Jefferson College of Life Sciences, Office of Postdoctoral Affairs, and Jefferson Postdoctoral Association

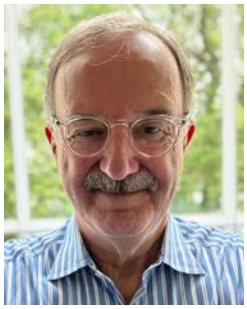
PRESENT

SEVENTEENTH POSTDOCTORAL RESEARCH SYMPOSIUM

SEPTEMBER 21, 2023

Thomas Jefferson University

KEYNOTE SPEAKER



Garret FitzGerald, MD, FRS

Robert L. McNeil, Jr., Professor in Translational Medicine and Therapeutics
Associate Dean for Translational Research
Director, Institute for Translational Medicine and Therapeutics
Perelman School of Medicine
University of Pennsylvania
Philadelphia, PA

Garret FitzGerald, MD, FRS, is the McNeil Professor in Translational Medicine and Therapeutics at the University of Pennsylvania in Philadelphia, where he directs the Institute for Translational Medicine and Therapeutics. Previously, he chaired the Department of Systems Pharmacology and Translational Therapeutics for more than 20 years.

His research has been characterized by an integrative approach to elucidating the mechanisms of drug action, drawing on work in cells, model organisms and humans. His work contributed fundamentally to the development of low-dose aspirin for cardioprotection. FitzGerald's group was the first to predict and then mechanistically explain the cardiovascular hazard from NSAIDs. He has also discovered many products of lipid peroxidation and established their utility as indices of oxidant stress in vivo. His laboratory was the first to discover a molecular clock in the cardiovascular system and has studied the importance of peripheral clocks in aging and in the regulation of cardiovascular and metabolic function.

FitzGerald has received the Boyle, Coakley, Harvey and St. Patrick's Day medals, the Lucian, Scheele, Spector and Hunter Awards and the Cameron, Taylor, Herz, Lefoulan Delalande, and Schottenstein Prizes. He is a member of the National Academy of Medicine, an honorary member of the Royal Irish Academy and the UK Academy of Medicine, a member of the Leopoldina and of the Accademia dei Lincei, a Fellow of the American Academy of the Arts and Sciences and of the Royal Society. He holds honorary degrees from UCD and RCSI in Dublin, Frankfurt, Edinburgh and King's College, London.

TABLE OF CONTENTS

ACKNOWLEDGEMENTS

The Jefferson Postdoctoral Research Symposium (PRS) is a combined effort of many people. The 2023 PRS Organizing Committee would like to thank:

- Lisa Kozlowski, PhD, Associate Dean, JCLS, for her twenty years of support, concern, and advocacy for Jefferson postdoctoral fellows
- Gerald B. Grunwald, PhD, Dean, JCLS, for his continued support of this event and all postdoctoral events and training at Jefferson
- Caitlyn Cardetti, PhD, Arijita Ghosh, PhD, Francesco De Pascali, PhD, Elham Javed, PhD, Arun Kumar Jannu, PhD, and Piyush Mishra, PhD, for their contribution to the overall PRS planning
- Dawn Berkbigler, PMP, BSW, for her administrative and project management skills
- Francesco De Pascali, PhD, and Elham Javed, PhD, for their contribution as oral presentation session moderators
- Carol Beck, PhD, Botond Igyarto, PhD, Caitlyn Cardetti, PhD, and Arijita Ghosh, PhD, for selecting the oral presentations
- Pamela Walter, MFA, Jefferson Office of Professional Writing, Publishing, and Communication, for coaching all postdoctoral participants on their presentation skills
- John Eisenbrey, PhD, Ulhas Naik, PhD, Francesco De Pascali, PhD, Arijita Ghosh, PhD, and Lisa Kozlowski, PhD, for selecting the Distinguished Mentor Award winner
- Our faculty judges for so willingly giving their time and constructive feedback
- The mentors, students, and staff who support the postdocs every day

17TH POSTDOCTORAL RESEARCH SYMPOSIUM

Thursday, September 21, 2023

PROGRAM AGENDA

Eakins Lounge, Jefferson Alumni Hall (JAH)

9:30-10:45	Poster Set-Up
11:00-12:00	Research Lightning Presentations
12:00-12:30	Lunch Break
12:30-2:00	Poster Presentations and Judging
2:00-3:30	Research In-Depth Presentations
3:30-4:00	Refreshment Break
4:00-5:00	**KEYNOTE ADDRESS:** ***"From Aspirin to Chronobiology | Reflections on Patience and Time"***

Garret FitzGerald, MD, FRS
Robert L. McNeil, Jr., Professor in Translational Medicine and Therapeutics
Perelman School of Medicine, University of Pennsylvania

5:00-5:30 Awards Ceremony

DISTINGUISHED MENTOR AWARD:

Joseph Tracy, PhD, ABPP/CN, *Professor, Department of Neurology*

Presented by: Lisa Kozlowski, PhD, Associate Dean, JCLS

POSTDOC PRESENTATION AWARDS

Presented by: Lisa Kozlowski, PhD, Associate Dean, JCLS, and
Caitlyn Cardetti, PhD, and Arijita Ghosh, PhD, 2023 PRS Organizing Committee Co-Chairs

5:30-6:00 Reception

2023 POSTDOCTORAL RESEARCH SYMPOSIUM ORGANIZING COMMITTEE

Caitlyn Cardetti, PhD
Co-Chair

Arijita Ghosh, PhD
Co-Chair

Dawn Berkbigler, PMP, BSW
Francesco De Pascali, PhD
Arun Kumar Jannu, PhD
Elham Javed, PhD
Lisa Kozlowski, PhD
Piyush Mishra, PhD

JEFFERSON POSTDOCTORAL ASSOCIATION

Jefferson Postdoctoral Association's (JPA) ultimate goal is to provide postdoctoral fellows with support to learn about the different professional paths that may fit their interests through a series of professional scientific training during the year in addition to creating friendly networking opportunities through multiple social events.

Our Academic Activities

- Postdoc Scientific Editing and Reviewing Team (PSERT)
- Postdoctoral Fellowship Application Program (PFAP)
- Technical Skills Seminar Series (TSSS)
- President's Talk (annual lecture by former JPA president)
- Postdoctoral Research Symposium (PRS)

Our Social Events

- National Postdoc Appreciation Week (NPAW) events
- Fall Bash
- Cultural festival celebrations
- Monthly social events

To continue improving the postdoctoral experience, we need your ideas, involvement and support! JPA offers opportunities to improve your professional development skill sets:

- **Leadership**
- **Communication**
- **Time management**
- **Event planning**
- **Marketing**
- **Budgeting**
- **Teamwork**
- **Networking and making valuable contacts**

For more information and to be part of the community, please contact **jpa@jefferson.edu**.

2023 DISTINGUISHED MENTOR AWARD NOMINEES

James S. Harrop, MD, MSHQS, FACS
Professor, Depts of Neurological and Orthopedic Surgery
Chief, Division of Spine and Peripheral Nerve Surgery
Director, Enterprise Neuroscience Quality and Safety
Professor, College of Population Health

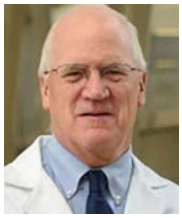
Erica Middleton, PhD
Institute Scientist
Research Department
Moss Rehabilitation Research Institute

Anna Pluciennik, PhD
Assistant Professor
Department of Biochemistry and Molecular Biology

Holly Ramage, PhD
Assistant Professor
Department of Microbiology and Immunology

Amit Srivastava, PhD
Assistant Professor
Department of Medicine
Cardeza Foundation for Hematologic Research

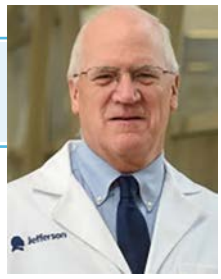
Jianxin Sun, PhD
Professor, Department of Medicine, Division of Cardiology
Associate Director, Center for Translational Medicine
Director, Vascular Biology and Therapeutics Program



Joseph Tracy, PhD, ABPP/CN
Professor, Department of Neurology
Director, Neuropsychology Division
Director, Cognitive Neuroscience & Brain Imaging Laboratory

Mudit Tyagi, PhD
Associate Professor
Center for Translational Medicine

2023 DISTINGUISHED MENTOR AWARD WINNER
Joseph Tracy, PhD, ABPP/CN



The Jefferson Postdoctoral Association and the Office of Postdoctoral Affairs established the Distinguished Mentor Award (DMA) to recognize the commitment and effort of Jefferson faculty members to the mentorship of postdoctoral fellows. The DMA recognizes faculty who stand out for guiding their postdoctoral fellows, listening to their goals and helping them to secure the milestones to reach those goals. This year's winner is Joseph Tracy, PhD, ABPP/CN, from the Department of Neurology, where he is Professor, Director of the Neuropsychology Division, and Director of the Cognitive Neuroscience and Brain Imaging Laboratory.

He received a BA in Psychology from Bowdoin College in Maine. He went on to receive an MA in Developmental Psychology from Columbia University and a PhD in Clinical Psychology from the New School for Social Research, both in New York City. He was a postdoctoral fellow and research associate at Rutgers University. He has held faculty appointments, including adjunct positions, at the Medical College of Pennsylvania Hahnemann University, Drexel University, LaSalle University and Rutgers University. He moved to Jefferson as a Clinical Associate Professor of Neurology and Radiology and is now a full professor in those departments. His research focuses on functional and structural brain connectivity in epilepsy as measured by resting state functional magnetic resonance imaging (rsfMRI), task-based functional magnetic resonance imaging (tfMRI), diffusion-weighted imaging (DWI), positron emission tomography (PET), and high-resolution anatomical MRI.

His current postdocs nominated him for this award. One nominator commented that "I have experienced unparalleled mentorship that has profoundly impacted my personal and professional growth." His deep understanding of the field allows him to provide "insights and guidance that have been invaluable in shaping research ideas." His nominator appreciated that he "provides clear and concise expectations" and that he has an "open-door policy" where he "actively listens and empathizes, showing genuine interest in my overall well-being." Tracy "fosters an inclusive lab environment where diversity is celebrated and all voices are valued and respected." "He is a passionate advocate for postdoctoral researchers." "He strikes the perfect balance between providing guidance and allowing me the freedom to develop independence in my research pursuits," says a nominator. Tracy "genuinely cares about his mentees' holistic development." Tracy also has an impressive list of former postdoctoral fellows who have gone on to a range of career paths. For all of these reasons, Dr. Joseph Tracy was chosen as this year's recipient of the DMA.

Research Lightning Presentations

EAKINS LOUNGE, JAH | 11:00AM–12:00PM

Moderator: Elham Javed, PhD

11:00 - 11:05	Lisa Kozlowski	Opening Remarks
11:05 - 11:13	Marilen Federico	Insight into Glycogen Synthase Kinase 3 Beta Localization within the Heart: Role on Ischemia-Reperfusion Injury
11:13 – 11:21	Prottoy Hassan	Stabilization of the ER-mitochondrial contacts by a synthetic interorganellar linker protects from NAFLD-induced mitochondrial permeability transition
11:21 - 11:29	William Lee	Molecular Basis for Maternal Inheritance of Human Mitochondrial DNA
11:29 - 11:37	Brian Montoya	When specific antibodies are absent, CD8+ T-cells induced by mRNA-LNP vaccines protect mice from lethal SARS-CoV-2 infection
11:37 - 11:45	Amy Shaver	Enzalutamide vs Abiraterone in Prostate Cancer Patients With and Without Type 2 Diabetes Mellitus
11:45 - 11:53	Qirui Zhang	Individual, Atypical Resting-stage Networks Contribute to Cognitive Reorganization in Temporal Lobe Epilepsy
11:53 - 12:00	Elham Javed	Closing Remarks

10 Insight into Glycogen Synthase Kinase 3 Beta Localization within the Heart: Role on Ischemia-Reperfusion Injury

Federico M[1], Tsai HY[1], Hurst S[2], Barraque F[1], Sheu SS[1,2]

[1]Center for Translational Medicine, Department of Medicine, Thomas Jefferson University, Philadelphia, PA, [2]Mitocare, Department of Pathology, Anatomy & Cell Biology, Thomas Jefferson University, Philadelphia, PA

Abstract: The heart requires ATP for every beating, which is mainly provided by the mitochondria through oxidative phosphorylation. During myocardial infarction (MI), the lack of oxygen promotes cell damage and apoptosis through the opening of the mitochondrial permeability transition pore (MPTP). Glycogen synthase kinase 3 beta (GSK3ß) is a cytosolic serine-threonine kinase, which has been shown to be upregulated under ischemia-reperfusion (I/R) modulating the MPTP. However, the role of mitochondrial GSK3ß (mtGSK3ß) has not been studied yet and could significate an alternative treatment of MI. We hypothesized that a small subset of GSK3ß is truncated and translocated to the mitochondrial matrix during I/R, which might modulate MPTP opening. To test our hypothesis, we studied GSK3ß expression in mitochondrial fractions isolated from differential centrifugation. We found GSK3ß present in purified mitochondria (Pmito) truncated at the C-terminal side. To evaluate if mtGSK3ß is involved in I/R injury, we subjected hearts to an I/R protocol. We found GSK3ß is being truncated and its expression was increased in Pmito from I/R-hearts compared to normoxia-hearts (controls). Using a GSK3ß inhibitor, SB216763 (SB21), and the Ca2+ die, we studied the role of mtGSK3ß on the MPTP regulation. MPTP Ca2+-sensitivity was reduced in crude mitochondria fraction vs Pmito, independently of SB21 presence. This data suggests that mtGSK3ß does not sensitize the MPTP opening at basal conditions. Since GSK3ß can be activated and inhibited by phosphorylation at T390 (pT390) and S9 (pS9) sites, respectively, we measure it on mtGSK3ß. We found pT390 is not present in Pmito likely missing during truncation, while pS9 is in low amount. All the data together showed that a small subset of GSK3ß is truncated and translocated within the mitochondrial matrix. Until now, we could not connect mtGSK3ß activity to the MPTP opening. Further studies will be carried out to test if the mtGSK3ß is active inside the mitochondria and what is the role of the enzyme on ischemic hearts and mitochondrial metabolism.

11 Stabilization of the ER-mitochondrial contacts by a synthetic interorganellar linker protects from NAFLD-induced mitochondrial permeability transition

Hasan P[1], Ghosh A[1], Mishra P[1], Santose JH[2], Hajnóczky G[1]

[1]MitoCare Center, Department of Pathology and Genomic Medicine, Thomas Jefferson University, Philadelphia, PA 19107, [2]Mechanistic Toxicology Branch (MTB), Division of Translational Toxicology (DTT), NIEHS/NIH, Research Triangle Park, NC 27709

NAFLD (Non-Alcoholic Fatty Liver Disease) is the most common chronic liver disease, a multifactorial metabolic syndrome with limited therapeutic cure, it demands better understanding. Mitochondria and endoplasmic reticulum (ER) collaborate in lipid metabolism, utilizing their close contacts (ERMC). We hypothesized that the ERMC are altered in NAFLD, and their stabilization with a synthetic interorganellar linker might decrease the NAFLD-induced hepatic injury. We used 60% High-Fat and choline-deficient diet (HFD) to induce NAFLD in mice. To stabilize ERMC a synthetic ERMC-linker was delivered in AAV8 specifically targets hepatocytes through tail-vein injection, and as a control, empty AAV8 was injected. After 3 weeks of HFD, the livers were harvested and mitochondria were isolated. On HFD, the liver weight to body weight showed 30% increase and the liver tissue displayed 40-50% increase in lipid content by histopathology. These parameters were unaltered by the linker. The livers from HFD also showed less close ERMC (0-20nm gapwidth) than that of regular diet by transmission electron microscopy. With the isolated mitochondria, a fluorometric Ca2+ clearance assay was done to evaluate Ca2+ overload and permeability transition induction that commonly mediates hepatocyte injury. Mitochondrial Ca2+ uptake was energized by malate-pyruvate and was isolated from other Ca2+ transport mechanisms by inhibitors of SERCA (thapsigargain) and NCLX (CGP37157). Repetitive Ca2+ boluses, were initially cleared but eventually, mitochondria failed to take up added Ca2+ and released all their Ca2+ content. The later was prevented by cyclosporin A, an inhibitor of the mitochondrial permeability transition. We found that in HFD mitochondria the Ca2+ release occurred earlier than in regular diet mitochondria. Furthermore, ERMC-linker expression in HFD effectively delayed the mitochondrial Ca2+ release. HFD model of NAFLD shows ER-mitochondrial physical uncoupling and tendency to mitochondrial permeability transition, which is reversed by reinforcement of ERMC via a synthetic linker.

17 Molecular Basis for Maternal Inheritance of Human Mitochondrial DNA

William Lee[1†], Angelica Zamudio-Ochoa[1†], Gina Buchel[1†], Petar Podlesniy[2], Nuria Marti Gutierrez[3], Margalida Puigros[2], Anna Calderon2, Hsin-Yao Tang[4], Li Li[5], Aleksei Mikhalchenko[3], Amy Koski[3], Ramon Trullas[2], Shoukhrat Mitalipov[3], and Dmitry Temiakov[1]

[1]Department of Biochemistry and Molecular Biology, Thomas Jefferson University, Philadelphia, PA, [2]Neurobiology Unit, Institut d'Investigacions Biomèdiques de Barcelona (IIBB-CSIC-IDIBAPS) and Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED), Barcelona, Spain, [3]Center for Embryonic Cell and Gene Therapy, Oregon Health & Science University, Portland, OR, [4]The Wistar Institute, Philadelphia, PA, [5]Department of Pathology, Thomas Jefferson University, Philadelphia, PA.

[†]These authors contributed equally to the abstract.

Uniparental inheritance of mitochondrial DNA (mtDNA) is an evolutionary trait found in nearly all eukaryotes. In many species, including humans, the sperm mitochondria are introduced to the oocyte during fertilization. The mechanisms hypothesized to prevent paternal mtDNA transmission include ubiquitination of the sperm mitochondria and mitophagy. However, the causative mechanisms of paternal mtDNA elimination have not been defined. We found that mitochondria in human spermatozoa are devoid of mtDNA and lack mitochondrial transcription factor A (TFAM), the major nucleoid protein required to protect, maintain, and transcribe mtDNA. During spermatogenesis, sperm cells express an isoform of TFAM, which retains the mitochondrial pre-sequence, ordinarily removed upon mitochondrial import. Phosphorylation of this pre-sequence prevents mitochondrial import and directs TFAM to the spermatozoon nucleus. TFAM re-localization from the mitochondria of spermatogonia to the spermatozoa nucleus directly correlates with the elimination of mitochondrial DNA, thereby explaining maternal inheritance in this species.

19 When specific antibodies are absent, CD8+ T-cells induced by mRNA-LNP vaccines protect mice from lethal SARS-CoV-2 infection

Montoya B[1], Melo-Silva C[1], Tang L[1], Kafle S[1], Lidskiy P[2], Bajusz C[3], Vadovics M[3], Chatterjee D[4], Scher G[1], Benitez J[1], Lin P[5], Baric R[6], Andino R[2], Pardi N[3], Sigal L[1]

[1]Department of Microbiology and Immunology, Thomas Jefferson University, Philadelphia, PA, [2]Department of Microbiology and Immunology, University of California, San Francisco, CA, [3]Department of Medicine, University of Pennsylvania, Philadelphia, PA, [4]Department of Neurology, Thomas Jefferson University, Philadelphia, PA, [5]Acuitas Therapeutics, Vancouver, BC, [6]Department of Microbiology and Immunology, University of North Carolina at Chapel Hill, Chapel Hill, NC

The role of CD8+ T-cells in SARS-CoV-2 pathogenesis or in vaccine-induced protection from lethal COVID-19 is unknown. Using mouse-adapted SARS-CoV-2 (MA30) in C57BL/6 mice, we show that CD8+ T-cells are unnecessary for the intrinsic resistance of females or the susceptibility of males to lethal SARS-CoV-2 infection. We also show that mice are protected from SARS-CoV-2 lethality and weight loss when vaccinated with two-proline stabilized full-length SARS-CoV-2 Spike (S-2P) mRNA-LNP vaccines, which induced antibodies and also CD8+ T-cells to the epitope VNFNFNGL, while mice vaccinated with mRNA-LNPs encoding only VNFNFNGL are protected from lethality but not from weight loss. CD8+ T-cell depletion ablates protection in VNFNFNGL but not in S-2P mRNA-LNP vaccinated mice, indicating that vaccine-induced CD8+ T-cells are dispensable when protective antibodies are present but are essential in their absence. Thus vaccine-induced CD8+ T-cells may be critical to protect against SARS-CoV-2 variants that mutate their protective antibody epitopes.

24 Enzalutamide vs Abiraterone in Prostate Cancer Patients With and Without Type 2 Diabetes Mellitus

Amy L. Shaver[1], Nikita Nikita[1], Krupa Gandhi[3], Swapnil Sharma[1], Scott W. Keith[3], Christopher C. Yang[4], and Grace Lu-Yao[1,2]

[1]Department of Medical Oncology, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, PA, [2]Sidney Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA, [3]Department of Pharmacology, Physiology, and Cancer Biology, Thomas Jefferson University, Philadelphia, PA, [4]College of Computing and Informatics, Drexel University, Philadelphia, PA

Background: Up to 18% of new cancer patients have Type 2 Diabetes (T2DM). Current guidance offers no clarity on therapy choices for comorbid prostate cancer (PCa)-T2DM patients. Since the PCa-T2DM population is growing and they face unique challenges from adverse events (AEs) requiring acute care utilization (ACU) it is important to ascertain which medication poses a lower AE threat. Methods: Men with primary PCa and T2DM treated with abiraterone (ABI, 2011) or enzalutamide (ENZ, 2012) were identified in the Surveillance, Epidemiology, and End Results (SEER)-Medicare database (1999-2019). Men were excluded with missing date of diagnosis, diagnosed at death, having HMO, or no continuous A & B coverage 12 months before diagnosis as well as 6 months continuous part D before and after treatment or until death. T2DM was identified using a CCI macro. ACU was calculated utilizing the ResDAC definition. Differences in emergency in-patient visits were evaluated with negative binomial models adjusted for demographic, disease, and socioeconomic factors. Results: The population of 11,163 men included 61.8% treated with ABI and 38.2% with ENZ. We identified 3044 (27.3%) men with T2DM, of which, 59.1% were treated with ABI and 40.8% with ENZ. Compared to those without T2DM those with T2DM had more ACU, regardless of medication, with a higher rate in the ABI than ENZ group, see table. Among diabetics, those with complications related to T2DM compared to those without experienced a higher ACU. The adjusted rate of ACU was 43% higher among those treated with ABI compared to ENZ (aIRR 1.43; 95% CI 1.28, 1.61). Overall mortality (15.7% vs 10.1%, p<0.01) and PCa-specific mortality (8.2% vs 5.3%, p<0.01) were worse in those with T2DM treated with ABI compared to ENZ. Conclusion: Outcomes for patients with T2DM are worse than for those without. PCa patients with comorbid T2DM may require a different targeted therapy than non-diabetics. Further study to evaluate comorbidity management in this population is warranted.

29 Individual, Atypical Resting-stage Networks Contribute to Cognitive Reorganization in Temporal Lobe Epilepsy

Qirui Zhang[1], Aaron Struck[2], Ankeeta A.[1], Sam J. Javidi[1], Stacy Hudgins[1], Michael R Sperling[1], Bruce Herman[2], Joseph I. Tracy[1]

[1]Farber Institute for Neuroscience, Department of Neurology, Thomas Jefferson University, Philadelphia, PA, [2]Department of Neurology, University of Wisconsin (Madison), Madison, WI

Rationale: Despite temporal lobe epilepsy (TLE) pathology, a significant subgroup of patients are able to maintain normative cognitive functioning. Here, we identify TLE patients with intact versus impaired cognitive profiles, and interrogate for the presence of both normative and highly individual intrinsic connectivity networks utilizing resting state fMRI. Methods: Sample was comprised of 88 TLE patients (right=52; left=36) and matched healthy controls (HC, n= 91) with fMRI resting state and neuropsychological (Npsych) performance data available on TLE. FMRI data was decomposed using FSL MELODIC independent component analysis yielding 30 substantive components. Based upon dice coefficient we quantified the degree of spatial match to 17 canonical, normative intrinsic connectivity networks (n-ICNs) and classified components for overall strong(r >.2), or poor(r < .15) match group. Strong match group indicated an individual's ICNs can be interpreted by n-ICNs; poor indicates highly individual/non-normative ICN components (i-ICNs). Results: K-means clustering produced two substantive clusters identified as having intact or impaired Npsych profiles. The degree of overall match to the n-ICNs varied by Npsych cluster group, mainly reflected by lower match (lower dice coefficient) in the impaired Npsych group. In particular, the number ICNs, variance explained, ICN GM volume, ICN strength, and network efficiency of strong matches ICNs decreases and these measures in poor match ICNs are increased. We also found these measures can be correlated with Npsych measures in general. In particular, strong match related measures showed a positive contribution, while poor match related measures showed a negative contribution. Conclusions: The level of non-normative, highly individual, but coherent systematic variance was higher in TLE patients with impaired Npsych profiles. We conclude that higher levels of non-normative and highly individual ICNs may be cognitively maladaptive, perhaps involved in epileptogenic signaling and pathology.

Early Discoveries Poster Presentations

EAKINS LOUNGE, JAH | 12:30PM–2:00PM

This section is intended for postdoctoral fellows either new to Jefferson or simply embarking on a new project to participate in PRS in a special way. In contrast to traditionally data-heavy scientific posters oftentimes representing a complete body of work, "Early Discoveries" posters focus on early ideas, hypothesis development and proposed methodology. This section is designed to encourage advancement of new projects and to provide an opportunity to stimulate discussions and receive constructive feedback from the research community at Jefferson.

Stephen Hurst	Development of an Optogenetic local calcium signaling system to model hotspot formation of the mitochondrial calcium uniporter in adult cardiomyocytes
Elham Javed	AKAP-dependent regulation of mitochondria in human airway smooth muscle
Victor Hugo Sanchez-Vazquez	Evaluating the role of the mitochondrial disaggregase protein, ClpB in mitochondrial Ca2+ signaling
Anuradha A Shastri	Metabolic interventions improve the radiation sensitivity of prostate cancer cells by altering their metabolic profile

12 Development of an Optogenetic local calcium signaling system to model hotspot formation of the mitochondrial calcium uniporter in adult cardiomyocytes

Hurst, S[1], Csordas, G[1]

[1]Department of Pathology & Genomic Medicine, Thomas Jefferson University, Philadelphia, PA

Background: Cardiomyocytes require a means to match energetic demand with supply. The current prevailing theory is that during high demand mitochondria utilize Ca2+ released from the SR during contraction stimulate the TCA cycle via Ca2+-responsive enzymes. However, in order to prevent futile cycling of Ca2+ and ATP we observed cardiac mitochondria are subdivided into a calcium intake zone and calcium extrusion zone. The MCU complex is preferentially localized to the intake zone adjacent to the junctional SR and the NCLX is maintained in the extrusion zone distal to junctional SR. In order to identify the Ca2+-dependent molecular mechanisms behind the redistribution of MCU in the inner mitochondrial membrane, we developed a series of optogenetic tethers to simulate the localized environment unique to the cardiomyocyte in a simplified cell system that can be easily manipulated at the genetic level. Using CRISPR-Cas9 we will knock in the tether into the AAVS1 safe harbor site of Cos7 cells, chosen for their flat morphology and elaborate mitochondrial and ER networks. To assemble the plasmid we had the individual components of the tether synthesized and combined them using homology directed cloning. The tether consists of two parts: a recently developed Calcium-permeable Channel Rhodopsin (CapCHR2) fused to the rapamycin-dependent dimerization domain and a fluorescent reporter protein to track localization. The complementary half consists of a mitochondrial outer membrane anchoring domain (AKAP) fused to FKBP and a calcium sensor jRCamP1b. The mitochondria is tethered to the Channel Rhodopsin in the presence of Rapamycin and calcium pulses will be controlled via stimulation with blue (405nm) light. Planned Experiments: 1) Characterization of the tether's trafficking, calcium conductance and rapamycin-dependent dimerization using both wide field fluorescent and super resolution microscopy and 2) Tag and edit the endogenous MCU & EMRE with split GFP/RFP tags to observe the distribution of functional (MCU+EMRE) vs total (MCU) complex +/- optogenetic stimulation.

14 AKAP-dependent regulation of mitochondria in human airway smooth muscle

Javed E[1], Villalba D[1], Valovatsy E[1], Shatzman AP[1], Lee K[1], Yan L[1], and Penn RB[1]

[1]Department of Medicine, Pulmonary and Critical Care Medicine, Center for Translational Medicine, Jane and Leonard Korman Respiratory Institute, Thomas Jefferson University, Philadelphia, PA

A-kinase-anchoring protein (AKAPs) are scaffold proteins that anchor the R-subunits of the cAMP -dependent protein kinase A (PKA) to control the magnitude and localization of cAMP-dependent signaling. Since cAMP/PKA signaling is the principal physiological and therapeutic means of inhibiting pathological airway smooth muscle (ASM) functions, understanding the cellular mechanisms that regulate the magnitude or duration of such signaling has been of intense interest to lung and lung disease research for decades. AKAP regulated PKA signaling affects mitochondrial morphology and essential mitochondrial functions, such as oxidative/phosphorylation and calcium buffering capacity. Previously, we identified AKAP9, AKAP12 (Gravin), AKAP78 (Ezrin), AKAP5, AKAP2 as the most abundantly expressed AKAPs in human ASM. Here, we assessed the role of Gravin, Ezrin, or both on mitochondrial morphology and function in human ASM cells. Preliminary data shows that knock down of either Ezrin, Gravin or both in human ASM cells, had increased mitochondrial -membrane potential and -ROS.

21 Evaluating the role of the mitochondrial disaggregase protein, ClpB in mitochondrial Ca2+ signaling

Sánchez-Vázquez VH[1], Cartes-Saavedra B[1], Cupo R[2], Shorter R[3], and Hajnóczky G[1]

[1]MitoCare Center, Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, PA, [2]National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, [3]Department of Biochemistry & Biophysics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

Mitochondrial protein homeostasis is regulated by chaperones which stabilize the newly synthetized proteins and assist in their folding into mature forms. However, disruption of the chaperone activity compromises mitochondrial function due to accumulation of aberrant proteins. Thus, cells possess protein disaggregases that restore functional form of the aggregated proteins. The Caseinolytic mitochondrial peptidase chaperone subunit B (ClpB) localized to the inner mitochondrial membrane (IMM) solubilizes aggregated proteins of the IMM and of the mitochondrial intermembrane space. The lack of ClpB showed solubility decrease of MICU1/2. MICU1/2 are the main gatekeepers of the mitochondrial Ca2+ uniporter complex that mediates Ca2+ uptake into mitochondria. Hence, we hypothesized that the lack of ClpB could affect mitochondrial Ca2+ signaling. To investigate it, we have studied cytoplasmic and mitochondrial Ca2+ dynamics in human haploid cells HAP I Wild-Type (WT), HAP I ClpB Knockout (KO) and HAP I ClpB rescued (RE) using epifluorescence simultaneous cytoplasmic and mitochondrial matrix Ca2+ imaging. We did not find differences between WT, KO and RE cells in the cytoplasmic Ca2+ rise upon discharge of the endoplasmic reticulum Ca2+ store by thapsigargin (Tg) and during Store Operated Ca2+ entry. However, KO cells showed a larger and more sustained mitochondrial Ca2+ signal induced by Tg as compared to WT and RE cells. Moreover, KO cells displayed a closer coupling of the mitochondrial Ca2+ rise with the cytoplasmic Ca2+ increase, while WT and RE cells showed a delay in the mitochondrial Ca2+ response after cytoplasmic Ca2+ rise. These data suggest that the lack of ClpB affects the gatekeeping governed by MICU1/2. To this end, we checked the level of MICU1/2 proteins. We did not observe changes in the MICU1/2 abundance in KO compared to WT and RE cells. Hence, these findings suggest that the lack of ClpB could impair the MICU1/2's gatekeeping function without changing their abundance.

23 Metabolic interventions improve the radiation sensitivity of prostate cancer cells by altering their metabolic profile

Shastri, A.A.[1], DeAngelis, T.[1], Francois, N.[1], Gomella, L.G.[2], Trabulsi, E.[2], Simone, N.L.[1]

[1]Department of Radiation Oncology, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, PA, [2]Department of Urology, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, PA

Background- Altered metabolism in cancer cells causes radiation (RT) resistance and increases risk of distant metastasis and worse treatment outcome in prostate cancer (PCa) patients. Tumors can metabolically reprogram their microenvironment, with c-myc driven tumors thriving in lipogenic metabolism and akt-driven tumors activating the glycolytic switch. In the present study, we used metabolic interventions (MI) to switch the metabolic profile of PCa tumors and improve sensitivity to treatment. Methods- We used 2 in vitro PCa models to evaluate effect of MI in RT efficacy: c-myc overexpressing Hi-Myc and PTEN knockout SKO cells. To determine if calorie restriction (CR) can switch metabolic profiles, both cell lines were treated with either complete or CR media (30% glucose+ 1% FBS) +/- 8Gy RT. We treated Hi-Myc cells with FASN inhibitor IPI-9119 +/- 8Gy to determine the effect of altering lipogenic metabolism on RT. In an IRB approved clinical trial, PCa patients were enrolled in a trial before definitive surgery to assess the effect of a 25% CR on serum biomarkers. The patients remained on the diet for 2-12 weeks with blood draws at baseline and morning of surgery. Results- Treating Hi-Myc cells with CR reduced cell viability by ~60% and 72% (p=0.001) alone and combined with RT, respectively. Treating SKO with CR showed ~24% and ~67% (p=0.001) decrease in cell viability alone and combined with RT, respectively. Treating Hi-Myc with IPI-9119 reduced viability by ~20% (p=0.01) compared to RT.16 patients were enrolled in the clinical trial. The patients on the dietary intervention showed downregulation of IGF-1R pathway with a decrease in serum levels of insulin, IGF-1 and increase in IGFBP1 (65%, p=0.001). Conclusions- Our data suggest that MI may switch metabolic profiles in both c-myc and akt models to sensitize them to RT. Changes in levels of patient serum biomarkers post-diet indicate that CR is able to alter the host metabolism to downregulate the IGF-1R pathway.

Ankeeta A	Targeted functional and structural measures of language laterality in epilepsy and their impact on other cognitive functions
Lakhikumar Adhikarimayum	DNA dependent protein kinase (DNA-PK) stimulates HIV transcription by promoting RNA polymerase II activity and recruitment of transcription machinery at HIV LTR
Michael H. Alexander	Trametinib treatment causes an increase in disease severity and reduced dermal immune cell infiltration in a mouse model of junctional epidermolysis bullosa
Mayuri Bhatia	Effect of DNA conformational states and accessory factors on FAN1-mediated processing of CAG extrusions
Bridget Curran	Investigating the role of MAP7 in promoting rVRG axon sprouting after cervical spinal cord injury
Arun Kumar Jannu	Myristoylation of the anchoring protein gravin by HDAC11 regulates B2AR localization and signaling
Sam Javidi	Exploring White-Matter Connectivity Underlying Focal to Bilateral Tonic-Clonic Seizures
Mandeep Kaur	Exploring the Impact of Donor-Specific Platelet-Derived Extracellular Vesicles on Endothelial Dysfunction
Melissa Molho	Defining the Role of Powassan Virus in Evading Host Antiviral Immunity
Stepan Nersisyan	Characterization of all small RNAs in and comparisons across cultured megakaryocytes and platelets of healthy individuals and COVID-19 patients
Raghavendra Singh	Synaptic dysfunction is associated with dysregulation of mitochondrial calcium homeostasis in MICU1KO mouse
Casey Stefanski	Metabolic adaptions promoting survival and invasion in drug tolerant melanoma cells
Nopprarat Tongmuang	Inhibiting Endothelial Mammalian Sterile 20-like Kinase 1 Attenuates Acute Lung Injury in Mice
Michael Young	Adaptations to the loss of IP3 receptor-mediated Ca2+ signaling

01 Targeted functional and structural measures of language laterality in epilepsy and their impact on other cognitive functions

A A[1], Zhang Q[1], Javidi S[1], Citro S[1], Sperling M[1], Tracy J[1]

[1]Neurology Department, Thomas Jefferson University, Philadelphia, PA

Rationale: The study aimed to understand the mechanisms underlying language laterality (LL) and its relationship with gray matter (GM) structure and cognitive functions. Key questions addressed were: (1) Does LL change correspond to changes in GM asymmetry? (2) Can targeted LL measures better differentiate temporal lobe epilepsy (TLE) patients from healthy controls (HCs) compared to standard measures? (3) Do LL asymmetries predict asymmetries in other cognitive functions, like memory? Methods: A total of 189 unilateral TLE patients (left=115; right=74) and matched HCs (115) underwent fMRI verb generation (VG) assessment for LL. Laterality indices (LIs: frontal, temporal, parietal) were calculated using the SPM Laterality Toolbox. Targeted LIs (TLIs) were created based on frontal, temporal, and parietal VG activation clusters. Structural laterality indices (SLIs) were derived from GM volume beneath the activation. Comparable fMRI verbal memory TLIs indices were calculated. Functional (TLI, SPM-LIs) and structural (SLIs) metrics were correlated. Discriminant function analysis determined the best TLE/HC discriminators; partial least squares (PLS) analyzed TLIs association with fMRI memory task TLIs. Results: TLIs/SLIs showed stronger functional/structural associations than standard LIs/SLIs, especially in left TLE (LTLE). The best discriminators of LTLE/HC were frontal and temporal TLIs/SLIs, primarily SLIs. Few discriminators were found for right TLE (RTLE), mostly involving SMA TLIs/SLIs. TLIs and SLIs reliably predicted verbal memory laterality, while standard LIs did not. TLI patterns predicted reorganization of cognitive functions, explaining 47% of variance in verbal memory TLIs. Conclusion: Targeted functional and linked-structural LL measures better differentiated TLE from HCs than standard measures. Targeted SLIs were the strongest discriminators. Correlations between TLIs and SLIs differed between groups, indicating sensitivity to TLE pathology. TLI patterns predicted cognitive reorganization, providing insights into LL and cognitive mechanisms in TLE.

02 DNA dependent protein kinase (DNA-PK) stimulates HIV transcription by promoting RNA polymerase II activity and recruitment of transcription machinery at HIV LTR

Lakhikumar Sharma Adhikarimayum and Mudit Tyagi

Center for Translational Medicine, Thomas Jefferson University, Philadelphia, PA

Current HIV therapy (Combination antiretroviral therapy) is able to suppress replication of HIV quite effectively, thereby reducing HIV/AIDS related mortality. Notably, despite of undetectable viremia for several years, the virus resurrects out of latent reservoirs and quickly once cART is interrupted. Thus, the presence of latent or transcriptionally silent HIV provirus is a major hurdle to HIV cure and has renewed interest in understanding the molecular mechanisms that control HIV. We discovered that DNA-dependent protein kinase (DNA-PK) facilitates HIV transcription by directly interacting with RNA polymerase II (RNAP II) complex recruited at HIV LTR promoter. To extend this finding and in our quest to define the molecular mechanisms involved, we evaluate the mechanism through which DNA-PK promotes HIV life cycle. Using different cell types, including peripheral blood mononuclear cells (PBMCs) from HIV-infected patients, we found that DNA-PK stimulates HIV transcription (initiation, pause-release and elongation); thus, augments HIV replication,

and reactivation of latent HIV. It achieves this by increasing phosphorylation of RNAP II C-terminal domain at Serine5 and Serine2, both through direct catalyzation and augmenting the recruitment of the positive transcription elongation factor (P-TEFb) at HIV LTR. Moreover, DNA-PK promotes euchromatin structure establishment at HIV LTR, involving the recruitment of Tripartite motif-containing 28 (TRIM28) and assisting the release of paused RNAP II through TRIM28 phosphorylation. Our study's clinical relevance is evident as DNA-PK inhibition or knockdown severely impairs HIV replication and reactivates latent HIV provirus in PBMCs from infected patients. Thus, supplementing current cART regimens with DNA-PK inhibitors may not only restrict HIV replication and protein production but also target HIV-associated malignancies. This research could pave the way for more effective HIV therapies in the future.

03 Trametinib treatment causes an increase in disease severity and reduced dermal immune cell infiltration in a mouse model of junctional epidermolysis bullosa

Alexander MH[1], Tartaglia G[1], Nyström A[2], Rosenbloom J[1] and South AP[1]

[1]Department of Dermatology and Cutaneous Biology, Thomas Jefferson University, Philadelphia, PA, [2]Department of Dermatology, University of Freiburg, Freiburg, Germany

Junctional epidermolysis bullosa (JEB) patients experience increased skin fragility due to a pathological deficiency in genes associated with epidermal adhesion, leading to severe blistering, granulated tissue formation and atrophic scarring. Previous work has demonstrated the therapeutic utility of the triterpenoid RTA408 in reducing skin fragility in a LAMC2 mutated JEB mouse model (Lamc2jeb mice). We evaluated the potential of combining RTA408 with trametinib, a MEK inhibitor previously shown to target fibrosis in other mouse models, for reducing disease severity in Lamc2jeb mice. Whilst RTA408 significantly reduced disease severity in monotherapy (P=0.015), trametinib failed to significantly alter severity trending toward an increase in severity and leading to early euthanasia in a proportion of treated animals. To examine if the difference in severity is related to immune cell infiltration, we conducted immunohistochemistry for the immune markers CD3, CD4 and CD45 in treated mouse skin. Following staining, the epidermal and dermal expression of these markers was analyzed using a positive pixel algorithm. Results revealed that while there were no changes in the epidermal expression of these markers for either RTA408 or trametinib, RTA408 did cause an increase in dermal expression of CD4 (P=0.0305) and a decrease in CD3 (P=0.0249). Conversely, trametinib treatment caused a universal reduction in CD3 (P=0.0038), CD4 (P=0.0003) and CD45 (P=0.0038) in the dermis. This broad reduction in immune markers was correlated with a significant reduction in epidermal thickness (P<0.0001) comparing treatment to control. This reduction was not observed in RTA408-treated mice. Together this data suggest that trametinib-induced MEK inhibition causes a reduction in both epidermal proliferation and immune cell infiltration/proliferation, with concurrent acceleration of skin fragility.

04 Effect of DNA conformational states and accessory factors on FAN1-mediated processing of CAG extrusions

Bhatia, M[1], Lakhina, A[1], Phadte, A[1], Pluciennik, A[1]

[1]Department of Biochemistry and Molecular Biology, Thomas Jefferson University, Philadelphia, PA

Huntington's disease (HD) is a neurodegenerative disorder caused by an aberrant expansion of the CAG repeat tract within the huntingtin (HTT) gene, leading to neuronal death primarily in the striatum and the cortex. Genome wide association studies have revealed the existence of genetic modifiers of the age of onset of the disease; these include several genes of the mismatch repair pathway (MSH3, MLH1, PMS1, and PMS2) as well as FAN1, a DNA interstrand cross-link repair gene. Findings in model systems indicate that knockout/knockdown of FAN1 promotes triplet repeat expansion, suggesting that FAN1 helps to maintain genetic stability of triplet repeats. Recent studies have reported that FAN1 can recognize, and process repeat-containing DNA sequences forming various secondary structures. The present study investigates the factors governing the nuclease activity of FAN1. In line with the literature on FAN1 processivity of extrusion-forming repeats on a forked substrate, we observed better processing rates for duplex DNA substrates harboring a (CAG)2 extrusion over the forked substrate. This prompted us to explore whether FAN1 is a sequence- or structure-specific nuclease. Thus, we have evaluated the effect of extrusion size on FAN1 nuclease activity by the varying number of (CAG)n repeats (n = 1 to 13) at lower ionic strength. Under physiological conditions, FAN1 requires accessory factors including PCNA and RFC for extrusion processing (Phadte et al. 2023, PNAS accepted). The PCNA-FAN1 interaction, that we showed using surface plasmon resonance (SPR), is required for this activity. We are further evaluating FAN1-PCNA complex using cryo-EM analysis. Overall, our study provides biochemical evidence for the extrusion size dependence of FAN1 activity and interplay with accessory factors, providing an insight into the FAN1 nuclease at physiological conditions.

08 Investigating the role of MAP7 in promoting rVRG axon sprouting after cervical spinal cord injury

Curran BM[1], Buckhaults KA[1], Cheng L[1], Tymanskyj SR[1], Lepore A[1], Ma L[1]

[1]Department of Neuroscience, Vickie and Jack Farber Institute for Neuroscience, Thomas Jefferson University, Philadelphia, PA

Axon regeneration can be achieved in different ways. While much attention has been focused on re-growth of injured axons, it is recognized that functional recovery can be achieved by axon sprouting or formation of axonal branches from either injured axons or spared axons. The molecular mechanism of axon sprouting is not well understood. Here, we investigate the role of MAP7 in axon sprouting or branch regeneration, because MAP7 is a microtubule-associated protein that is enriched at branch junctions and stabilizes microtubules to prevent branch retraction. Using a rat spinal cord (SC) injury model involving the respiratory function, we assessed whether MAP7 can promote axon sprouting after injury. Specifically, recombinant adeno associated virus-2 (AAV2) was injected unilaterally to express MAP7-EGFP or EGFP alone (as control) in the rostral ventral respiratory group (rVRG) of the medulla of adult female rats. AAV2-mCherry virus was co-injected to label rVRG axons. Four weeks post injection, half of the animals underwent SC hemisection at the cervical level 2 (C2) and in the side contralateral to the injection site. After 4 weeks of recovery, animals were tested for their respiratory function using electromyography recordings of the diaphragm, followed by perfusion for tissue collection. To visualize rVRG axons, cross sections (30µm) were cut from the cervical SC (C1-C5), and imaged by confocal microscopy after antibody staining. Images were then analyzed using Fiji (ImageJ). To automate the analysis, several macros were developed to identify and quantify labeled rVRG axons at the different cervical levels and in different SC regions (gray vs white, ipsilateral vs contralateral). We

performed a systematic analysis of these axonal profiles between four experimental conditions (injury vs non-injury and EGFP vs MAP7-EGFP) to determine the potential correlation of axonal sprouting with changes in respiratory functions. These data will provide the first analysis of MAP7 in promoting axon sprouting/branch regeneration after SC injury in vivo.

13 Myristoylation of the anchoring protein gravin by HDAC11 regulates B2AR localization and signaling

Jannu AK[1], Javed E[1], Robinson EL[2], Valovatsky E[1], Yan L[1], Lee K[1], McKinsey TA[2], Penn RB[1]

[1]Department of Medicine, Center for Translational Medicine, Jane & Leonard Korman Respiratory Institute, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, PA, [2]Department of Medicine, Division of Cardiology, University of Colorado Anschutz Medical Campus, Aurora, CO

The beta 2 adrenoceptor (B2AR) is the prototypical G Protein Coupled Receptor (GPCR). Activation of the B2AR on airway smooth muscle (ASM) causes relaxation of contracted airways, and B2AR agonists (beta-agonists) are used to reverse acute bronchospasm during asthma exacerbations. When activated chronically, the B2AR is desensitized, which limits its therapeutic efficacy. Strategies that avoid or overcome B2AR desensitization therefore represent potential therapies. Key signaling proteins in the B2AR-Gs pathway are protein kinase A (PKA or A kinase), and the scaffolding protein A kinase anchoring protein kinase (AKAP). Our recent findings support the hypothesis that lysine myristoylation of the AKAP gravin promotes the subcellular distribution of the B2AR to plasma membrane lipid rafts. Histone deacetylase (HDAC11) is shown to demyristoylate gravin, causing it (and the B2AR) to distribute outside of lipid rafts. Click chemistry data demonstrates that HDAC 11 inhibition by FT895, a highly specific HDAC11 inhibitor, significantly increases gravin myristoylation in human ASM cells. FT895 treatment of human ASM for 30 min promoted phosphorylation of the PKA substrates VASP and HSP20. Pretreatment with B2AR inverse agonist ICI118551 for 30 min inhibited FT895-stimulated PKA activity, suggesting this activity is B2AR-dependent. Following chronic beta-agonist treatment, FT895-treated human ASM cells retained the ability to stimulate PKA activity, whereas beta-agonist-mediated signaling exhibited desensitization. Functionally, FT895 had an inhibitory effect on PDGF-stimulated migration of HASM cells, comparable to that of ISO. Collectively, our data suggest that HDAC11, via its regulation of gravin myristoylation, is a novel regulator of B2AR localization and signaling, and FT895 represents a novel treatment of adjunct for diseases managed by beta-agonists.

15 Exploring White-Matter Connectivity Underlying Focal to Bilateral Tonic-Clonic Seizures

Javidi S[1], A A[1], He X[2], Zhang Q[1], Kry Y[1], Citro S[1], Sperling M[1], Tracy J[1]

[1]Farber Institute for Neuroscience, Department of Neurology, Thomas Jefferson University, Philadelphia, PA, [2]University of Science and Technology of China, Department of Psychology, Hefei, Anhui, P.R. China

Focal to bilateral tonic-clonic seizures (FBTCS+) is one of the most challenging temporal lobe epilepsy (TLE) subtypes in terms of disease severity and treatment response. Current studies have implicated subcortical-cortical connectivity, and commonly take a regional/nodal approach that is agnostic to abnormalities related to changes in the white matter (WM) that may carry epileptogenic signaling between regions. We take this pathway approach by interrogating the integrity of WM sources indexed by diffusion-tensor-derived WM streamlines (STR). First, we test for FBTCS+ and FBTCS- differences in whole brain network-level graph measures. Second, we focus on individual STRs and examine their association with clinical variables that may be associated with FBTCS+ risk. We acquired T1-weighted and diffusion-weighted HARDI images on 22 FBTCS-, 43 FBTCS+ and 105 matched healthy participants (HP), processed with QSIprep and DSIstudio to obtain STR connectome matrices (AAL atlas, 90 regions of interest). We re-oriented the AAL STR matrices of the right TLE group to match the ictal (.i) and non-ictal (.ni) tracts of the left TLE group. Subsequently, we transformed the connectivity matrix into a 4005x4005 STR connectome matrix and calculated graph metrics (degree, betweenness, eigenvalue centrality, clustering coefficient). We performed ANOVA on individual STR with permutation testing to account for type I error and imbalanced sample sizes. We also reported associations between graph metrics and clinical variables. Our approach yielded important information not just about regions involved in abnormality, but the broader structural circuit expressing that abnormality. Two key findings appeared. TLE demonstrated contrasting SC abnormalities for the ictal and non-ictal amygdala, consistently involving frontal pathways, suggesting even in the absence of FBTCS amygdala-frontal pathways are selectively affected. FBTCS+ findings showed reliable interhemispheric abnormalities pointing to the specific SCs that may support the unique seizure propagation features of this group.

16 Exploring the Impact of Donor-Specific Platelet-Derived Extracellular Vesicles on Endothelial Dysfunction

Kaur M[1], Gupta M[1], Yadav SK[1], Srivastava AK[1]

[1]Department of Medicine, Sidney Kimmel Medical College, Thomas Jefferson University, Cardeza Foundation for Hematologic Research, Philadelphia, PA

Introduction: Traumatic injuries induce endothelial dysfunction, causing organ dysfunction. Platelet transfusion helps maintain barrier integrity, but has limitations (short shelf life, storage lesion, lung injury). Platelets-derived extracellular vesicles (PEVs) are platelet-secreted nanoparticles with reparative abilities, offering an alternative to cell therapy. Our previous findings showed PEVs effectively mitigate vascular permeability. This study explores the therapeutic impact of PEVs from different donors on lung endothelial barrier dysfunctions. Methods: PEVs were isolated from platelet-rich plasma of 5 male and 5 female donors using tangential flow filtration. Comprehensive characterization was performed. Pulmonary endothelial cells (HULEC-5a) were pretreated with PEVs obtained from distinct donors (3.29x109 per reaction). Cells were exposed to thrombin (0.2U/ml, 1 hour). Barrier permeability was evaluated through transendothelial electrical resistance (TEER) measurements, and tight junction protein expression was analyzed by immunostaining. Results: TEM analysis showed uniform, sphere-shaped PEVs with no discernible differences between male and female PEVs. PEVs had a microparticle origin (168.94$\pm$66 nm) and expressed CD41, CD9, and CD63. In vitro findings showed male and female PEVs significantly mitigated thrombin-induced barrier permeability, with female PEVs being more effective. Conclusion: PEVs have potential for addressing trauma-induced endotheliopathy. Our findings reveal sex-related disparities in PEV activity and donor-specific variations in PEV transfusion efficacy.

18 Defining the Role of Powassan Virus in Evading Host Antiviral Immunity

Molho M[1], O'Mara M[1], Blanco-Melo D[2], Johnson J[3], Ramage H[1]

[1]Department of Microbiology and Immunology, Thomas Jefferson University, Philadelphia, PA, [2]Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Center, Seattle, WA, [3]Department of Microbiology, Icahn School of Medicine at Mount Sinai, New York, NY

Flaviviruses are enveloped, positive-strand RNA viruses comprised of several human pathogens accounting for significant morbidity and mortality worldwide. Powassan virus (POWV) is an emerging, neurotropic tick-borne flavivirus endemic in North America. POWV infection is fatal in 10-15% of cases exhibiting neurological symptoms and half of those surviving neurological disease have long-term issues. Currently, there are no specific antiviral treatments nor approved vaccines for POWV, underscoring the importance of deciphering the cellular mechanisms controlling this virus. Flavivirus-host interactions can modulate Type I interferon expression and other antiviral pathways. However, it is unknown if these mechanisms are conserved during POWV infection. We sought to identify POWV proteins that antagonize the expression of Type I interferons and interferon-stimulated genes (ISGs). We co-transfected mammalian cells with each of the ten POWV proteins together with a Firefly luciferase reporter under the control of the IFN-beta or ISRE promoter and stimulated the cells to elicit Type I IFN and ISGs expression. We found that POWV NS5 protein inhibits luciferase expression downstream of the IFN-beta and ISRE promoters, indicating a role in antagonizing Type I IFN signaling. Further, western blot analysis showed that POWV NS5 expression inhibits phosphorylation of TYK2 and STAT1 in response to IFN-beta. In addition, to understand the host response to POWV in the central nervous system, we infected HMC3 cells, a human microglial cell line that is targeted by flaviviruses, and performed a transcriptomic analysis to identify changes in gene expression during infection. We observed significant upregulation of the Type III interferons (IFN-lambda) and several ISGs that have not been previously studied in POWV infection. To complement these studies, we have also used a proteomics approach to identify changes to the host cell proteome during infection. Together, these data will define both virus and host-specific mechanisms controlling POWV infection.

20 Characterization of all small RNAs in and comparisons across cultured megakaryocytes and platelets of healthy individuals and COVID-19 patients

Nersisyan S[1], Montenont E[2], Loher P[1], Middleton EA[2,3], Campbell R[2,4], Bray P[2,5], Rigoutsos I[1]

[1]Computational Medicine Center, Thomas Jefferson University, Philadelphia, PA, [2]University of Utah Molecular Medicine Program, University of Utah, Salt Lake City, UT, [3]Division of Pulmonary Medicine, Department of Internal Medicine, University of Utah, Salt Lake City, UT, [4]Division of General Medicine, Department of Internal Medicine, University of Utah, Salt Lake City, UT, [5]Division of Hematology and Hematologic Malignancies, Department of Internal Medicine, University of Utah, Salt Lake City, UT

Background: The small non-coding RNAs (sncRNAs) in megakaryocytes (MKs) and platelets are not well characterized. Neither is the impact of SARS-CoV-2 infection on the sncRNAs of platelets. Methods: We used deep sequencing to profile sncRNAs from MKs cultured from cord blood-derived CD34+ cells; platelets from healthy donors; and platelets from patients with moderate and severe SARS-CoV-2 infection. We also profiled AGO-bound sncRNAs from the cultured MKs. We used state-of-the-art bioinformatic tools to map the sequencing reads to the human reference sncRNA sequences and for the downstream analysis. Results: We exhaustively characterized the sncRNAs in MKs and platelets and can account for ~95% of all sequenced reads. We found that MKs primarily comprise microRNA isoforms (isomiRs), tRNA-derived fragments (tRFs), rRNA-derived fragments (rRFs), and Y RNA-derived fragments (yRFs) in comparable abundances. The platelets of healthy donors showed a skewed distribution by comparison: 56.7% of all sncRNAs are yRFs, 34.4% are isomiRs, and less than 2.0% are tRFs and rRFs. Most isomiRs in MKs and platelets are either non-canonical, non-templated, or both. The non-canonical isomiRs do not match the miRNA sequence listed in miRBase. The non-templated isomiRs have one or more As, Cs, Gs, or Us added to their 3′ ends. When comparing MKs and platelets from healthy donors, we found numerous isomiRs, tRFs, rRFs, and yRFs showing opposite enrichments or depletions, including molecules from the same parental miRNA arm, tRNA, rRNA, or Y RNA. The sncRNAome of platelets from COVID-19 patients is skewed compared to healthy donors: only 19.8% of all sncRNAs are yRFs, with isomiRs increasing to 63.6%, and tRFs, rRFs more than tripling their presence to 6.1%. Conclusions: The findings show that the sncRNAomes for MKs and platelets are very rich. The findings also suggest complex mechanisms that sort MK sncRNAs into platelets and the possibility of sncRNA uptake by platelets from non-MK cells. SARS-CoV-2 infection acutely changes the relative proportions of sncRNAs in platelets.

25 Synaptic dysfunction is associated with dysregulation of mitochondrial calcium homeostasis in MICU1KO mouse

Raghavendra Singh[1] and György Hajnóczky[1]

[1]Department of Pathology & Genomic Medicine, Thomas Jefferson University, Philadelphia, PA

Mitochondrial clearance of intracellular calcium and ATP production during neuronal stimulation play a crucial role in neuronal health, and modulating Ca2+ dependent synaptic function. MICU1 enables Ca2+ entry into mitochondria through MCU, and Human loss of function mutation of MICU1 is linked to learning difficulties, muscle weakness, and fatigue. In the previous study, we have demonstrated the mitochondrial Ca2+ overload as inducer of cell death in MICU1KO. In the present study we asked, if MICU1 regulation of mitochondrial calcium entry influences the local synaptic intracellular calcium buffering and neurotransmitter-vesicle fusion during synaptic activity. We found WT and KO neurons with similar global cytoplasmic [Ca2+] ([Ca2+]c) responses during electrical stimulation (ES). In KO neurons, mitochondrial matrix [Ca2+] ([Ca2+]m) rise was ensued even at 50nM increase in [Ca2+] c upon low pulse (10-30) field stimulation (20V, 10Hz), and it was tightly coupled to the [Ca2+]c increase. In WT neurons, high pulse (150) field stimulation (40V, 20Hz) was required for a [Ca2+]m rise, and it lagged behind the [Ca2+]c rise. Furthermore, at the sub-optimal field stimulation the presynaptic local [Ca2+]c rise was attenuated by the presence of mitochondria in KO neuron but not in WT. Moreover, synaptic (SV) fusion was suppressed in KO neurons at all the ES parameter used, particularly, the secretory response evoked by repetitive suboptimal ES seemed to be greatly inhibited in KO neurons. Notably, mitochondrial presence suppressed SV fusion immensely only in KO. In addition, blocking recodification of alkaline trapped vesicles by bafilomycin-A1 led to a larger maximal ES-evoked secretory response in WT than KO, suggesting that exocytosis per se is affected in MICU1 KO neurons. Thus, our results highlight the specific contribution of MICU1-gated mitochondria in the regulation of Ca2+-dependent exocytosis of neurotransmitter vesicles by modulating local intracellular Ca2+ levels at the neuronal processes.

26 Metabolic adaptions promoting survival and invasion in drug tolerant melanoma cells

Casey D. Stefanski[1], Glenn L. Mersky[1], Timothy J. Purwin[1], and Andrew E. Aplin[1,2]

[1]Department of Pharmacology, Physiology, and Cancer Biology, Thomas Jefferson University, Philadelphia, PA, [2]Sidney Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA

Minimal residual disease (MRD) eludes therapeutic efforts selecting resistant and invasive subpopulations contributing to poor prognosis in melanoma patients. Previously, we discovered a SOX10-deficient melanoma cell population within MRD associated with drug tolerance and invasion. RNA-sequencing and gene set enrichment of SOX10-deficient cells demonstrated an enriched glycolytic gene signature. In addition, increased expression of MCT4, the lactate exporter, was observed in SOX10-deficient cells suggestive of enhanced glycolysis. However, MCT4 inhibition did not affect SOX10-deficient cells survival. Using the Seahorse Analyzer, we observed that SOX10-deficient cells had reduced glycolysis and glycolytic capacity. Simultaneously, we determined SOX10-deficient cells had slightly slower flux through glycolysis and the tricarboxylic acid cycle suggesting SOX10-deficient cells do not rely on glycolysis for cell survival. To investigate other metabolic pathways in drug resistant models, several disrupted metabolic pathways were identified including the arachidonic acid pathway. Prostaglandin reductase 1 (PTGR1), a member of arachidonic acid metabolism, was increased in drug resistant cells. We will assess whether genetically silencing PTGR1 inhibits resistant cell growth. Additionally, the expression of the arachidonic acid related enzyme aldo-keto reductase family 1 member C3 (AKR1C3) was increased in drug resistant cells, which is elevated in the previously reported Rambow et al. invasive melanoma gene signature. To determine whether AKR1C3 is necessary for invasive cell behavior in drug resistant cells, we will pharmacologically inhibit AKR1C3 in spheroid outgrowth assays. Future studies will evaluate the importance of arachidonic acid metabolism in promoting the invasive phenotype in resistant cells. Metabolic adaptations in drug tolerant melanoma cells will be functionally investigated to identify novel therapeutic opportunities.

27 Inhibiting Endothelial Mammalian Sterile 20-like Kinase 1 Attenuates Acute Lung Injury in Mice

Tongmuang N[1], Guo Z-F[2], Li C[1], Zhang C[1], Hu L[1], Capreri D[1], Zuo M-X[1], Summer R[1], Sun J[1]

[1]Thomas Jefferson University, Philadelphia, PA, [2]Changhai Hospital, Second Military Medical University, Shang Hai Shi, China

Please contact the postdoc presenter for information about this abstract.

28 Adaptations to the loss of IP3 receptor-mediated Ca2+ signaling

Young MP[1], Booth D[1], Hajnóczky G[1], Joseph SK[1]

[1]Department of Pathology & Genomic Medicine, Thomas Jefferson University, Philadelphia, PA

The activation of IP3 receptor (IP3R) Ca2+ channels generates agonist-mediated Ca2+ signals that regulate a wide range of biological processes. It is therefore surprising that CRISPR-induced loss of all three IP3R isoforms (TKO) generates HEK293 and HeLa cell lines that can survive, grow and divide, albeit more slowly than wild-type cells. Under basal conditions no major metabolic or bioenergetic changes are observed in TKO cells. In an effort to understand the mechanisms used by these cells to adapt to the absence of Ca2+ signaling, we have examined the activity of key Ca2+ dependent transcription factors (NFAT,CREB,NFκB) using luciferase-reporter assays, phosphoprotein immunoblots and whole genome transcriptomic studies.

Research In-Depth Presentations

EAKINS LOUNGE, JAH | 2:00PM – 3:30PM

Moderator: Francesco De Pascali, PhD

2:00 - 2:05	Lisa Kozlowski	Opening Remarks
2:05 - 2:20	Aurélie Bouteau	Steady-state Langerhans cells induce antibody responses through an IL-6 and type I interferon-independent but CD80/CD86-dependent mechanism
2:20 - 2:35	Ali Calderon-Aparicio	S6K1 signaling pathway is a target to overcome radio-resistance of lung cancer
2:35 - 2:50	Benjamin Cartes-Saavedra	The mitochondrial Ca2+ uniporter gatekeeper, Micu1 is required for mitochondrial fusion dynamics
2:50 - 3:05	Kristen C. Davis	A Neurexin / Neuroligin network underlies sexually dimorphic central synapse formation
3:05 - 3:20	Chiara Scopa	Exploring a Novel Pathway: JUN Upregulation Initiates Transposable Element-Driven Innate Immunity Cascade in Alzheimer's Disease and Related Dementias
3:20 - 3:30	Francesco De Pascali	Closing Remarks

05 Steady-state Langerhans cells induce antibody responses through an IL-6 and type I interferon-independent but CD80/CD86-dependent mechanism

Aurélie Bouteau[1], Sandra M Zurawski[2], Gerard Zurawski[2], and Botond Z Igyártó[1]

[1] Department of Microbiology & Immunology, Thomas Jefferson University, Philadelphia, PA, [2] Baylor Scott & White Research Institute, Dallas, TX

The traditional danger model states that the immune system requires a danger signal for professional antigen-presenting cells, such as dendritic cells (DCs), to initiate adaptive immune responses, including the production of protective antibodies. However, our recent findings challenge this model by revealing that Langerhans cells (LCs), a specific type of dendritic cell found in the skin epidermis, can trigger protective antibody responses against foreign antigens without the need for a danger signal. Investigating how LCs facilitate adaptive immune responses in steady-state conditions holds great potential for advancing our understanding of immune response induction and regulation. Furthermore, it offers promising opportunities for developing more effective immunotherapeutic strategies to combat autoimmune and infectious diseases. In this study, we utilized a well-established antigen-targeting model in steady-state conditions to explore the underlying mechanism by which LCs support T follicular helper (Tfh) cells and antibody responses. Using bone marrow chimeras, the Cre/Lox system, and blocking antibodies, we made several key discoveries. Firstly, we found that IL-6, a crucial factor in inducing Tfh cells and antibody responses during inflammatory conditions, does not contribute to LC-mediated adaptive immune responses in steady-state environments. Additionally, we determined that type I interferon signaling is not required in this context. However, our data indicate that the induction of humoral immune responses by steady-state LCs depends on membrane-bound co-stimulatory molecules, specifically CD80/CD86. These findings strongly suggest that adaptive immune responses against foreign antigens, in the absence of inflammation, occur through a distinct mechanism from the one proposed by the traditional danger model, and does not involve the participation of inflammatory cytokines.

06 S6K1 signaling pathway is a target to overcome radio-resistance of lung cancer

Calderon-Aparicio A[1], Simone N[1]

[1] Department of Radiation Oncology, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, PA, USA

Lung cancer is the leading cause of cancer mortality worldwide. In USA, it will be responsible for the 21% of deaths by cancer in 2023. Although radiation is a mainstay of lung cancer treatment, tumor response to radiation is variable. Clinically, it has been found that patients with metabolic dysfunction have worse therapeutic outcomes against standard therapies. Metabolic targets such as S6K1, a downstream kinase of the mTOR pathway which regulates several cellular processes such as translation, ribosome biogenesis, and cell growth, are associated with lung cancer progression and radiation resistance. We sought to understand the role of S6K1 in radio-resistance of lung cancer and whether its inhibition can increase the therapeutic ratio of radiotherapy. To determine the importance of S6K1 in cancer outcomes, we performed expression analysis of lung cancer patients from TCGA database and showed that S6K1 overexpression was associated with a reduction of the overall survival. The radio-sensitivity of 4 different lung cancer cells lines was determined. At 6Gy, the A549 cells had 5% cell death and were most radiation resistant compared with H661, H226 and H23 which had a 20%, 43% and 55% cell death respectively. The resistant cells were also treated with a highly specific inhibitor of S6K1, PF-4708671, which was noted to improve the therapeutic efficacy of radiation, by reducing the survival cell fraction when combined with radiation, in comparison with radiation or drug alone. In vitro assays showed that the phospho-activation of S6K1 and its downstream target S6 are increased in resistant cells. Likewise, immunoblot analysis showed that radiation increases the phosphorylation of S6K1, suggesting that its activation post-radiation could lead to radio-resistance in lung cancer. In conclusion, S6K1 inhibition improves the therapeutic effect of radiotherapy in lung cancer and should be considered a therapeutic target. Studies oriented to determine the mechanisms of S6K1 in radio-resistance are being performed.

07 The mitochondrial Ca2+ uniporter gatekeeper, Micu1 is required for mitochondrial fusion dynamics

Cartes-Saavedra B.[1], Chakrabarti R.[1], Hasan P.[1], Berezhnaya E.[1], Perocchi F.[2], Hajnóczky G.[1]

[1] MitoCare Center for Mitochondrial Imaging Research and Diagnostics, Department of Pathology and Genomic Medicine, Thomas Jefferson University, Philadelphia, PA, [2] Institute of Neuronal Cell Biology, Technical University of Munich, Munich, Germany

Introduction: Mitochondria are multifaceted organelles that provide energy for the main cellular processes. Mitochondrial Ca2+ (Ca2+m) signaling and mitochondrial fusion are central in organelle bioenergetics and quality control. Ca2+m uptake is mediated by the mitochondrial calcium uniporter complex (mtCU), a pore composed of a core (Mcu), a scaffold (Emre), and the mtCU gatekeepers Micu1 and Micu2. However, how mitochondrial fusion dynamics and Ca2+m signaling are connected remains elusive. In this work, we address how the loss of the Micu1 impairs mitochondrial dynamics and its relationship with Ca2+mt homeostasis. Material and Methods: We have created an acute inducible KO using a CRE-Lox recombination system. Micu1fl/fl MEFs cells were infected with a CRE or Null adenovirus for 72 hr to induce the recombination. To follow mitochondrial fusion dynamics, infected Micu1fl/fl MEFs cells or MCU/EMRE/MICU1 KO HeLa (3KO) cells, were transfected with a mitochondrial-targeted photoswitchable proteins mtPAGFP /mtDsRed or mtDendra2. For Ca2+ measurements, cells were transfected with an outer mitochondrial membrane-Ca2+ (OMMRCaMP) sensor or a matrix-Ca2+ sensor (mtRCaMP). Actin staining was done using Phalloidin. Results: Micu1 loss showed mitochondrial fragmentation and fusion inhibition, increased OMM, and matrix resting Ca2+. These changes lead to a peri-mitochondrial actin polymerization around the mitochondria. Dystabilization of the actin cytoskeleton and Micu1 rescue experiments in the Micu1 KO MEFs or 3KO HeLa show restoration of mitochondrial fusion dynamics. Discussion: Our results shows that Micu1 loss leads to mitochondrial fusion impairment, with Ca2+m dysregulation and peri-mitochondrial actin polymerization, an important player on fusion dynamics as demonstrated in our experiments. Our results suggests, that Micu1 have a dual role on fusion dynamics, one independent of the mtCU relevant for cristae stabilization and fusion, and an MCU-dependent role that maintains the Ca2+m, required to prevent the peri-mitochodrial actin and fusion loss.

09 A Neurexin / Neuroligin network underlies sexually dimorphic central synapse formation

Davis, K.C.[1], Mosca, T.J.[1]

[1]Department of Neuroscience, Farber Institute for Neuroscience, Thomas Jefferson University, Philadelphia, PA

Please contact the postdoc presenter for information about this abstract.

22 Exploring a Novel Pathway: JUN Upregulation Initiates Transposable Element-Driven Innate Immunity Cascade in Alzheimer's Disease and Related Dementias

Scopa C.[1,2], Barnada S.M.[1], Cicardi M.E.[2], Singer M.[2], Trizzino M.[1,3] and Trotti D.[2]

[1]Department of Biochemistry and Molecular Biology, Thomas Jefferson University, Philadelphia, PA, USA, [2]Jefferson Weinberg ALS Center, Vickie and Jack Farber Institute for Neuroscience, Department of Neuroscience, Thomas Jefferson University, Philadelphia, PA, USA, [3]Department of Life Sciences, Imperial College London, London, UK

Alzheimer's Disease and Alzheimer's Disease Related Dementias (AD/ADRD) are characterized by genomic instability, which leads to abnormal chromatin relaxation and mobilization of transposable elements (TEs). Importantly, aberrant TE mobilization can lead to neurotoxicity, inflammation, and cell death, but the underlying mechanisms remain poorly understood. By combining functional genomics with differentiation of familial and sporadic AD patient-derived iPSCs into hippocampal progenitors and cerebral organoids, we identified that the upregulation of c-JUN in the context of Alzheimer's disease models triggers the decondensation of genomic regions containing TEs. This leads to the cytoplasmic accumulation of TE-derived RNA-DNA hybrids, activation of the cGAS-STING cascade, and increased cleaved caspase-3, suggesting the initiation of programmed cell death and ensuing neurodegeneration. Significantly, inhibiting c-JUN effectively blocks downstream molecular processes. Additionally, we identify the activation of the TE-cGAS-STING axis, also in the context of C9orf72-linked ALS/FTD. This finding was consistent in both our in vitro model using cerebral organoids differentiated from C9orf72 patient derived iPSCs and our in vivo model.Our study not only sheds light on the role of TEs in the development of ADRD but also opens up new possibilities for developing therapeutic strategies and biomarkers that can counteract disease progression and enable early, pre-symptomatic diagnosis of ADRD.

DIRECTORY OF PRESENTERS

NO.	NAME	DEPARTMENT	EMAIL
01 P	Ankeeta A	Neurology	axl666@jefferson.edu
02 P	Lakhikumar Adhikarimayum	Biochemistry and Molecular Biology	lakhikumar.adhikarimayum@jefferson.edu
03 P	Michael H. Alexander	Dermatology	michael.alexander2@jefferson.edu
04 P	Mayuri Bhatia	Biochemistry and Molecular Biology	mayuri.bhatia@jefferson.edu
05 RI	Aurélie Bouteau	Microbiology and Immunology	aurelie.bouteau@jefferson.edu
06 RI	Ali Calderon-Aparicio	Radiation Oncology	ali.calderonaparicio@jefferson.edu
07 RI	Benjamin Cartes-Saavedra	Pathology/MitoCare	benjamin.cartessaavedra@jefferson.edu
08 P	Bridget Curran	Neuroscience	bridget.curran@jefferson.edu
09 RI	Kristen C. Davis	Neuroscience	kristen.davis2@jefferson.edu
10 RL	Marilen Federico	Center for Translational Medicine	marilen.federico@jefferson.edu
11 RL	Prottoy Hassan	Pathology/MitoCare	prottoy.hassan@jefferson.edu
12 E	Stephen Hurst	Pathology/MitoCare	stephen.hurst@jefferson.edu
13 P	Arun Kumar Jannu	Center for Translational Medicine	arunkumar.jannu@jefferson.edu
14 E	Elham Javed	Center for Translational Medicine	elham.javed@jefferson.edu
15 P	Sam Javidi	Neurology	sam.javidi@jefferson.edu
16 P	Mandeep Kaur	Hematology	mandeep.kaur@jefferson.edu
17 RL	William Lee	Biochemistry and Molecular Biology	william.lee@jefferson.edu
18 P	Melissa Molho	Microbiology and Immunology	melissa.molho@jefferson.edu
19 RL	Brian Montoya	Microbiology and Immunology	brian.montoya@jefferson.edu
20 P	Stepan Nersisyan	Computational Medicine Center	stepan.nersisyan@jefferson.edu
21 E	Victor Hugo Sanchez-Vazquez	Pathology/MitoCare	victorsanchez.vazquez@jefferson.edu
22 RI	Chiara Scopa	Center for ALS	chiara.scopa@jefferson.edu
23 E	Anuradha A Shastri	Radiation Oncology	anuradha.shastri@jefferson.edu
24 RL	Amy Shaver	Medical Oncology	amy.shaver@jefferson.edu
25 P	Raghavendra Singh	Pathology/MitoCare	raghavendra.singh@jefferson.edu
26 P	Casey Stefanski	Pharmacology, Molecular Physiology, & Cancer Biology	casey.stefanski@jefferson.edu
27 P	Nopprarat Tongmuang	Center for Translational Medicine	nopprarat.tongmuang@jefferson.edu
28 P	Michael Young	Pathology/MitoCare	michael.young@jefferson.edu
29 RL	Qirui Zhang	Neurology	qirui.zhang@jefferson.edu

E=Early Discoveries Poster Presentation *RI=Research In-Depth Presentation*

P=Poster Presentation *RL=Research Lightning Presentation*