution retrospective study was performed of 156 adult patients with spinal metastases treated with single- or 3-fraction SBRT from 2008 to 2019. Demographics and baseline characteristics, radiographic data, and minimum 3-month follow-up post-treatment outcomes were recorded.

Results: Of the 156 patients included in the study, 70 (44.9%) underwent single fraction SBRT (median total dose 1700 cGy) and 86 (55.1%) underwent 3-fraction SBRT (median total dose 2100 cGy). At baseline, higher proportion of patients in the 3-fraction group had worse baseline profile including severity of pain (p<0.05), average use of pain medication (p<0.001), and functional scores compared to that in the single-dose fraction cohort. At 3-month follow-up, although there was no significant difference in the mean pain medication usage both between and within the two groups, the 3-fraction cohort experienced a greater frequency of improved pain outcomes compared to the single-fraction group (p<0.05).

Patients treated with single-dose and 3-fraction SBRT demonstrated similar improvements in Modified Rankin Scale scores (p=0.0008 and p<0.0001, respectively) with no significant difference in Karnofsky Performance Scale scores.

Conclusion: A greater frequency of patients who received fractionated delivery of spinal SBRT achieved significant pain relief with similar functional outcomes compared to those treated with single-fraction. Future work is needed to further establish the relationship between fractionation schedule and clinical outcomes.

POSTER 11

Pre-operative risk factors associated with prophylactic muscle flaps and peri-operative factors associated with subsequent post-operative complications in spine surgery

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Surgical closure of complex spinal procedures presents a challenge due to potential for poor wound healing and infections. Paraspinal flaps have been implemented in an attempt to decrease the likelihood of post-operative complications. Our study sought to identify pre-operative factors that impact the decision to perform prophylactic trunk flap closure and assess rates of and risk factors for wound disruption/infection in patients receiving prophylactic trunk flaps.

The National Surgical Quality Improvement Program(NSQIP) database was queried for all patients undergoing spinal surgeries from 2005-2017. Pre-and peri-operative variables including steroid use, preoperative transfusion, medical comorbidities, ASA classifications, wound classification, and operative time were extracted. Uni and multivariate analyses were performed to assess patient risk factors influencing surgical site infection(SSI) and wound disruption and to delineate which pre-operative factors increased the likelihood of patients receiving flap closures a priori.
Trunk flaps were performed on 758 patients; 301,670 patients did not receive a flap. Overall 29 (3.83%) patients in the flap group experienced SSI while 5154 (1.71%) did in the non-flap group (p<0.0001). Pre-operative steroid use (OR 0.5; p<0.0001), wound infection (OR 0.24; p<0.0001), elevated WBC count (OR 1.034; p<0.0001), low hematocrit (OR 0.94; p<0.0001), and preoperative transfusion (OR 0.22; p=0.0068) were significantly associated with utilization of a trunk flap. Perioperative factors including a contaminated or infected wound (OR 4.72; p<0.0001), ASA classification of severe disease (OR 1.92; p=0.024), and longer operative time (OR 1.001; p=0.0024) were significantly associated with postoperative wound disruption.

Our results suggest that patients with more comorbidities and a higher burden of illness are more likely to receive prophylactic trunk flaps at the time of spinal procedures. Additionally, regardless of these baseline factors, certain perioperative conditions place both patients who do and do not receive flaps at risk for wound disruption.

**POSTER 12**

**The DREAMER Study: A randomized controlled trial Developing a Real-time EEG-guided Anaesthesia Management curriculum for Educating Residents**

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Different anaesthetic drugs and patient factors are associated with unique EEG spectrogram patterns. Yet, it is unclear how to best teach trainees to interpret EEG spectrogram waveforms for intraoperative anaesthetic titration or what effect such educational interventions might have on clinical outcomes. We developed an EEG electronic-learning curriculum (ELC) that covered EEG spectrogram-guided anaesthetic titration. Anaesthesiology residents were randomized to receive this ELC versus standard residency curriculum alone. We hypothesized that the ELC group would have improved knowledge of EEG and administer lower aaMAC fraction (the primary outcome) to patients >60 years. ELC group residents showed a significantly greater EEG knowledge increase than control residents (6-point increase on test knowledge; 95% CI (3.50 to 8.88), p<0.001). There was no significant aaMAC difference in patients cared for by the ELC versus control group (p=0.23), though the percentage of patients who received >1 aaMAC was lower in the ELC group (p=0.027). Patients cared for by the ELC group versus control group had a reduced hospital length of stay (2.47 days versus 3.73 days, respectively) (p=0.039). An EEG spectrogram-guided anaesthetic titration ELC was associated with no difference in mean aaMAC administered to older adults, though it led to a reduction in the percentage of patients who received high anesthetic dosages >1 aaMAC, improved resident knowledge, and a reduced hospital length of stay. Future studies are warranted to replicate these results and to determine if modifications of this curriculum can lead to further clinical practice changes and improved patient outcomes.
POSTER 13
Worsening depressive symptoms after an emergency department visit for low back pain are associated with persistent pain and disability

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More than 2.5 million U.S. emergency department (ED) visits each year are for low back pain (LBP). Nearly half of these patients report persistent pain and functional disability 3 months later. While baseline depression has been shown to predict these poor outcomes, little is known about whether persistent pain and disability correlate with worsening depression. This is a secondary analysis of 362 patients seen at an urban ED with LBP who completed the Roland-Morris Disability Questionnaire (RMDQ), a 0-10 pain numeric rating scale (NRS), and Patient Health Questionnaire depression subscale (PHQ-9) at their ED visit and 3 months later. Linear regression analysis was used to determine the association between changes in depression severity from index ED visit to 3-month follow-up, and changes in RMDQ and pain scores over the same period. Models were adjusted for age, gender, race, ethnicity, education, and depression severity at baseline. At the index ED visit, median PHQ score was 0 (IQR 0,4) and median RMDQ score was 22 (IQR 17,24). At one week, median pain score was 6 (IQR 2,8). At 3 months, median change in PHQ from baseline was 0 (IQR -24,23), change in RMDQ was -8 (IQR -20,0), and change in pain score was -1 (IQR -3,0). After adjusting for potential confounders, worsening depression score between the ED visit and 3 month follow-up was associated with worsening function (B=0.85, 95% CI=0.68-1.03) and pain scores (B=0.11, 95%CI=0.05-0.17). The 3-month disability and pain intensity outcomes were more strongly correlated with change in depression than with baseline depression scores. Future work among ED patients with LBP should consider progressive depressive symptoms as a potentially modifiable risk factor for persistent pain and disability.

POSTER 14
An Internally Randomized Comparison on the Impact of Instrument Navigation on Time and Radiation during Percutaneous Transforaminal Lumbar Interbody Fusion Through Kambin's Triangle

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Background: Minimally invasive techniques in spinal fusion have resulted in smaller incisions, minimized blood loss, shorter hospital stays, and faster recovery time. Unfortunately, one drawback of minimally invasive techniques is the increased reliance on fluoroscopy and subsequent increase in exposure to ionizing radiation. Much of the radiation utilized in these procedures occurs during localization and hardware implantation. Intraoperative instrument navigational technology has emerged to aid in these processes, thereby reducing radiation exposure. TrackX integrates intraoperative fluoroscopy with instrument trackers, from which subsequent changes in instrument positioning are displayed in real-time without any additional radiation.

Purpose: Compare radiation output, fluoroscopy time, and number of images between standard C-arm fluoroscopy and instrument navigation for patients undergoing percutaneous transforaminal lumbar interbody fusion through Kambin's triangle.

Study design: internally randomized control trial

Eligible Population: adult patients undergoing index percutaneous transforaminal lumbar interbody fusion through Kambin's triangle.

Methods: Radiation emitted, x-rays taken, and fluoroscopy time for two individual tasks from the percutaneous minimally invasive transforaminal lumbar interbody fusion (percTLIF) were recorded between instrument navigation (TrackX) and conventional C-arm fluoroscopy. The tasks include placement of the initial percutaneous dilator to the appropriate disc
space and the placement of a single pedicle screw. Each patient was randomized to undergo placement of the initial dilator with or without instrument navigation. For multilevel cases, each level was randomized in an alternating fashion to undergo each task with instrument navigation or conventional fluoroscopy.

Results: Twenty-three cases were included in analysis. For the first task of placing the initial dilator at the appropriate entry point to the disc space, 9 control points were compared against 21 study points where an average of 299.87 seconds (P = 0.0022), 14 fluoroscopic images (P=0.0014) and 7.39 mGy (P=0.0112) were saved as a direct result of the TrackX instrument navigation system. Similarly, for pedicle screw insertion, 31 control points were compared against 17 study points where an average of 398.27 seconds (P <0.001), 8 x-rays (P <0.001) and 17.37 mGy (P <0.001) were saved. This amounts to almost 5 minutes saved during dilator access and 6.6 minutes saved per screw; leading to projected time savings of 31.5 minutes for a 1-level TLIF when only the first dilator and screwdriver are tracked.

Conclusions: C-arm-based instrument navigation is an efficacious method of facilitating hardware placement for percutaneous TLIF while simultaneously reducing the radiation exposure, time, and number of fluoroscopic images. This is the first instrument navigational system that reduces operative time and improves surgeon efficiency.

POSTER 15

Percutaneous lumbar interbody fusion with an expandable cage through Kambin’s triangle: initial results and feasibility

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Minimally-invasive transforminal lumbar interbody fusion is a common procedure in lumbar spine fusion. Typically, facetectomy is necessary to access the disc space for cage placement. Most authors have described the use of endoscopy to insert static cages through this approach or the use of a porous allograft-containment mesh. In this study, we describe percutaneous access to the disc and insertion of an expandable cage through Kambin’s triangle without facetectomy. The objective of this study was to determine the clinical, and radiographical outcomes and feasibility of totally percutaneous lumbar interbody fusion (percLIF) with the insertion of an expandable cage through Kambin’s triangle.

A retrospective review of patients undergoing single-level percLIF without the use of an endoscope for grade 1 lumbar spondylolisthesis via Kambin’s triangle with an expandable cage was performed. Demographic information, Oswestry disability index, pre- and postoperative radiographic factors, perioperative data, and complications were recorded from the electronic medical record.

Eleven total patients (two males) were included in this study. Anterior disc height significantly improved at six weeks, however, lost significance at six months. Posterior disc height significantly improved at six weeks and six months. Oswestry disability index was significantly improved by 24.2% from baseline to 12 months postoperatively (p=0.033).

Initial experiences have shown than percLIF without the use of an endoscope with an expandable cage through Kambin’s triangle is a safe and clinically efficacious procedure for reducing grade 1 lumbar spondylolisthesis and radiculopathy.
Communication Didactics in Obstetrics and Gynecology Residency: A National Survey

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Introduction: Delivery of excellent Ob/Gyn care hinges on effective communication strategies. Improved communication between physicians, patients and colleagues facilitates shared decision-making and fosters success in interprofessional teams. Despite this, no prior study has investigated the national landscape of communication training during Ob/Gyn residency.

Methods: Residents and PDs at nationwide accredited programs were emailed anonymized surveys. Topics included status of dedicated communication didactics, frequency of challenging interactions, and attitudes towards communication training. Responses were analyzed using descriptive statistics.

Results: 45 PDs and 215 residents responded. 98.1% of residents reported challenging clinical communication at least monthly, with many reporting these interactions weekly (47.9%), daily (30.0%), and multiple times a day (11.7%). 28 programs (62.2%) reported their residents receive formal communication training. Certain topics were less frequently taught, yet cited by residents as particularly challenging – such as “diffusing conflict amongst colleagues” and dealing with an “angry patient or family member.” PDs consistently overestimated residents’ communication competence as compared to self-evaluations. The largest discrepancy was between the percentage of PDs who felt their residents were “Independently” able to have difficult conversations with Interdisciplinary Colleagues, versus residents who felt “Independently” competent in this domain (85.7% vs. 50.2%). A majority of both PDs (77.8%) and residents (67.0%) endorsed trainee interest in communication didactics.

Conclusion: Communication receives relatively infrequent didactic time during residency. Traditionally emphasized topics – such as delivery of bad news – were considered less difficult than interpersonal dynamics and conflict resolution. Residents frequently encounter challenging communication interactions, and both PDs and residents are interested in dedicated didactics. Ultimately, communication training appears feasible, necessary, and may comprise a critical aspect of training the next generation of Ob/Gyns.

Can the p50 of red blood cells be modulated while preserving the Bohr effect?

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Background
The Bohr effect describes the effect of pH on oxygen affinity(increased p50 = lower oxygen affinity); within the pH range of 6.0 to 8.5, oxygen affinity decreases as a function of decreasing pH. This results in increased oxygen delivery to tissues that are more acidic secondary to increased metabolism and improved oxygen uptake into the RBCs in areas that are less acidic, such as lung tissue.

Myo-Inositol tripyrophosphate (ITPP) is a molecule that has been shown to pass through the RBC plasma membrane and allosterically modify hemoglobin, and, in human whole blood samples, ~40% shift in p50 was seen at concentrations from 60-120mM . Our aim is to confirm that ITPP does not abrogate the Bohr effect.

Methods
Preliminary experiments were conducted to determine the effect of increasing concentrations of ITPP on p50 under normal and acidotic conditions. We incubated 10mL PRBC’s at 37°C for 1 hour with ITPP at concentrations of 0mM, 30mM, 60mM, 90mM, 120mM, and 240mM. Automated tonometry using Clark oxygen electrode (Hemox Analyzer; TCS Scientific,
New Hope, PA) determined the oxygen affinity of each sample, in triplicate, using buffers at pH 6.8 or 7.4. Per manufacturer’s instructions, 5mL of buffer, 20 μL of 25% bovine serum albumin, and 10 μL of antifoaming agent were mixed with 50 μL whole blood. The mixture was exposed to decaying oxygen tension by insufflation of nitrogen gas, while dual-wavelength spectrophotometry at 560nm and 570nm was used to measure changes in oxyhemoglobin.

Results
A mixed linear regression model with fixed effects for ITPP concentration and pH was used. In this model, the effects of both ITPP concentration and pH were significant (Figure 1). A 10 mM increase in ITPP concentration was associated with an increase in p50 of .435 (95% confidence interval [.108, .762]; p-value = .0116). A pH of 7.4 was associated with a p50 which is 13.71 lower when compared with a pH of 6.8 (95% confidence interval [8.69, 18.74]; p-value < .0001).

Conclusion
In these preliminary experiments the Bohr effect is conserved, which may have important safety implications for clinical research using ITPP in patients with tissue acidosis.

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POSTER 18
Congenital Cytomegalovirus Infection Impairs Maternal-Fetal Antibody Transfer and Enhances Neonatal Antibody Production

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Background – Congenital cytomegalovirus (cCMV) infection is the most common vertically transmitted infection worldwide; however, neonatal humoral immunity in the setting of cCMV infection has been poorly characterized. CMV can infect the placenta and cause degradation of the neonatal Fc receptor (FcRn), which transfers IgG antibodies from mother to fetus, yet transplacental maternal antibody transfer has not been examined in cCMV.

Methods – We used a case-control cohort of infants from the Carolinas Cord Blood Bank, including CMV-infected, CMV-exposed, and CMV-uninfected infants. Cases and controls were matched on race and maternal age. We measured total IgG and antigen-specific IgG concentrations in paired maternal and infant cord blood plasma samples to assess the IgG transfer efficiency in infected versus uninfected dyads. We also measured infant IgA and IgM production in cord blood samples to evaluate neonatal antibody production.

Results – Our study showed decreased transfer efficiency of IgG in infants with cCMV compared to uninfected infants. The transfer efficiency of neonatal pathogen-specific IgG, including anti-tetanus, anti-pertussis, anti-hepatitis B, and anti-respiratory syncytial virus antibodies was decreased in mother-infant pairs with cCMV. The IgG transfer efficiency was intact in CMV-exposed infants, suggesting this decreased antibody transfer is not driven by maternal serostatus. Infants with cCMV infection also had increased production of both IgA and IgM compared to uninfected controls.

Discussion – Our preliminary results suggest impaired maternal-fetal antibody transfer occurs in the setting of cCMV. This could be due to CMV-mediated degradation of FcRn or a result of CMV-induced maternal hypergammaglobulinemia, which has been shown to compromise IgG transfer in other chronic maternal infections. The precise immune consequences of cCMV on passive maternally-derived immunity and the developing neonatal antibody repertoire requires further investigation.
POSTER 19

Maternal alum-adjuvanted recombinant HIV Env vaccine does not enhance autologous virus neutralization in HIV-infected pregnant women


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Preventive strategies beyond ART will be required to end the pediatric HIV epidemic. A maternal vaccine capable of boosting neutralizing antibody (nAb) responses against circulating viruses in HIV-infected pregnant women could effectively decrease mother-to-child transmission of HIV. Yet, it is not known if an HIV envelope (Env) vaccine administered to infected pregnant women can enhance autologous virus neutralization.

Here, we assessed autologous virus nAb responses in maternal plasma samples obtained from AIDS Vaccine Evaluation Group (AVEG) Protocols 104 and 102, historical Phase I safety and immunogenicity trials of recombinant HIV Env subunit vaccines in HIV-infected pregnant women (NCT00001041). AVEG 104 participants were randomized to receive 300 µg Env subunit MN recombinant gp120 with alum adjuvant or alum alone. AVEG 102 participants were randomized to receive 640 µg Env subunit recombinant gp160 or placebo. HIV Env-specific maternal plasma binding and neutralizing responses were characterized before and after vaccination in 15 AVEG 104 (n=10 vaccinee, n=5 placebo) and 2 AVEG 102 (n=1 vaccinee, n=1 placebo) participants. Single genome amplification (SGA) was used to obtain HIV env gene sequences from autologous viruses for pseudovirus production in pre- and post-vaccination plasma of HIV-infected pregnant vaccinees (n=6 gp120, n=1 gp160) and placebo recipients (n=3).

We detected an increase in MN gp120-specific IgG binding in the vaccinee group between the first immunization visit and the last visit at delivery (p=0.027, 2-sided Wilcoxon test). However, no difference was observed in the neutralization potency of maternal plasma collected at delivery against autologous viruses isolated from early or late pregnancy. Thus, immunization strategies capable of more potent B cell stimulation will likely be required to effectively boost autologous virus nAb responses in pregnant women and synergize with ART to further reduce infant HIV infections.

POSTER 20

Retrospective machine learning approach to analyze chest radiographs for applicability in patient surveillance, diagnosis, and prognosis

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Machine Learning is concerned with constructing algorithms which process data by example. This requires large data sets to provide comprehensive representative examples. Neural networks are layers of nonlinear computational nodes, allowing multiple levels of abstraction. Convolutional neural networks are structured to simulate the human visual cortex by integrating nearby features. [1,2]

Over the past decade, neural networks have become the leading contenders in image classification due to an explosion of parallel processing power and labeled examples. ImageNet contains 15 million images, allowing computer algorithms to reach human performance in identifying snapshots of real-world objects.

The purpose of this study is to develop a machine learning framework for the analysis of chest radiographs, and assess the feasibility and data characteristics of such a framework within the Duke University Health System (DUHS). With the recent publication of over 500,000 chest films by Stanford, Beth Israel, and the NIH, it has become feasible to develop a system trained primarily on chest radiography data. We aim to:

• Develop a machine learning framework for the analysis of chest radiographs using a convolutional neural network model with the advantage of these large published datasets.
• Apply this model broadly to chest radiographs within DUHS to evaluate baseline data characteristics and the feasibility
of using such a model for:

- Correlative analysis, e.g. evaluating features that are shared among patients with a given diagnosis, age, laboratory values, or condition.
- Diagnostic analysis, e.g. an electronic "sniffer" algorithm to diagnose the acute respiratory distress syndrome in high-risk patients.
- Prognostic analysis, e.g. an algorithm to predict disposition (home, ward, ICU) of emergency department patients based on chest films.

References:

POSTER 21

Differential Peptide and Protein Expression in Human Cerebrospinal Fluid in Patients with and without Postoperative Cognitive Dysfunction

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Introduction: Perioperative Neurocognitive Disorders (PND) occur in up to ~40% of the ≥16 million adults age ≥60 who undergo surgery each year, and are associated with decreased quality of life, increased one-year mortality, and a possible increased dementia risk.[1, 2] Strategies for managing PND are limited by our poor understanding of their underlying mechanisms, which are thought to involve neuroinflammation, glial activation, and disruption of the blood-brain barrier.[3] However, few studies have evaluated these processes by analyzing human cerebrospinal fluid (CSF) samples, and none have described CSF proteome-wide comparisons between patients with and without PND. We hypothesized that mass spectroscopy-based unbiased proteomic analysis may provide a powerful tool for identifying pathways underlying PND pathogenesis.

Methods: CSF was collected from 14 patients age ≥60 years before, 24 hours after, and six weeks after major non-cardiac, non-neurological surgery. Eight patients had PND and six were cognitively normal after surgery. Unbiased proteomic analyses were performed by the Duke Proteomics and Metabolomics core facility using hybrid quadrupole/time-of-flight tandem mass spectrometry, and statistical comparisons of peptide levels between PND and cognitively-affected patients were performed using a repeated measures mixed model.

Results: The repeated measures mixed model revealed significant changes in peptides levels from seventeen complement and complement-associated proteins between patients with versus without PND at six weeks post-surgery. No significant differences in peptide levels were identified between groups or time points alone.

Conclusions: These data demonstrate the feasibility of using unbiased proteomic analysis for evaluating CSF proteomic changes that may underlie PND, and suggest a possible role for complement activation within the central nervous system in PND pathogenesis.

References:
[3] Safavynia SA. Front Psychiatry. 2018
POSTER 22

Single Cell Transcriptomic Analysis Identifies Differences in Skeletal Muscle Macrophages in a Murine Model of Hindlimb Ischemia and a Human Critical Limb Ischemia Patient

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Introduction: Critical limb ischemia (CLI), the most severe form of peripheral arterial disease, results in limb loss in up to 50% of patients. However, CLI patient outcomes do not always correlate with limb ischemia severity. In fact, the skeletal muscle response to ischemia is an emerging area of interest. Skeletal muscle recovery is highly dependent on the reparative and regenerative abilities of macrophages. The role of macrophages in muscle regeneration and limb salvage in the chronically ischemic limb remains unknown.

Methods: Single-cell RNA sequencing (scRNA seq) was performed on C57BL/6J (BL6J, N=1) and BALB/cJ (N=1) skeletal muscle (tibialis anterior, TA) harvested 72 hours following hindlimb ischemia (HLI). TAs from BL6J and BALB/cJ were also collected for histological analysis at 24, 48, 72, 96, and 120 hours post-HLI (N=1). Additionally, scRNA seq was performed on both healthy (proximal specimen) and ischemic (distal specimen) tissue collected from a human CLI patient undergoing below-the-knee amputation.

Results: At 72 hours post-HLI, BALB/cJ (N=2) mice displayed greater tissue loss compared to BL6J (N=2) mice. Laser Doppler perfusion imaging confirmed identical ischemic insult between strains. UMAP analysis revealed a decreased macrophage population in BALB/cJ mice. Gene expression analysis also revealed differences in macrophage polarization and monocyte recruitment. Expression of Kruppel-like factor 4, a marker of regenerative M2 macrophages, was decreased in BALB/cJ mice. Furthermore, C5aR1 expression was decreased in BALB/cJ mice; the C5a-C5aR1 signaling axis is a key regulator of monocyte recruitment. Histological analysis of C57BL/6J and BALB/cJ TAs also showed increased F4/80 (murine pan-macrophage marker) staining up to 120 hours following HLI. Additionally, UMAP analysis of human CLI samples revealed decreased macrophage cell population in distal (ischemic) compared to proximal (healthy) muscle.

Discussion: Taken together, these findings suggest both quantitative and qualitative defects in macrophages are partly responsible for the development of CLI. Further research into monocyte recruitment and macrophage polarization in the setting of limb ischemia are warranted.

POSTER 23

Robotically-Aligned Optical Coherence Tomography for Automatic Retinal Imaging of Freestanding Subjects

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Current clinical optical coherence tomography (OCT) systems require stabilization of patient heads, usually with a chin and head rest, to reduce motion artifacts in the images. This limits the use of these OCT systems for those who cannot be stabilized in this way, such as unconscious, bedbound, posturally-limited, and very young patients. Using a robot-mounted retinal OCT scanner with face and eye tracking capabilities, we demonstrate high quality OCT imaging of freestanding subjects’ eyes. Our automatic OCT system consisted of a custom retinal scanner mounted on a 6 degree-of-freedom robot arm, a custom 100 kHz swept-source OCT engine with a motorized reference arm, and two fixed face tracking RGB-D cameras. The retinal scanner had a 100 mm working distance for subject comfort, a 16-degree retinal field of view, and a fast steering mirror (FSM) at the retinal conjugate plane for pupil pivot aiming. An inline pupil camera shared the OCT objective to provide lateral pupil tracking via the FSM whereas two offset pupil camera formed stereo pairs for axial pupil tracking via the motorized reference arm. The face tracking cameras detected facial landmarks using OpenFace 2.0 to
guide alignment until the pupil entered the scanner’s tracking field of view. Pupil tracking, face tracking, and robot control operated at 350 Hz, 30 Hz, and 125 Hz, respectively. We evaluated the system by imaging a model eye as well as 6 human subjects consented under an IRB-approved protocol. We corrected residual axial motion through registration of adjacent B-scans. Model eye imaging showed tracking bandwidth at up to 5.6 Hz laterally and 6.7 Hz axially as well as accuracy of 36.6 μm laterally and 63.6 μm axially. Human imaging yielded OCT volumes of the fovea that were suitable for retinal evaluation in all subjects.

**POSTER 24**

**UV-Induced ENTPD1 expression on immunosuppressive memory T cells in human cutaneous squamous cell carcinoma**

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Ultraviolet (UV) radiation and immunosuppression are two major risk factors for cutaneous squamous cell carcinoma (cSCC) and previous studies have shown a role for immunosuppressive regulatory T cells in the pathogenesis of these tumors. Our recent work has demonstrated that purinergic signaling plays a previously unrecognized role in DNA damage repair (DDR) and we hypothesized that dysregulation of purinergic signaling in the tumor microenvironment may lead to carcinogenesis due to failure of DDR. In order to investigate whether immunosuppressive tumor-associated T cells functioned to suppress DDR via purinergic signaling, we examined the expression ENTPD1 (CD39) within human cSCCs. ENTPD1 is an endonucleotidase that catalyzes the conversion of extracellular ATP to ADP, ultimately leading to elevated extracellular AMP and adenosine (ADO) levels. We found that ENTPD1 expression is significantly increased on Tregs within human cSCC when compared to T cells isolated from blood or non-lesional skin (p<0.05). Accordingly, the concentrations of extracellular ADP, AMP, and ADO are increased in tumors when compared to normal skin (p<0.05). We find that increased ADO concentrations downregulate expression of a nucleosomal adaptor protein (NAP), an important component of the DDR pathway. Using a murine IL27 receptor KO model, we show that UV-induced ENTPD1 expression is IL27-dependent and IL27 expression blocks UV-induced DNA damage repair in an in vitro keratinocyte model. In a mouse model of UV-induced cSCCs, inhibition of ENTPD1 with POM1 resulted in early reduction of tumor growth. Interestingly, ENTPD1 expression is significantly higher in human cSCCs that metastasize compared to those that are non-metastatic (p<0.01). Together, these data suggest a role for IL27-mediated increased ENTPD1 expression on regulatory T cells within cSCCs that acts to mitigate effective DDR to promote carcinogenesis and metastasis. This serves to further elucidate the role of the immune system in regulating carcinogenesis and provides several potential targets for therapeutic advancements.
POSTER 25

The SANDMAN Study: Sleep Apnea, Neuroinflammation, & Cognitive Dysfunction Manifesting After Non-cardiac surgery

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Up to 40% of older patients will develop postoperative cognitive dysfunction (POCD), a syndrome of thinking/memory deficits that occurs 1-12 months after surgery and is associated with decreased quality of life, long-term cognitive decline, and increased mortality. One possible risk factor for POCD is obstructive sleep apnea (OSA), a frequently undiagnosed disorder characterized by repetitive interruptions in breathing during sleep. OSA is prevalent in older surgical patients and can be diagnosed with home sleep apnea tests (HSAT), which estimate the apnea-hypopnea index (AHI). Increased AHI (ie, OSA severity) has been associated with long-term cognitive decline and postoperative delirium. Yet, no study has examined the role of OSA in POCD. Neuroinflammation, which is hypothesized to underlie POCD, might be increased in OSA patients, since OSA is associated with peripheral inflammation. In SANDMAN, we are determining the extent to which OSA severity is associated with POCD and neuroinflammation. SANDMAN is a sub-study of INTUIT, in which 200 patients age ≥60 undergoing major non-cardiac surgery undergo blood and cerebrospinal fluid (CSF) sampling and cognitive testing before, and 24 hrs and 6 wks after surgery. CSF cytokines (IL-8, IL-6, MCP-1, and G-CSF) will be measured with multiplex ELISA assays. In SANDMAN, 80 INTUIT patients will also complete preoperative HSAT to diagnose OSA (AHI>5). The association of AHI with postoperative cognition and CSF cytokines will be assessed via multivariable regression models. As of 10/1/2019, 51 SANDMAN patients have completed HSAT (mean AHI=11; SD 15) with 61% positive for OSA, including 18% with moderate OSA (AHI 15-29.9) and 12% with severe OSA (AHI >30). SANDMAN is an ongoing study assessing the relationship between OSA, neuroinflammation and POCD severity. Our findings could guide intervention strategies to prevent POCD, including preoperative treatment of OSA.

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POSTER 26

Comparative behavioral and task fMRI in Focal Dystonia during increasingly complex motor task

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Dystonia is brain disorder which causes involuntary twisting movements. Writer’s cramp (WC) is a focal hand dystonia which occurs selectively during the task of writing and suggests a problem with the brain’s ability to accurately access motor skill programs. Development of long-lasting treatments is contingent on understanding the relationship of dystonia circuit abnormalities to disease symptoms. Task-based fMRI studies in WC subjects show decreased striatal BOLD activity. But much less is known about how abnormal task-based fMRI activity relates to clinical measures of dystonia. The goal of this study was to evaluate the relationship between clinical features of dystonia and changes in BOLD activity in brain regions known to play a role in dystonia. Methods: 8WC and 8HV were clinically phenotyped using automated writing measures. The automated measures were used to categorize WC subjects into mild or moderate symptom severity. Subjects then underwent structural and functional imaging using MRI. During fMRI runs, subjects performed 3 motor tasks of increasing motor complexity in a block design: 1) finger flexion-extension 2) 4 element sequence tapping task and 3)
sentence writing. All statistical analyses was performed in FSL software. Results: After writing task, WC subjects differentiate into mild and moderate subsets outside the fMRI. Fmri of HV subjects demonstrates increase BOLD activity in left striatum during all 3 motor tasks. In contrast, WC subjects show reduction in striatal activity during finger flexion-extension, and writing. Within the WC subsets, there is decline in BOLD activity in the striatum in association with dystonia clinical outcome severity during all 3 motor tasks, with moderate subtype showing greater decline in striatal BOLD activity compared to mild subtype. Conclusion: Our study demonstrates that clinical measures of dystonia correlate with striatal brain activity in a dose-dependent manner. This extends prior work by demonstrating a relationship between striatal activity and clinical disease severity.

POSTER 27

Development of a Duke Pediatric and Congenital Heart Center Biorepository

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Background
Pediatric cardiovascular disease is often heritable and investigations into the genetic causes of congenital heart disease have yielded insights critical for diagnosis, treatment and prognosis of these diseases. The Duke Pediatric and Congenital Heart Center provides a rich collaborative environment for coupling deep clinical phenotyping of children, adults and their families with genetic, cellular and biospecimen-based research if a comprehensive program can be established. This requires access to well-annotated, ethically consented biospecimens which has the potential to accelerate the pace of translational research through immediate availability of biospecimens that otherwise would take many years to accumulate.

Objective
To build a Duke Pediatric and Congenital Heart Center Biorepository of blood, surgical tissue and autopsy tissue samples of patients and their families to serve as a substrate for collaborative research.

Methods
Following IRB approval, subjects were recruited from Duke University Hospitals with inclusion criteria comprising those who have been evaluated for, or diagnosed with, a sudden cardiac death-predisposing disease, congenital structural heart defects, post-mortem subjects who have died of a suspected sudden cardiac death, or subjects undergoing medical and surgical interventions. Infants, children and adults as well as clinically affected and unaffected parents and family members were included. The exclusion criteria comprised subjects unable or unwilling to give informed consent due to no legal guardian or parent or, those who have declined the review and release of their genetic information for research. Samples of whole blood, surgical waste, or autopsy tissues were collected. Whole blood was aliquoted into PAX gene DNA and RNA tubes for storage of genomic DNA and serum DNA/RNA, respectively. Tissue was frozen on liquid nitrogen and stored at -80C. Detailed demographic and clinical data, including cardiac evaluation and genetic testing, was abstracted. Subject recruitment was registered in Duke OnCore. Samples were de-identified and coded before registration in Duke LabVantage. Samples were paired with detailed clinical information entered in Duke RedCap.

Results
From 12/03/18 to 09/17/19 a total of 68 subjects were recruited and enrolled. 46 blood samples and 2 autopsy tissues were collected. Among the 68 subjects, 29 were diagnosed with congenital arrhythmia syndromes. These include ventricular tachycardia (6, 20.7%), LQTS (6, 20.7%), AV block (4, 13.8%) and SVT (2, 6.9%). Of the 11 patients with cardiomyopathy, left ventricular hypertrophy (4, 36.4%) and ARVC (3, 27.3%) was the predominant type. Congenital/structural heart diseases such as bi-leaflet mitral valve prolapse (3, 42.9%) and hypoplastic left heart syndrome (2, 28.6%) was prevalent. All the 28 probands (100%) remained genotype negative following routine genetic panel testing for the appropriate diagnosis. Among these genotype-negative individuals there were 11 families, 3 trios and 14 probands.

Conclusion
As biobanks become mainstream sources of research material, the Duke Pediatric and Congenital Heart Center Biorepository will be an essential platform to promote multi-disciplinary research in heritable causes of heart disease. The identification of over 2 dozen individuals with congenital heart disease, yet who are negative for variants using established clinical testing provides a substrate for pilot studies using expansive genetic studies for discovery.
POSTER 28

Characterizing the Phenotype of Glycogen Storage Disease Type IX (gamma): A Platform for Designing Liver-Directed AAV Gene Therapy

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Glycogen storage disease type IX (GSD IX) is one of the most common forms of glycogen storage disorders, accounting for 25% of cases with an estimated frequency of 1 in 100,000 patients. GSD IX is a rare, monogenic, metabolic disorder where a mutation in a gene encoding the phosphorylase kinase (Phk) enzyme leads to liver disease. While symptoms generally improve with age, some patients have symptoms that persist and progresses to liver fibrosis, cirrhosis, liver failure and cancer. These patients have a mutation specifically in the (gamma) subunit of Phk, a disease subtype known as GSD IX (gamma). Despite the life-threatening severity of GSD IX (gamma), there has been no research into developing treatments. Therefore, the purpose of this project is to design and optimize a therapy for the treatment of GSD IX (gamma). Prior to treatment design, we need biological models that reflect our patient phenotype. Our lab is characterizing the first mouse model for GSD IX (gamma). Preliminary results already show that our KO mice reflect GSD IX patient phenotype – KO mice have higher blood liver enzymes, liver glycogen content, and liver size relative to heterozygous and wild type controls. With a biological model in place, we will start designing and producing an optimized AAV gene therapy. By designing and optimizing a liver-directed AAV gene therapy and testing this therapy in our mouse model, this project has the potential to provide a treatment for patients with GSD IX (gamma) and to inform the treatment of other monogenic, liver diseases.

POSTER 29

Novel Gwt1 inhibitor, APX2104, protects against Invasive Aspergillosis in Neutropenic Mouse model.

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\textit{A. fumigatus} is the leading agent in invasive aspergillosis (IA), a lethal pulmonary infection among immunocompromised patients worldwide. The most effective therapies for IA include triazole, echinocandin, and ambisomal therapies. Concerns about toxicity and resistance to these antifungal therapies have been globally reported, so new, safe, and effective therapeutics are imperative. We assessed the \textit{in vitro} and \textit{in vivo} efficacy of a gwt1 inhibitor, APX2104, with various strains of \textit{A. fumigatus}. APX2041, the active-drug of APX2104, had over a 16-fold lower minimum effective concentration (MEC) value \textit{in vitro} when compared to voriconazole, caspofungin, and ambiosome treatments against various \textit{A. fumigatus} strains, including echinocandin- and azole-resistant strains. APX2104 was shown to be non-toxic in immunocompetent mice at a dose of 60 mg/kg once per day (QD) with survival of 4 of 4 (100%). Toxicity related deaths, 3 of 9 (33%), were seen at dosages of 78 mg/kg, so 60 mg/kg became our standard dose for APX2104. In our IA challenge study, mice were immunocompromised with both cyclophosphamide days -2/+3 and cortisone acetate days -1/+6. Immunocompromised mice were infected with 12 mL via aerosolized \textit{A. fumigatus} CEA10 spores at a concentration of 1x10\textsuperscript{9} spores/mL (Day 0). APX2104 treatment started day +1 and ended day +7. Treatment of APX2104 prolonged survival of 13 of 15 (86%) mice, while 6 of 15 (40%) mice survived with no treatment. Consistent with our survival studies, H&E and GMS histological samples also demonstrate that APX2104 treatment decreased aspergillosis burden within the lungs of neutropenic mice, when compared to the non-treated group. Further studies will compare APX2104 to current therapeutics and other resistant strains \textit{in vivo}. Our preliminary findings suggest that APX2104 is a potential therapeutic for IA, and is a plausible solution for antifungal resistance.