Ohio Physiological Society

39th Annual Meeting
University of Cincinnati
October 10–11, 2025

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OPS2025 Program

Friday, October 10 *University of Cincinnati, Medical Campus–East*	
2:00–5:00 pm	**Registration** *Atrium, CARE/Crawley Building, 3230 Eden Avenue*
4:00 pm	**Opening Session** *Kowalewski Auditorium, Kowalewski Hall, 3255 Eden Avenue* **Opening Remarks** Karthickeyan Chella Krishnan, PhD *OPS President* **Welcome Address** Teresa M Reyes, PhD *Senior Associate Dean for Basic and Translational Research and Professor, Pharmacology, Physiology & Neurobiology* *University of Cincinnati College of Medicine* **Keynote Address** Chair: Karthickeyan Chella Krishnan, PhD **Finding your own path to make an impact** Katsu Funai, PhD *University of Utah*
5:45 pm	**Reception** *Atrium, CARE/Crawley Building, 3230 Eden Avenue*
6:45 pm	**Banquet** *Kaplan Reception Hall, CARE/Crawley Building, 3230 Eden Avenue*

Saturday, October 11

University of Cincinnati, Medical Campus–East

8:00–9:00 am	**Registration** | **Coffee & Pastries** *Atrium, CARE/Crawley Building, 3230 Eden Avenue*
9:00 am	**Oral Session A** *Kowalewski Auditorium, Kowalewski Hall, 3255 Eden Avenue* **Oral Presentations** Chairs: Kesha Dalal, BS and Cory W Baumann, PhD 1. Effect of charged polymers and charged lipids on the biophysical study of membrane proteins Evelyn A Okorafor (Graduate Student) | Miami University 2. Restoring T cell power: mRNA nanoparticles boost T cell immunity in head and neck cancer Anjali Iyer (Undergraduate Student) | University of Cincinnati 3. The human glucocorticoid receptor variant rs6190 protects the heart from metabolic stress Ashok Daniel Prabakaran (Postdoctoral Fellow) | Cincinnati Children's Hospital **Data Blitz A** 8A Buckles 26A Kronk 33A Ojha 43A Sathyanarayana 11A Collins 29A Mattam 34A Oyebode 49A Thapa 15A Franco 30A Mia 36A Paxhia-Poppaw 22A Kamau 32A Nur 39A Ren
10:30 am	**Refreshments** *Atrium, CARE/Crawley Building, 3230 Eden Avenue*
10:45 am	**Poster Session A** *Atrium, CARE/Crawley Building, 3230 Eden Avenue*
11:45 pm	**Lunch** *Kaplan Reception Hall, CARE/Crawley Building, 3230 Eden Avenue*

12:45 pm	**Oral Session B** *Kowalewski Auditorium, Kowalewski Hall, 3255 Eden Avenue* **Oral Presentations** Chairs: Francisca Akhigbe, DVM and Ellen Gagliani, PhD 4. Sting–IL-6 signaling in sensory neurons mediates cisplatin-induced neuropathic pain Yasmin Sahlloul (Graduate Student) | University of Cincinnati 5. Mutation in polymerase gamma increases the severity of trauma induced intervertebral disc degeneration in a mouse model Abduallah Ahmed (Undergraduate Student) | Northeast Ohio Medical University 6. Role of ACC1 in rewiring chondrocyte metabolism during obesity and injury-associated osteoarthritis Anupama Binoy (Postdoctoral Fellow) | Ohio University **Data Blitz B** 3B Ansari, 14B Foltz, 24B Kondapalli, 39B Rezaei 7B Bostick, 15B Frazier, 31B Nolt, 42B Saini 8B Cagle, 20B Hyrne, 33B Onyeagba, 49B Umerani 11B Coughlin, 21B Jones, 34B Oyetunji
2:15 pm	**Refreshments** *Atrium, CARE/Crawley Building, 3230 Eden Avenue*
2:30 pm	**Poster Session B** *Atrium, CARE/Crawley Building, 3230 Eden Avenue*
3:30 pm	**Oral Session C** *Kowalewski Auditorium, Kowalewski Hall, 3255 Eden Avenue* **Oral Presentations** Chairs: Corbin R Azucenas, BS and Joshua Benoit, PhD 7. IL-3/IL-3 receptor contributes to skeletal sexual-dimorphism in a pre-clinical model for non-syndromic autosomal recessive intellectual disability Gabrielle T Robinson (Graduate Student) | Northeast Ohio Medical University 8. Role of muscle-specific FSP27 in energy production and whole-body glucose Rabia Basri (Graduate Student) | Ohio University 9. Cartilage-specific deletion of acetyl-CoA carboxylase 1 (ACC1) disrupts growth plate development and alters skeletal growth Shadi Moradi (Graduate Student) | Ohio University
4:15 pm	**Group Photo** *Kresge Circle, 231 Albert Sabin Way*
4:30 pm	**Business Meeting and Awards** *Kowalewski Auditorium, Kowalewski Hall, 3255 Eden Avenue*

Posters

Atrium, CARE/Crawley Building, 3255 Eden Avenue

Poster Session A | 10:45 – 11:45 am | Presenters: A Posters

Poster Session B | 2:30 – 3:30 pm | Presenters: B Posters

Presenting author is indicated by underline if not the first author

1A	Sleep-like states in mosquitoes impact pre- and post-blood feeding behavior and physiology Oluwaseun M Ajayi, Diane F Eilerts, Clément Vinauger, Joshua B Benoit
1B	Post-transcriptional regulation of adrenal–heart crosstalk in heart failure with preserved ejection fraction Francisca Akhigbe, Kayla Lux, Tian Liu, Ningjing Song, Jayme McReynolds, Christoph Rau, Yibin Wang, Chen Gao
2A	LRRC14B is essential for cardiac function via sarcomeric protein quality control Olukunle Akinborewa, Ashok Prabarakan, Hima Bindu Durumutla, Hannah Latimer, Mattia Quattrocelli
2B	Shear stress-induced calcium signaling dynamics in TIE2-L914F mutant endothelial cells in venous malformations Pardis Amini, Elisa Boscolo
3A	Sub-second release of neurochemicals from CD4+CD25+ regulatory T cells (Tregs) Thepuni Kalu Arachchillage, Jordan Seibold, Ashley E Ross
3B	Role of acute alcohol-induced acetylation in tauopathy Aisha Ansari, Usman Sabir, Takhar Kasumov
4A	Demographic and medical factors associated with speech-evoked EEG in preterm infants Mir Ashraf, Chelsea Blankenship, Lauren Petley, David Moore, Lisa Hunter
4B	Erythroid-specific, inducible CDAN1Δ/Δ mouse model phenocopies congenital dyserythropoietic anemia type-Ia Corbin R Azucenas, Aikaterini Voulgaridou, Sidharth Sen, Yasmin El Gammal, Athina Ntoumaziou, Mary Risinger, Katie G Seu, Lee Edsall, Matthew Weirauch, Leah Kottyan, Nathan Salomonis, Theodosia A Kalfa
5A	Membrane topology and dynamics of the antimicrobial peptide gp28: lipid-specific interactions revealed by EPR spectroscopy Binaya Baral, Nancy Rotich, Evelyn Okorafor, Andrew Morris, Gary Lorigan
5B	Combining immune checkpoint inhibitors and anti-angiogenesis approaches: treatment of advanced non-small cell lung cancer Tate Barney, Anita Thyagarajan, Ravi P Sahu
6A	Fat-specific protein 27 (FSP27) regulates intramuscular fat storage for skeletal muscle function Chloe C Becker, Bijinu Balakrishnan, Mark Slayton, Rabia Basri, Hebaallaha Hussein, Ishika Puri, Kate Tenerowicz, Kaia Mckinney, Lillian Ijoma, Andrew Pugh, Scott Jobe, Vishva M Sharma, Vishwajeet Puri
6B	Altered nighttime sleep and activity patterns as mechanisms of ectoparasite resistance Joshua B Benoit, Joy Bose, Hailie Talbott, David A Lewis, Ashley Webster, Oluwaseun M Ajayi, Michal Polak
7A	*Withdrawn*
7B	Long-term stability of urinary and kidney protein biomarkers for diabetic kidney disease Nadia Bostick, Unmesha Thanekar, Sridevi Gutta, Mohammad Saklayen, Khalid M Elased

8A	A rapid, non-destructive, specific method for intervertebral disc imaging with KI-enhanced micro-CT Madison M Buckles, Abdulkadir Nur, Nada H Warda, Huzafa Khanzada, Amogh Kankanwadi, Ethan Hyrne, Abduallah Ahmed, Mohammad Y Ansari
8B	Determining changes in gene expression from microgravity through qRT-PCR Samuel Cagle, Joey Barhorst, Emma Linneman, Emma Simone, Cena Hornberger, Emily Greulach, Marie Mortreux, Hanna Wetzel, Kelly Crowe
9A	Purines dynamically mediate astrocyte Kaejaren CN Caldwell, Ashley E Ross
9B	Engineering bacteria for a sustained release of mycosporine-like amino acid, shinorine, for gut and neurodegenerative disorders Abram Canowitz, Nitin S Kamble, Saqib Sange, Bhavesh Gabani, Nathan Muck, Komalpreet Kaur, Nathaniel Garay, Pankaj Desai, Gary Gudelsky, Nalinikanth Kotagiri
10A	Exploring the effect of cortisol on antibody production Maitreyee Chavan, Addison Lowe, Courtney Sulentic
10B	Circadian disruption by artificial light at night alters activity and male mating in the tsetse fly *Glossina morsitans morsitan* Bruna Ciuffa Maria, Brian Weiss, Joshua B Benoit
11A	Gut microbiome and type 1 diabetes: a possible link Colby Collins, McKenzie Paul, Olivia Deichman, Michael Kennedy
11B	Characterization of Nrac, a nutritionally regulated adipose and cardiac-enriched microprotein Taylor Coughlin, Aaron M Gibson, Jiuzhou Huo, and Catherine A Makarewich
12A	TRPV4-mediated mitochondrial dynamics: a novel mechanism regulating endothelial function and angiogenesis Kesha K Dalal, Venkatesh Katari, Narendra Kondapalli, Sailaja Paruchuri, Charles K Thodeti
12B	FAK activation by M64HCl promotes osteoclastogenesis: a potential therapeutic strategy for high bone mass disorders Ernesto Solorzano, Michael DiSabato, Alhussain Ojaym, Mitchell W Bailey, Shahab Yazdanpanah, Marc D Basson, Fayez F Safadi
13A	Decoding fibroblast heterogeneity in severe fibrotic lung disease HH Ediga, CP Vemulapalli, V Sontake, Anil G Jegga, SK Huang, Nishant Gupta, Francis X McCormack, SK Madala
13B	Comparative effects of canagliflozin and pioglitazone on urinary ACE2 shedding and renal injury in diabetic mice Siri Chandana Minikuri, Unmesha Thanekar, Nadja Alexis Bostick, Khalid M Elased
14A	Investigating NDM-4 antibiotic resistance mechanisms through structural analysis of NDM variants Anastasiia Evstifeeva, Richard Page
14B	Airway inflammation and fear: elucidating brain nodes and cellular substrates Corey Foltz, Emily Allgire, Rebecca Ahlbrand, Ian Lewkowich, Renu Sah
15A	Investigating foraging behavior via the insulin/IGF-1 pathway in *C. elegans* Sofia Franco, Ansley Varisco, Hanna N Wetzel, Kelly E Crowe, Michael Nitabach, Kaiden Price

15B	Adipose-specific overexpression of NDUFV2 attenuates cardiometabolic comorbidities in females in a “2-hit” mouse model of HFpEF James Frazier, Ushodaya Mattam, Noble Kuman Talari, Ashish Rao Sathyanarayana, Brook Hemmelgarn, Karthickeyan Chella Krishnan
16A	Chronic ethanol exposure triggers multi-organ dysfunction via gut-liver axis perturbation Muni Swamy Ganjayi, Thomas Krauss, and Cory W Baumann
16B	The quantitative assessment of computational simulations involving vulnerabilities in miniature excitatory postsynaptic current detection Hanna Ghouse and Kathy Engisch
17A	Evaluation of saposin C-dioleoylphosphatidylserine nanovesicles for drug delivery to the placenta Ameya Gourisetty, Josephine Link, Ahmet Kaynak, Xiaoyang Qi, Braxton Forde
17B	Diabetes mellitus impairs regenerative fibroblast activation Jaedyn Haverstock, Jenna Green, Kimberly Wagner, Anne-Karina Perl
18A	Perioperative fluid conservation guidelines did not negatively impact early postoperative clinical outcomes during the nationwide IV fluid shortage due to Hurricane Helene Jonah Heidel, Corey Hughes, Kevin Hatton, Brian Abiri, Dung Nguyen, Jamie Boggs, Andrew Singerman, Aric Schadler, Devlin McGrath
18B	Neurokinin signaling promotes proper conduction and restricts cardiomyocyte number in the zebrafish heart Lindsay N Helock, Hannah N Gruner, Bradley Davidson, Joshua S Waxman
19A	Dry conditions shift mosquito behavior and blood feeding Christopher J Holmes, Souvik Chakraborty, Oluwaseun M Ajayi, Melissa R Uhran, Ronja Frigard, Crystal L Stacey, Emily E Susanto, Shyh-Chi Chen, Jason L Rasgon, Matthew DeGennaro, Yanyu Xiao, Joshua B Benoit
19B	The kissing bug likely has a single functional eye photoreceptor Syeda Farjana Hoque, Michael Meece, Shubham Rathore, Amartya Tashi Mitra, Samantha Gass, Paige Crawford, Zoe Carter, Noelia Lander, Elke K Buschbeck, Joshua B Benoit
20A	Identifying a novel protein protecting against atherosclerosis and vascular dysfunction Hebaallaha Hussein , Bijinu Balakrishnan, Rabia Basri, Chloe Becker, Vishva Sharma, Ramiro Malgor, Mahmood Khan, Noyan Gokce, Vishwajeet Puri
20B	Age-progressive and sex-dependent bone phenotype in mice lacking Atp13a2 Ethan Hyrne, Abdulkadir Nur, Nada H Warda, Huzafa Khanzada, Amogh Kankanwadi, Madison M Buckles, Abduallah Ahmed, Mohammad Y Ansari
21A	*Withdrawn*
21B	Neurovascular LAT1 signaling in the DRG as a driver of neuropathic pain David Jones, Nesia Zurek, Yasmin Sahlloul, Jun-Ming Zhang, Temugin Berta, Sascha Alles
22A	Lipin1 restoration mitigates cardiomyopathy progression in Duchenne muscular dystrophy John Karanja Kamau, Hongmei Ren
22B	Oxidative stress induces mitochondrial DNA leakage in chondrocytes Amogh Kankanwadi, Nada H Warda, Abdulkadir Nur, Madison M Buckles, Huzafa Khanzada, Ethan Hyrne, Abduallah Ahmed, Mohammad Y Ansari
23A	Cardiomyocyte-specific TRPV4 deletion attenuates adverse cardiac remodeling via modulation of protein kinase G signaling Venkatesh Katari, Kesha Dalal, Narendra Kondapalli, Sailaja Paruchuri, Charles Thodeti

23B	Queuosine derived from the microbiome influences the physiology of mosquito larvae through altered tyrosine metabolism Melissa Kelley, Patrick A Limbach, Joshua B Benoit
24A	Study of age- and sex-related changes in the tail vertebrae of Atp13a2 knockout mouse Huzafa Khanzada, Abdulkadir Nur, Nada H Warda, Ethan Hyrne, Amogh Kankanwadi, Madison M Buckles, Abduallah Ahmed, Mohammad Y Ansari
24B	TRPV4 mechanotransduction mediates TGF-β2–induced endothelial-to-mesenchymal transition (EndMT) via Rho/Snail pathway Narendra Kondapalli, Venkatesh Katari, Kesha Dalal, Sailaja Paruchuri, Charles K Thodeti
25A	Distinct regulation of apolipoprotein j in pathological and physiological skeletal muscle conditions Thomas A Krauss, Muni Swamy Ganjayi, Cory W Baumann
25B	The role of the CD44 receptor in post-traumatic and age-related osteoarthritis Trinity A Kronk, Alexander Powell, Zachary Oatley, Abdelrahman Boghdady, Hakem Altawil, Anas Bakdalieh, Gabrielle T Robinson, Layth Khawaja, Emily Arellano, Michael DiSabato, Sharon Usip, Hope Ball, Fayez F Safadi
26A	Gpnmb overexpression delays progression of post-traumatic and age-related osteoarthritis Trinity A Kronk, Zachary Oatley, Alexander Powell, Abdelrahman Boghdady, Christian Mineo, Hakem Altawil, Anas Bakdalieh, Layth Khawaja, Emily Arellano, Gabrielle T Robinson, Jalal Jwayyed, Michael J DiSabato, Sharon Usip, Hope Ball, Fayez F Safadi
26B	Osteoactivin/Gpnmb, a novel therapeutic for post-traumatic osteoarthritis Trinity A Kronk, Alexander Powell, Zachary Oatley, Christian Mineo, Shahabeddin Yazdanpanah, Abdelrahman Boghdady, Adam Sanchez, Hakem Altawil, Anas Bakdalieh, Gabrielle Robinson, Layth Khawaja, Bryce Pember, Kenneddy Nkachukwu, Michael J DiSabato, Abdigadir Khalif, Sharon Usip, Hope C Ball, Fayez F Safadi
27A	Drying habitats increase mite parasitism of their fly hosts Gabrielle LeFevre, Joy Bose, Ann Miller, David Lewis, Hailie Talbott, Chandrima Das, Emily Susanto, Lyn Wang, Oluwaseun M Ajayi, Shyh-Chi Chen, Michal Polak, Joshua B Benoit
27B	Bioamine disruption leads to memory deficits in the whip spider *Phrynus marginemaculatus* Sidney T Ley, Nicholas A Brown, Gabriella H Wolff, Nicholas R Gookin, Patrick Casto, Daniel D Wiegmann, Verner P Bingman
28A	The effects of cocaine on sialyltranaferase levels in rat skeletal muscle Emma Linnemann, Taylor Thomas, Kelly Crowe, Hanna Wetzel, Jayme McReynolds
28B	Sex differences in endocannabinoid regulation of stress-cocaine interactions in rats Claire Lopez, Andrew D Gaulden, Erin A Tepe, Sierra S Rollins, Nicolas Wiles, Kristin Chase, Jayme R McReynolds
29A	Sex differences and the role of plasma extracellular vesicles in HFpEF pathology Ushodaya Mattam, James Frazier, Noble Kuman Talari, Karthickeyan Chella Krishnan
29B	The expanded version of the RNA binding protein PABPN1 is functionally insufficient and causes a dominant-negative RNA export defect in a cellular model of OPMD Allison Mezzell, Katherine Vest
30A	Inhibition of cardiomyocyte GLUT1 ameliorates KLF5 activation and diabetic cardiomyopathy Sobuj Mia, Kajol Thapa, Georgios Siokatas, Karthi Sreedevi, Alexey Zaitsev, Junco Warren, Konstantinos Drosatos

30B	Investigating radiation sensitivity of proton therapy-treated HNSCC murine cells Sushruth Muthuluru, Margaret Nelson, Maria Lehn, Ashley Karns, Dalia El-Gamal, Trisha Wise-Draper
31A	Disengaging hypoxia inducible factors 1 alpha (HIF-1α) regulation from hypoxia Yu Sun, Maradumane Mohan, Kate Stenson, Anushruti Ashok, Sathyamangla V Naga Prasad
31B	Microglia-selective expression of APOE2 improves remyelination even in the presence of CNS APOE4 Georgia Nolt, Lesley Golden, Shealee Thorpe, Jessica Funnell,, Isaiah Stephens,, Gabriela Hernandez, Steven MacLean, Chloe Lucido, Chesney Brock, Darcy Adreon, Holden Williams, Josh Morganti, Lance Johnson
32A	Atp13a2 deficiency triggers chondrocyte inflammation and exacerbates spontaneous osteoarthritis severity in an aging mouse model Abdulkadir Nur, Ethan Hyrne, Huzafa Khanzada, Madison M Buckles, Nada H Warda, Amogh Kankanwadi, Abduallah Ahmed, Mohammad Y Ansari
32B	Next-generation 3D-printed scaffolds enhance auricular cartilage regeneration in pediatric microtia Alhussain A Ojaym, Hope C Ball, Trinity A Kronk, Gabrielle T Robinson, Ananth S Murthy, Fayez F Safadi
33A	Characterizing the mechanism of norepinephrine transporter in secondary lymphoid organ Sarbeshwar Ojha, Ashley E Ross
33B	Egg viability is improved by tick burrowing into moist soil Kosisochukwu Onyeagba, Harshita Nune, Sarah Salem, Logan McGinnis, Pia U Olafson, Joshua B Benoit
34A	miR-146a overexpression protects and stabilizes the muscle environment in Duchenne muscular dystrophy Olumide E Oyebode, Dema M Herzallah, Hanna S Rakhangi, Mariana Ramallo, Edana A Ottney, Michael C Ostrowski, Sudarshana M Sharma, Jennifer M Peterson
34B	Absence of chloride intracellular channels (CLICs) offers resistance to hypoxia via differential regulation ERK and AKT pathways Ibukunoluwa Oyetunji, Savanna Spitnale, Sarah Seeley, Maxwell Sutherland, Soichi Tanda, Mark Berryman, Harpreet Singh, Shubha Gururaja Rao
35A	*Withdrawn*
35B	Exploring the efficacy of pantoprazole-based approaches for cancer treatment Ashni Patel, Anita Thyagarajan, Ravi P Sahu
36A	Interaction between human APOE polymorphisms and sex differences in hippocampal mitochondrial functions in lean and obese mice Zoe Paxhia-Poppaw, Ushodaya Mattam, Brook Hemmelgarn, Noble Kumar Talari, Karthickeyan Chella Krishnan
36B	Modulation of fear behavior and neuroimmune alterations in a model of allergic asthma in female mice Taylor M Peach, Renu Sah
37A	Exploring the allocation of copper to mitochondria during myoblast differentiation Alexandra Perez, Jason Fivush, Dina Secic, Megan Bischoff, Ushodaya Matta, Karthickeyan Chella Krishnan, Maria Czyzyk-Krzeska, Katherine Vest
37B	Exploring the responses of therapeutic outcomes and adverse effects of aurora kinase inhibitors in diverse human malignancies N Pothamsetty, A Thyagarajan, RP Sahu
38A	Loss of FSP27 impairs cognitive function via disruption of neuro-metabolic pathways Andrew Pugh, Aarav Bhasin, Connor Aleshire, Rabia Basri, Chloe Becker, Hebaallaha Hussein, Kaia Mckinney, Kate Tenerowicz, Bijinu Balakrishnan, Murali Vijayan, Ishika Puri, Vishwajeet Puri

38B	How female sex affects mitochondria in Alzheimer's disease Harshini Ramasubramanian, Zoe Paxhia-Poppaw, Brook Hemmelgarn, Karthickeyan Chella Krishnan
39A	Role of growth hormone in post-traumatic osteoarthritis Siqi Ren, Abhijit Sukul, Huanhuan Liu, Anna E Miller, John Kopchick, Shouan Zhu
39B	The effects of systemic gene therapy with AAV-lipin1 on model Duchenne muscular dystrophy skeletal muscle Bahar Rezaei, Pooneh Hajmirza Mohammadi Kamalabadi, Hongmei Ren, Andrew A Voss
40A	Metabolomic profiling uncovers a sex-specific bone phenotype in a pre-clinical model of non-syndromic-autosomal recessive intellectual disability Gabrielle T Robinson, Bailey C Deevers, Trevor M Wentworth, Robert L Smallwood, Xiaohang Wang, Liang Li, Fayez F Safadi
40B	Regional variability of lipid content in normal versus diabetic hearts and coronary microvessels Hunter Rode, Sanju Gudla, David Cunningham, Patricia E McCallinhart, Aaron J Trask
41A	Repurposing aurora kinase A and B inhibitors to enhance immunotherapy in non-small cell lung cancer J Sabbasani, A Thyagarajan, RP Sahu
41B	Protein glutathionylation is essential in acute myeloid leukemia through OxPhos regulation Paula Saez-Raez, Tianyi Ling, Mike Adam, Nathan Salomonis, Courtney L Jones
42A	An initial evaluation of body protective compound 157 (BPC-157) a peptide, as treatment for musculoskeletal pain Sameer Samad, Moazzam Nafees, Muhammad A Munir
42B	Does zinc deficiency promote renal inflammation? Diksha Singh Saini, Hannah Barrett, Clintoria R Williams
43A	Role of PKLR overexpression and knockdown in cholesterol biosynthesis Ashish Rao Sathyanarayana, Ushodaya Mattam, Zoe Paxhia-Poppaw, Anidya Soni, Karthickeyan Chella Krishnan
43B	Characterizing the functional properties of a malarial parasite homolog of the iron transporter DMT1 Ethan C Schuebel, Kade M Loveridge, Corbin R Azucenas, Adham Atwan, Kylee Armour, Paul Sigala, Bryan Mackenzie
44A	Comparative analysis of diphenylbutylpiperidine class of compounds for cancer treatment: evidence from single vs. combination approaches Maia Prem Sethi, Anita Thyagarajan, Ravi P Sahu
44B	Hemochromatosis, hepcidin, ferritin, and transferrin in cancer: mechanistic insights and clinical implications Mansi Sharma, Anita Thyagarajan, Ravi P Sahu
45A	Immune checkpoint inhibitor cardiotoxicity screening: using a single test to diagnose a condition Anish Sharma, Hannah Dempsey, Rekha Chaudhary
45B	Adipocyte subpopulations regulate growth hormone action Sohana Siyar, Rita Sharma, Edward List, John J Kopchick, Kevin Y Lee
46A	Investigating how CHIP autoubiquitination shapes its interaction with Hsp70 Shreesti Shrestha, Vivian Vukcevich, Richard C Page
46B	Ultrasound pressure fields visualized by fast object-oriented C++ ultrasound simulator (FOCUS) Sydnie Singh, Kevin Haworth

47A	UTCOMLS third-year subject exam and clerkship performance: benchmarking against national data Mooskan Singhal, Sami Sarrouj, Delaney Mcgranahan, Mahesh Muddaluri, Kayla Gray, Bindu Menon, Jeremy Laukka
47B	Cardiomyocyte KLF5 inhibits miR-30-5p family in ischemic cardiomyopathy via stimulation of 3 circular RNAs Georgios Siokatas, Matthew Hoffman, Nikolaos Mylonas, Konstantinos E Hatzistergos, Craig H Selzman, Stavros G Drakos, Konstantinos Drosatos
48A	Stress induced RNA decay in cardiac hypertrophy Ningjing Song, Sriram Ravindran, Tian Liu, Shuxun (Vincent) Ren, Yibin Wang, Christoph D Rau, Chen Gao
48B	APOE4 protects against metabolic dysfunction-associated steatotic liver disease (MASLD) by increasing mitochondria Noble Kumar Talari, Ushodaya Mattam, Jeyashree Alagarsamy, Zoe Paxhia-Poppaw, Brook Hemmelgarn, Karthickeyan Chella Krishnan
49A	Ventricular and sex-specific remodeling of GLUT1 in a mouse model of HFpEF Kajol Thapa, Erjola Rapushi, Georgios Siokatas, Sobuj Mia, Matilda Valianou, Konstantinos Drosatos
49B	Topical imipramine and amitriptyline block experimental ultraviolet B radiation-induced erythema in rosacea subjects Aadil Umerani, Craig Rohan, Jade Bryant, Avital Savin, Jeffrey Travers
50A	Unraveling fibroblast and lung cell heterogeneity in fibrotic lesions through single-nucleus RNA sequencing Chanukya P Vemulapalli, Harshavardhana H Ediga, Priyanka Singh, Vishwaraj Sontake, Hikaru Miyazaki, Dimitry Popov, Martin B Jensen, Steve K Huang, Nishant Gupta, Frank McCormack, Satish K Madala
50B	Phospholamban R14del cardiomyopathy develops independent of PLN aggregation through SR–mitochondrial disruption JP Verry, Omar Brito-Estrada, A Apfelbaum, J Huelsman, AM Gibson, K Haghighi, F Stillitano, EG Kranias, CA Makarewich
51A	The effect of genotypic mutations on NCCR-Driven BK polyomavirus gene expression Tiana A Walder, Taylor Hurst, Heidi L Meeds, Steven B Kleiboeker, Assem Ziady, Anthony Sabulski, Sonata Jodele, Alix E Seif, Stella M Davies, Benjamin L Laskin, Jason T Blackard
51B	Retinal pathways to the midbrain: characterizing olivary pretectal nucleus circuits in light-driven physiology Burgundy A Walters, Rosheeta Shaw, Diego C Fernandez
52A	The cross-link between mitochondrial DNA mutations in the polymerase gamma mutator mouse and the severity of traumatic osteoarthritis Nada H Warda, Abdulkadir Nur, Amogh Kankanwadi, Madison M Buckles, Huzafa Khanzada, Ethan Hyrne, Abduallah Ahmed, Mohammad Y Ansari
52B	Using qPCR to detect *E. coli* in water samples Grace Wiltsey, Eilee Ossont, Ellie Gagliani
53A	Evaluating the efficacy of a 3D-printed partial occlusion device (POD) in rat femoral artery microsurgical anastomosis revision Shahabeddin Yazdanpanah, Yuzhu Huang, Jonas Zhao, Elan Shukhmakher, Omer Bilal, Abraham Joshua Johnson, Hui Zhang, Sharon C Usip, Jennifer Baccon, Fayez F Safadi, Yelena Akelina
53B	A 3D-cardiac organoid model to mimic myocardial infarction in a dish Adel Kanaan, Salvia Zafar, Syed A Ashraf, Divya Sridharan, Mahmood Khan

OPS2025 Keynote Lecturer

Katsu Funai, PhD

Associate Professor

Department of Nutrition & Integrative Physiology
Diabetes & Metabolism Research Center
Molecular Medicine Program
Eccles Institute of Medical Genetics

University of Utah
Salt Lake City, Utah

Katsu Funai is an associate professor of nutrition and integrative physiology at the University of Utah. His lab has been continuously funded by the National Institutes of Health (NIH) to study the role of lipids in bioenergetics. Funai, from Japan, received his BS/MS at Boston University and earned his PhD at the University of Michigan. He was a postdoctoral fellow at Washington University–St Louis. Funai opened his lab at East Carolina University in 2013. He moved to the University of Utah in 2017 and, since that time, he has mentored 15 graduate students, 9 postdoctoral fellows, and 34 undergraduate or postbaccalaureate students as their primary research advisor. Together, these scholars have been the recipients of a total of 72 awards (49 of which were extramural) including fellowships from the NIH and from the American Heart Association. On average, PhD students in the Funai lab have published 2.8 first-author papers in their 4.4 years in his laboratory. Email: kfunai@utah.edu

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Abstracts

OPS2025 Keynote Address

Finding your own path to make an impact

Katsu Funai

Department of Nutrition & Integrative Physiology, University of Utah, Salt Lake City, Utah

In the last 12 years, my laboratory has studied mitochondrial oxidative phosphorylation as a critical cellular process that responds to changes in nutrient supply or energy demand to promote metabolic adaptations. We have identified key new mechanisms by which these adaptations alter propensities for metabolic diseases. Establishing research niche is an essential process for achieving research independence and autonomy, but it is a difficult journey filled with uncertainties. Exploration of the unknown by definition prompts us to distance ourselves from things that are familiar. I believe a key answer to this challenge is to harness diversity in each of our experiences. Through the lens of my own career, it is clear that my success was shaped by my choice to pursue topics that felt relevant to me, even if there were clear obstacles. The ability to lead a team of scientists, the courage to develop new ideas, methods, and models, and the patience to persevere when times are tough, all came from channeling in my personal experiences.

Oral Presentations

Oral Presentation # 1

Effect of charged polymers and charged lipids on the biophysical study of membrane proteins

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Membrane proteins are crucial targets for drug development; however, studying them using biophysical and magnetic resonance spectroscopic techniques is challenging due to the need for a membrane-like native environment, which helps maintain stability and integrity outside the native cellular environment. Recently, polymers such as Styrene Maleic Acid (SMA) have become valuable tools for studying these proteins within lipid bilayers due to their ability to solubilize membrane proteins in their native environments. However, limitations in the use of SMA copolymers have led to the development of SMA derivatives. In this study, we explore the effect of the charge properties of these SMA derivatives on the lipid bilayer encapsulating membrane proteins, which may also carry charges. We employed neutrally charged, positively charged, and negatively charged SMA-derivative copolymers (SMA-Neut, SMALP-BZ30, SMA-Pos, SMA Glu, and SMA-AE) to investigate their impact on bilayers composed of 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC), 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphoglycerol (POPG), and 9:1 molar ratio mixture of POPC and POPG. Techniques such as dynamic light scattering (DLS), electron paramagnetic resonance (EPR), and solid-state nuclear magnetic resonance (ssNMR) were utilized to characterize the interactions between the polymers and the lipid bilayers. Our findings indicate that the electrostatic interactions between charged polymers and lipids can significantly alter the native environment of the bilayer, potentially affecting the stability and function of encapsulated membrane proteins. These results underscore the importance of considering polymer-lipid electrostatic interactions when selecting SMA derivatives or other charged polymers for biophysical studies of membrane proteins, as the choice of polymer can significantly impact the integrity and behavior of the lipid bilayer system.

Oral Presentation # 2

Restoring T cell power: mRNA nanoparticles boost T cell immunity in head and neck cancer

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Head and neck squamous cell carcinoma (HNSCC) is an aggressive malignancy with poor immunotherapy response rates, with only ≈20% of patients benefiting

from current treatments. T cell-mediated cytotoxicity is critical for effective anti-tumor immunity; however, tumor-infiltrating T cells in HNSCC exhibit functional impairment, in part, due to downregulation of Kv1.3 potassium channels, which are essential for calcium-dependent effector functions. We developed a targeted mRNA nanoparticle-based strategy to restore Kv1.3 expression in T cells and enhance their antitumor function. Kv1.3 mRNA was synthesized via in vitro transcription (IVT) and encapsulated within lipid nanoparticles (NPs) functionalized with anti-CD5 antibodies (CD5-NPs) to ensure T cell specificity. CD5-NPs demonstrated selective T cell attachment and endocytosis, effectively delivering Kv1.3 mRNA into the cytosol. In vitro, Kv1.3 mRNA delivery resulted in upregulated Kv1.3 expression and increased interferon-γ secretion in a dose-dependent manner. In vivo, humanized NSG mice bearing Cal27 HNSCC xenografts treated with Kv1.3 mRNA-loaded NPs exhibited enhanced CD8+ T cell infiltration and granzyme B expression within the tumor microenvironment, indicating the restoration of cytotoxic function. These findings support the therapeutic potential of nanoparticle-mediated Kv1.3 mRNA delivery as a novel immunotherapy platform to overcome T cell dysfunction and improve HNSCC treatment outcomes.

Oral Presentation # 3

The human glucocorticoid receptor variant rs6190 protects the heart from metabolic stress

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Objective: Insulin resistance is a key metabolic insult in heart failure with preserved ejection fraction (HFpEF). The human coding variant rs6190 (NR3C1 gene; c.71G>A, p.R24K) is a glucocorticoid receptor (GR) single nucleotide polymorphism (SNP) that is associated with improved cardiometabolic fitness in small cohorts with heterozygous carriers. However, the SNP mechanism of action remains undetermined. The objective of this study is to determine the extent to which the GR SNP protects heart metabolic function under metabolic stress through transcriptional changes. Methods and Results: We probed the large UK Biobank cohort and confirmed the beneficial SNP effect on cardiometabolic health parameters like BMI, body composition and glycemia for the first time across the zygosity scale (non-carriers, heterozygous, homozygous). We generated SNP-genocopying mice and found that the variant is indeed sufficient in homogenous genetic background conditions to protect the heart from the metabolic stress imposed by high-fat diet. Transcriptional and epigenomic profiling in heart unveiled the diacylglycerol kinase eta (gene name, Dgkh) as hyper-transactivation target of the mutant GR. Through gain- and loss-of-function genetic manipulations in heart in vivo, we found that Dgkh is indeed required and sufficient for the SNP effect on cardiac insulin sensitivity and metabolic flexibility. Moreover, the zygosity dependent SNP effect on Dgkh transactivation and insulin sensitivity was translatable to human iPSC-derived cardiomyocyte-like cells in isogenic conditions. Conclusions: Taken together, our data provides a cardiomyocyte-autonomous mechanism of cardiometabolic protection for this SNP, while discovering a new function for the diacylglycerol kinase eta in heart.

Oral Presentation # 4

Sting–IL-6 signaling in sensory neurons mediates cisplatin-induced neuropathic pain

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Viral infections commonly cause temporary pain and discomfort. These infections can sometimes lead to persistent painful neuropathies, highlighting an important link between viral recognition mechanisms and neuropathic pain. Our previous research established that stimulator of interferon genes (STING) signaling activation in sensory neurons is crucial for viral recognition and pain processing. Notably, the chemotherapy agent cisplatin, known to cause painful neuropathy, triggers the release of mitochondrial DNA (mtDNA) and activates STING signaling in acute kidney injury. We therefore hypothesized that cisplatin-induced painful neuropathy occurs through STING signaling activation in sensory neurons. Our findings demonstrate that wild-type (WT) mice treated with cisplatin developed mechanical hypersensitivity, characteristic of neuropathic pain. This response was accompanied by

increased cytosolic mtDNA levels and elevated expression of STING and pro-inflammatory cytokine interleukin 6 (IL-6) transcripts in dorsal root ganglia (DRGs), while type I interferon (IFNB1) remained unchanged. Consistent with these findings, conditional knockout mice lacking STING expression in nociceptive DRG neurons (Nav1.8-Cre;STINGfl/fl) showed reduced mechanical hypersensitivity after cisplatin exposure and failed to upregulate IL-6 in DRGs. Similarly, systemic administration of the STING antagonist C-176 attenuated mechanical hypersensitivity and normalized DRG IL-6 expression. Furthermore, IL-6-deficient mice exhibited the same phenotype as those with STING deletion or blockade, while loss of the interferon receptor (IFNAR) had no effect. These results confirm that STING operates through an IL-6-dependent downstream pathway after cisplatin exposure, which is independent of IFN signaling. Collectively, our findings reveal a novel mtDNA-STING-IL-6 signaling axis within sensory neurons that connects viral mechanisms to painful neuropathies, potentially offering new therapeutic targets.

Oral Presentation # 5

Mutation in polymerase gamma increases the severity of trauma induced intervertebral disc degeneration in a mouse model

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Introduction: Polymerase Gamma (PolgA) is the key enzyme responsible for the replication of mitochondrial DNA. Mutations in PolgA can interfere with mitochondrial function and impair tissue repair. Most individuals over the age of 40 develop some form of intervertebral disc degeneration (IDD). This generally happens as a result of aging or trauma. The purpose of the study was to observe the effect of mutation in the proofreading domain of PolgA on trauma-induced IDD. Methods: Annular needle puncture surgery (NPS) was performed on 10–12-week-old wild-type (WT) and PolgA mutant mice (n=5 per group), with the adjacent disc serving as a sham control. Two weeks after NPS, mice were euthanized and their tails were collected, fixed in 10% neutral buffered formalin, and decalcified. Subsequently, processed tissues were embedded, sectioned at 7 µm, and stained with Hematoxylin & Eosin, Alcian Blue & Picrosirius Red, and Picrosirius Red alone. Slides were scanned on an Olympus VS-120 slide scanner, and Olympus VS-ASW software was used to assess inflammation, nucleus pulposus (NP) height and width. Results: Compared to healthy discs, NPS significantly reduced NP width in both WT and PolgA mutant mice. PolgA mutant showed significantly reduced disc height after NPS, whereas the difference in wild-type mice wasn't significant. Notably, PolgA mutant NP width was lower than WT; however, the difference was not statistically significant. Interestingly, the aspect ratio of the disc in PolgA mice was significantly higher than the aspect ratio in WT mice. Alcian blue staining showed a reduction in the extracellular matrix in PolgA mutant compared to WT mice. The PS Red staining revealed higher fibrosis in the PolgA mutant damaged disc, compared to WT mice discs. Conclusion: The mutation in PolgA resulted in an increased severity of trauma-induced degeneration of intervertebral discs in mice.

Oral Presentation # 6

Role of ACC1 in rewiring chondrocyte metabolism during obesity and injury-associated osteoarthritis

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Aging and obesity are major risk factors for osteoarthritis (OA), but how they interact to disrupt cartilage metabolism remains unclear. Previously, we reported that protein post-translational malonylation (MaK) is increased in obesity and is associated with dysregulated cellular metabolism in chondrocytes. Interestingly, the enzyme that produces the precursor for MaK, acetyl-CoA carboxylase 1 (ACC1), is significantly increased in cartilage in both aging and obesity conditions. We hypothesized that ACC1 upregulation drives MaK, altering chondrocyte metabolism and promoting OA progression. To test this, we generated *ACC1-CKO* (*Aggrecan-Cre^{ERT2}:ACC1$^{flox/flox}$*) mice by crossing *Aggrecan-Cre^{ERT2}* mice with WT mice (ACC1$^{flox/flox}$) and used tamoxifen injections (100 mg/Kg of body weight) to induce knockout cartilage specifically. Two cohorts were studied: (1) WT and *ACC1-CKO* mice fed a low-fat diet (LFD, 10% fat) or high-fat diet (HFD, 60% fat) for 25 weeks, and (2) WT and *ACC1-CKO* mice subjected to non-invasive anterior cruciate ligament rupture (ACLR) to model post-traumatic OA (PTOA). There were no notable

metabolic differences detected between WT and *ACC1-CKO* mice. Histopathological analysis followed by OARSI and Mankin scoring of the mice knee joints from the diet study revealed that *ACC1-CKO* mice exhibited decreased cartilage damage and limited loss of proteoglycan staining even in HFD group. *ACC1-CKO* mice subjected to non-invasive ACLR showed protection against the development of PTOA compared to WT controls. Targeted metabolomics revealed that ACC1 loss altered glycolytic, pentose phosphate, and TCA cycle intermediates, with accumulation of branched-chain and aromatic amino acids. Proteomic analysis of anti-MaK enriched proteins showed reduced malonylation of enzymes involved in glycolysis, amino acid biosynthesis, pentose phosphate pathway, TCA cycle, and pyruvate metabolism. Functionally, ACC1 deletion suppressed basal mitochondrial respiration, enhanced glycolysis, and increased GAPDH activity, consistent with reduced GAPDH malonylation. Overall, cartilage-specific ACC1 knockout protected against both obesity-induced OA and PTOA by reprogramming chondrocyte metabolism toward a glycolytic phenotype and reducing enzyme malonylation. These findings establish ACC1 as a key regulator of cartilage metabolism and OA pathogenesis.

Oral Presentation # 7

IL-3/IL-3 receptor contributes to skeletal sexual-dimorphism in a pre-clinical model for non-syndromic autosomal recessive intellectual disability

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Intellectual disability (ID) affects 1–3% of the global population, with a U.S. pediatric prevalence of 2.2% between 2019 and 2021. While X-linked causes of ID are well characterized, many autosomal-recessive forms remain incompletely defined. One such disorder is non-syndromic autosomal-recessive ID (NS-ARID) caused by mutations in TRAPPC9, which has been associated with microcephaly, obesity, and skeletal abnormalities. Recent reports suggest additional skeletal and dental manifestations, though the mechanisms linking TRAPPC9 dysfunction to bone remain unknown. Interestingly, TRAPPC9 knockout (KO) mice exhibit sex-dependent behavioral differences, raising the possibility of similar effects in skeletal homeostasis. To address this, we investigated bone mass, osteoclast activity, and cytokine signaling in male and female TRAPPC9 KO mice at 6–8 weeks and 30–35 weeks of age. Bone architecture was analyzed by micro-computed tomography, serum cytokines quantified by Olink multiplex assays, and osteoclast differentiation assessed from bone marrow precursors. Expression of interleukin-3 (IL-3) and its receptor CD123 was evaluated in humeri by qPCR. Our results revealed a striking sexual dimorphism. While young KO mice showed no difference in bone volume fraction (BV/TV), aged KO females displayed significantly increased BV/TV, whereas aged KO males exhibited reduced BV/TV. Serum profiling demonstrated elevated IL-3 levels in KO females but not males. Correspondingly, IL-3 expression was consistently upregulated in females at both ages, while males showed reduced expression when young but increased levels with age. CD123 expression followed a parallel pattern: enhanced in females and decreased in males. These findings indicate that TRAPPC9 regulates bone homeostasis in a sex-dependent manner, potentially mediated through IL-3 signaling and its effects on osteoclast differentiation. This is the first study to define the skeletal phenotype of TRAPPC9 KO mice, providing novel.

Oral Presentation # 8

Role of muscle-specific FSP27 in energy production and whole-body glucose

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Skeletal muscle (SkM) plays a central role in whole-body energy metabolism, influencing systemic glucose homeostasis, substrate utilization, and overall metabolic health. Our study identifies Fat- Specific Protein 27 (FSP27), previously characterized in adipose tissue, liver and endothelium, as a key modulator of energy

metabolism in skeletal muscle. FSP27 is highly expressed in SkM, and global Fsp27 knockout (Fsp27-/-) mice display markedly impaired energy balance and muscle function. To assess the muscle-specific role of FSP27 in SkM metabolism, we generated a musclespecific Fsp27 knockout mouse model (M-Fsp27-/-). These mice exhibited significantly reduced ATP levels, citrate levels, and reduced energy expenditure compared to their floxed littermate controls, which highlights the critical role of SkM FSP27 in maintaining muscle observed in both sexes, indicating no sexual dimorphism. Mechanistically, we found that FSP27 interacts with lactate dehydrogenase A (LDHA), and its expression inversely correlates with lactate production in SkM, suggesting a regulatory role in glycolytic flux and substrate preference. M-Fsp27-/- mice displayed reduced exercise endurance and muscle strength, reinforcing the physiological impact of impaired energy metabolism. Supporting these findings, our human data reveal a positive correlation between SkM FSP27 expression and performance metrics such as aerobic capacity, muscle strength, and responsiveness to exercise training, which are closely linked to efficient metabolic function and glucose homeostasis. As a systemic outcome, M-Fsp27-/- mice exhibited impaired glucose and insulin tolerance, highlighting the downstream impact of muscle energy deficiency on whole-body glucose homeostasis. Collectively, our findings establish FSP27 as a novel regulator of skeletal muscle energy metabolism, exerting effects on substrate utilization and whole-body glucose homeostasis.

Oral Presentation # 9

Cartilage-specific deletion of acetyl-CoA carboxylase 1 (ACC1) disrupts growth plate development and alters skeletal growth

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Acetyl-CoA carboxylase 1 (ACC1) is the rate-limiting enzyme for de novo fatty acid synthesis, yet its role in cartilage and skeletal development is poorly defined. We investigated how cartilage-specific ACC1 deletion affects chondrocyte maturation, growth plate organization, and bone modeling. ACC1 conditional knockout (ACC1-CKO) mice were generated by crossing Aggrecan-CreERT and ACC1^fl/fl mice, with Cre activation induced via tamoxifen during early postnatal development. Body weight, length, and composition were measured at one month, and bone microarchitecture was analyzed at four months using micro-computed tomography (micro-CT). Growth plate morphology and chondrocyte dynamics were assessed with Safranin O/Fast Green staining, immunohistochemistry (COLX, OSX, PCNA), and TUNEL assays. ACC1-CKO mice showed reduced body size and fat mass, with lean mass unaffected. Histology revealed severe disorganization of proliferative chondrocyte columns, contrasting with the well-aligned columns in wild-type controls. At four months, micro-CT demonstrated decreased trabecular bone volume, thickness, and density, indicating compromised bone quality. Immunostaining showed extended COLX expression into the proliferative zone, decreased OSX, elevated PCNA, and increased apoptosis, suggesting disrupted coordination of proliferation and differentiation. These results identify ACC1 as a crucial regulator of chondrocyte lipid metabolism and endochondral ossification. Loss of ACC1 uncouples lipid synthesis from growth plate regulation, leading to stunted skeletal growth and abnormal bone architecture. Beyond its role in osteoarthritis, ACC1 acts as a metabolic checkpoint linking lipid biosynthesis to chondrocyte maturation. Targeting ACC1 may provide therapeutic opportunities to support growth plate integrity, cartilage repair, and bone health.

Poster Presentations

Poster # 1A

Sleep-like states in mosquitoes impact pre- and post-blood feeding behavior and physiology

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Sleep occurs in most, if not all, animal species, including insects, where this state influences different biological processes such as cognition, reproduction, and immunity. However, little is known about sleep in blood-feeding arthropods, especially mosquitoes. Here, we characterized sleep-like states in mosquitoes using conventional behavioral correlates, evaluated the impact of sleep deprivation on important indices of vector competence, and determined the influence of

blood meals on the behavioral rhythms of activity and sleep. Posture metrics revealed a clear distinction between awake and sleep-like states in multiple mosquito species, which correlated with a decrease in stimulation by host cues. Infrared monitoring of activity showed that mosquitoes have different periods of prolonged immobility influenced by species and sex. Nighttime and daytime sleep deprivation through the delivery of vibration stimuli resulted in sleep rebound in *Aedes aegypti* and *Anopheles stephensi*, respectively, and caused the suppression of host landing and blood feeding in *Ae. aegypti*. Furthermore, the ingestion of vertebrate and artificial blood diets by *Ae. aegypti* showed that hemoglobin intake is linked to reduced post-feeding activity and increased sleep amounts in mosquitoes. Lastly, short periods of sleep deprivation in *Ae. aegypti* during the post-blood feeding period of inactivity did not alter egg production and timing of deposition. Altogether, these results suggest that sleep-like states occur in mosquitoes and influence aspects of mosquito biology important for disease transmission.

Poster # 1B

Post-transcriptional regulation of adrenal–heart crosstalk in heart failure with preserved ejection fraction

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Introduction: Heart Failure with Preserved Ejection Fraction (HFpEF) is a rising unmet medical need with limited effective treatment. HFpEF has multiple risk factors including obesity, hypertension, and diabetes. Chronically elevated catecholamine level is a hallmark of metabolic disorders and heart failure. However, the role of catecholamine in the pathogenesis of HFpEF remains unknown. We have previously identified glutamyl-prolyl-tRNA synthetase 1(EPRS) as a gene significantly involved in adrenal gland growth post chronic isoproterenol treatment and a novel regulator for catecholamine synthesis through regulating key enzymes expression at post-transcriptional level through its noncanonical function. Methods: High fat diet (HFD) and N(ω)-nitro-L-arginine methyl ester (L-NAME) were utilized to induce HFpEF in C57B/L mice and the catecholamine synthesizing protein expression changes in adrenal gland were measured. An adrenal gland specific EPRS knockout mouse model was established through crossing EPRSfl/fl with PNMT-Cre (EPRS-aKO) and subjected with L-NAME/HFD induced HFpEF. Cardiac contractile and diastolic functions were determined. Glucose tolerance and insulin tolerance tests were exploited to examine the metabolic impact of ERPS inactivation in adrenal gland. Masson Trichrome staining was performed to determine cardiac fibrosis. Exercise endurance test was also performed. Results: After 14 weeks of L-NAME/HFD challenge, we observed a significant induction of EPRS and catecholamine synthesizing enzymes protein expression in adrenal gland. EPRS-aKO mice were protected from obesity and diabetes compared to the control based on glucose tolerance and insulin tolerance tests. Further, EPRS-aKO mice were protected from L-NAME/HFD induced cardiac dysfunction based on improved left ventricular diastolic function and decreased expression of pathological markers as well as improved exercise endurance level. EPRS inhibition decreased cardiac hypertrophic response based on decreased cardiomyocyte cross sectional area. Conclusion: Our results demonstrate EPRS regulatory role in HFpEF pathogenesis. Targeting the newly identified EPRS-adrenal-heart crosstalk may serve as a basis for novel therapies for HFpEF.

Poster # 2A

LRRC14B is essential for cardiac function via sarcomeric protein quality control

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Introduction: Leucine Rich Repeat Containing 14B (LRRC14B) is a cardiac-enriched gene with a completely unknown function. Analysis of the GTEx dataset identified LRRC14B as one of the most highly enriched transcripts in the heart. It is cardiomyocyte-specific and down-regulated in heart failure (HF), yet its function remains completely unknown. Objective: To elucidate the functional and mechanistic role of LRRC14B in the heart. Methods & Results: We generated Lrrc14b knockout (Lrrc14b-null) mice, using wild-type (WT) littermates as controls. Lrrc14b-null mice developed

progressive systolic dysfunction, with reduced ejection fraction (EF) and left ventricular (LV) dilation from 6 to 12 months of age in both sexes, without evidence of hypertrophy or fibrosis. Notably, we re-expressed Lrrc14b in Lrrc14b-null mice with a MyoAAV-Lrrc14b vector, and systolic function was rescued in both sexes. Lrrc14b contains LRR motifs known to mediate protein-protein interactions, thus, we queried the BioGRID database and found that LRRC14B was predicted to interact with BAG3 and HSPA8, core components of the chaperone assisted selective autophagy (CASA) complex. This complex mediates sarcomeric protein quality control (SQPC), which is essential for Z-disc stability and myofibrillar organization. Co-immunoprecipitation confirmed these interactions. Lrrc14b was further required to maintain normal protein (but not mRNA) levels of Bag3 and Hspa8, and for proper Bag3 localization. Autophagy was impaired in Lrrc14b-null hearts, as shown by accumulation of LC3-I over LC3-II, p62 and ubiquitin-conjugated proteins. Furthermore, we identified the cardiomyocyte-specific Z-disc protein Nebulette as a myofibrillar Lrrc14b interactor that accumulates in the insoluble protein fractions of Lrrc14b-null hearts. Conclusion: LRRC14B is essential for postnatal cardiac function, stabilizing CASA and maintaining SQPC. These findings position LRRC14B as a promising target for HF research.

Poster # 2B

Shear stress-induced calcium signaling dynamics in TIE2-L914F mutant endothelial cells in venous malformations

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Introduction: Venous malformation (VM) is a chronic disease mainly seen in the head and neck region of young children and manifest in dilated veins causing chronic pain, swelling, and in advanced cases, coagulopathy and spontaneous bleeding. Yet no targeted curative treatments have been developed. Sporadic VMs are usually caused by somatic mutation in TEK gene, encoding EC receptor tyrosine kinase TIE2. TIE2-L914F is the most common sporadic point mutation leading to ligand independent hyperactivation of TIE2 and cellular overgrowth. TIE2 is expressed in endothelial cells (ECs) and is essential for vascular development and in adult, for vascular remodeling and homeostasis. ECs form the inner lining of blood vessels and therefore, are constantly under the laminar shear stress by blood flow. In ECs both TIE2 and mechanosensitive calcium channels are required for the EC to respond to shear stress. Under flow, the intracellular $[Ca^{2+}]_i$ rises in a dose dependent manner. Elevated intracellular Ca^{2+} binds to a calcium binding protein called Calmodulin (CaM). When intracellular Ca^{2+} rises, CaM binds directly to the cytoplasmic tail of TIE2 leading to TIE2 dephosphorylation and reduced receptor activation. This Ca^{2+}/CaM mediated inhibition of TIE2 acts as a negative feedback mechanism to regulate angiogenesis during vascular development. While TIE2 downstream pathways and its role in the response to shear stress have been studied, the functional and phenotypical changes as well as the role of calcium signaling and dynamics in EC expressing the TIE2 mutation L914F in response to shear stress are still poorly understood. Methods: We used ibidi pump system to apply precise, reproducible, and unidirectional flow to wild type and L914F mutated human umbilical vein endothelial cells (HUVECs), enabling physiologically relevant modeling to study the effects of this mutation on proliferation, phenotype, and intracellular Ca^{2+} concentration of ECs under physiological and pathological shear stress.

Poster # 3A

Sub-second release of neurochemicals from CD4+CD25+ regulatory T cells (Tregs)

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The neuroimmune system is a complex network in which neurochemicals released by immune and neuronal cells act as critical messengers, regulating communication and functional responses in the body. Neuro-immune interactions are thought to contribute to the progression of neurodegenerative diseases. Therefore, identifying the primary neurochemicals released from immune cells can help understand the dynamics of neuroimmune signaling and molecular mechanism of neuroinflammation. While research has explored neuro-immune interactions, studies on the rapid release of neurochemicals within immune cells are limited. Here, we have discovered that Tregs, a specialized subset of T lymphocytes that play a crucial role in preventing autoimmunity, are capable of releasing neurochemicals on a sub-second time scale. We have used Fast Scan Cyclic Voltammetry (FSCV); a powerful electrochemical technique with excellent spatial and temporal resolution

to detect neurochemicals in this sub-second time scale. Our findings so far demonstrate that Tregs produce different types of neurochemicals on the same timescale as neurons. Given that neurochemicals suppress Treg function and are linked to neurological disorders, this project will advance understanding of how Treg-derived neurochemicals may be harnessed for therapeutic benefits in the future.

Poster # 3B

Role of acute alcohol-induced acetylation in tauopathy

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Background: Alzheimer's disease (AD) is a major concern in aging populations, and evidence suggests alcohol intake may accelerate brain aging and elevate AD risk. Normal aging involves altered proteostasis and cognitive decline, regulated in part by tau phosphorylation and acetylation. In AD, tau and histone acetylation are disrupted; however, the impact of alcohol on acetylation-dependent tauopathy remains unclear. Method: This study examined the effects of time- and dose-dependent acute alcohol exposure on tauopathy markers were assessed with EtOH-d6- and ^2H_2O-labeled mass spectrometry tracing alcohol's impact on cortical acetylation and tau turnover, respectively Results: A single EtOH dose (5 mg/g BW) transiently elevated Tau174ac (peaking at 2 h) and progressively increased TauS202p and total tau in 9-month-old htau mice ($P<0.05$). Higher EtOH doses (3–5 mg/g BW) promoted acetylation-dependent tau accumulation, whereas acute EtOH exposure elevated H4K16 and H3K9 acetylation at all doses, accompanied by increased CBP and MOF1 expression, without changes in Sirt1, Sirt6, or other KATs/KDACs linked to tau or histone acetylation. Mass spectrometry showed EtOH-d6-derived acetate contributed to histone but not tau acetylation. A ^2H_2O-based turnover study revealed faster turnover of multiple proteins, but reduced turnover of tau and synuclein in tauopathy mice versus wild-type. Phosphorylated tau proteoforms also exhibited longer half-lives than native forms, suggesting alcohol may exacerbate tauopathy indirectly by impairing tau turnover. Conclusion: These findings suggest that alcohol-induced disruptions in brain acetylation may accelerate cognitive decline by driving epigenetic changes and impairing tau turnover. Future studies will examine the effects of chronic alcohol exposure on tauopathy and test whether histone acetylation–mediated transcriptional changes in tau degradation pathways contribute to its progression.

Poster # 4A

Demographic and medical factors associated with speech-evoked EEG in preterm infants

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Background: Infants born very and extremely preterm (≤ 32 weeks gestational age [GA]) are at elevated risk for speech and language disorders (SLD), yet there is currently no reliable biomarker to identify which infants will be affected. Early neural measures such as the speech-evoked Mismatch Response (MMR) may serve as predictors of language outcomes, but the influence of medical and demographic factors on MMR remains underexplored. Objective: This study performed an exploratory analysis to investigate associations between medical and demographic factors and MMR area in preterm infants at 3 months corrected age (CA). Methods: Ninety-two very (28–32 weeks GA) and extremely (< 28 weeks GA) preterm infants were recruited from five NICUs across Cincinnati and underwent speech-evoked EEG at 3 months CA. MMR area (250–550 ms) was then calculated from responses averaged across five frontal electrodes. Relevant demographic and medical factors were prospectively collected. Data were analyzed with generalized linear regression, adjusting for age and examining interactions. Results: Mismatch Response area was significantly associated with race ($p < 0.001$), Maternal Education Level (MEL) ($p < 0.001$), GA ($p < 0.001$), and Bronchopulmonary Dysplasia (BPD) grade ($p = 0.005$). Reduced MMR area was observed among infants of color and those with lower GA, whereas infants with higher MEL and no BPD exhibited more robust MMR responses. Brain abnormality scores were not significantly associated with MMR area. Conclusion: These findings demonstrate that demographic (race, MEL) and medical factors (GA, BPD) significantly influence early speech-evoked neural responses in preterm infants, highlighting the importance of considering social and perinatal

variables when interpreting EEG biomarkers. Future work will compare preterm and full-term cohorts and assess associations between MMR area and 3-year language outcomes to inform early risk stratification and intervention.

Poster # 4B

Erythroid-specific, inducible CDAN1Δ/Δ mouse model phenocopies congenital dyserythropoietic anemia type-Ia

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Congenital dyserythropoietic anemias (CDAs) are a heterogenous group of inherited blood diseases, characterized by ineffective erythropoiesis, hemolysis, secondary iron overload, and the presence of bi- or multinucleated erythroblasts in the bone marrow (BM). CDA types are classified by their causative gene mutations, when known. CDA type-Ia (CDA-Ia) is caused by biallelic pathogenic variants in the CDAN1 gene, which encodes Codanin-1, a highly conserved protein. The typical clinical presentations for CDA-Ia include hemolytic anemia with relative reticulocytopenia, suggesting ineffective erythropoiesis, binucleated erythroblasts in the BM, and, under transmission electron microscopy (TEM), a "Swiss cheese" appearance in the heterochromatin of erythroid precursors. This observation and the role of CDAN1 in erythropoiesis are still not fully understood, highlighting the need for more investigations. Previous efforts to make an erythroid-specific deletion of CDAN1 in mice utilized the constitutive erythroid-restricted Epor-cre recombinase. This model was embryonal lethal by mid-gestation due to severe anemia, allowing for limited in vivo studies. To circumvent the embryonal lethality, we used an inducible, erythroid-restricted cre recombinase, Gata1creERT2. We generated control and experimental mice via weaning 4-week-old mice onto tamoxifen chow for 2–3 months. Codanin-1-deficient (CDAN1Δ/Δ) mice have a macrocytic anemia and have evidence of secondary iron loading. Flow cytometry of CDAN1Δ/Δ erythroblasts revealed a reduction in late-stage erythroblasts not only in the bone marrow but also in the spleen, compared to controls, demonstrating this hallmark of ineffective erythropoiesis both in medullary and extramedullary erythropoiesis. CDAN1Δ/Δ erythroblasts presented with the "Swiss cheese" phenotype under TEM. After flow sorting discrete BM erythroblast populations, we assayed for chromatin accessibility, and our preliminary analysis suggests differential gene accessibility between control and CDAN1Δ/Δ erythroblasts. In conclusion, we have generated a reliable model of CDA-Ia which we will use as a platform to investigate the role of CDAN1 in chromatin organization and condensation during erythropoiesis.

Poster # 5A

Membrane topology and dynamics of the antimicrobial peptide gp28: lipid-specific interactions revealed by EPR spectroscopy

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We investigated the structural dynamics and membrane topology of gp28, a cationic antimicrobial peptide encoded by the ϕKT podophage, which infects Escherichia coli. Using electron paramagnetic resonance (EPR) spectroscopy with site-directed spin labeling (SDSL), we examined gp28's conformational behavior in different lipid bilayers, including POPC, POPE, and POPC/POPG (3:1). Our results show that gp28 exhibits strong lipid-specific interactions. In the negatively charged POPC/POPG bilayers, the peptide displayed reduced mobility, consistent with tighter lipid–peptide interactions, whereas its behavior in neutral bilayers such as POPC or POPE was more dynamic. Spectral analysis of both vesicles and mechanically aligned samples further revealed differences in orientation and topology: helical regions of gp28 aligned parallel to the membrane surface, a configuration that promotes electrostatic engagement with lipid headgroups and contributes to membrane destabilization. These findings provide mechanistic insight into gp28's role in bacterial lysis, demonstrating how lipid composition modulates peptide insertion, alignment, and activity. More broadly, the study highlights the power of EPR spectroscopy for probing membrane-active peptides and suggests that gp28's lipid-dependent interactions are central to its antimicrobial function. In conclusion, our work advances understanding of gp28's structural and functional properties, laying the groundwork for future studies of

its activity in diverse membrane environments and supporting the potential of phage-derived peptides as novel antimicrobial agents.

Poster # 5B

Combining immune checkpoint inhibitors and anti-angiogenesis approaches: treatment of advanced non-small cell lung cancer

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The integration of immune checkpoint inhibitors (ICIs) with anti-angiogenic agents has emerged as a promising therapeutic strategy for non-small cell lung cancer (NSCLC). Angiogenesis contributes not only to tumor growth but also to immune evasion through abnormal vasculature and a hypoxic microenvironment. Combining ICIs with vascular endothelial growth factor (VEGF) inhibitors has the potential to normalize tumor vasculature, enhance immune cell infiltration, and improve treatment efficacy. Currently, the only FDA-approved regimen combining an ICI and VEGF inhibitor in NSCLC is atezolizumab/bevacizumab with chemotherapy. However, early clinical evidence indicates that the combination of nivolumab, a programmed death-1 (PD-1) inhibitor, and bevacizumab, a VEGF inhibitor, is associated with encouraging clinical outcomes and a favorable adverse effects profile. This approach may be particularly beneficial in patients lacking sensitizing mutations in EGFR, ALK, or ROS1, where targeted therapies are less effective. This study evaluates the therapeutic potential of nivolumab and bevacizumab in NSCLC. While results to date are promising, most available data come from early-phase or small-scale trials, underscoring the need for more robust evidence. Emphasis should be placed on longitudinal sampling to monitor changes in the TME and immune system functionality. Future research should focus on developing more comprehensive biomarker panels that combine immune markers, angiogenesis markers, and characteristics of the TME. Gaining a better understanding of resistance mechanisms could help inform the design of combination therapies and improve how treatments are timed to extend patient response.

Poster # 6A

Fat-specific protein 27 (FSP27) regulates intramuscular fat storage for skeletal muscle function

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Fat-specific protein 27 (FSP27) results lipid metabolism in adipose tissue. We recently demonstrated that despite exhibiting higher oxidative metabolism, 10-month-old global Fsp27-/- mice displayed reduced skeletal muscle (SkM) function. We hypothesized that chronically elevated oxidative metabolism during the period of 10 months might cause cumulative muscle stress or inefficiency, causing gradual decrease in muscle function. To test our hypothesis, we performed muscle endurance and strength tests using the treadmill running endurance test and 4-limb hanging grid, respectively, at 6 and 2 months of age. These tests were performed on both male and female Wild Type and Fsp27-/- mice. Surprisingly, Fsp27-/- mice showed reduced running endurance and muscle strength as early as 2 months, as we previously observed in 10-month-old mice. The Fsp27-/- mice also displayed lower adipose and SkM triglyceride levels, suggesting FSP27 as a promoter of intramyocellular triglyceride storage, a required fuel source for muscle function. As opposed to our hypothesis, the data indicates that the absence of Fsp27 caused the depletion of intramuscular and adipose triglyceride stores, limiting the availability of lipid-derived energy during muscle function.

Poster # 6B

Altered nighttime sleep and activity patterns as mechanisms of ectoparasite resistance

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Parasites negatively impact host fitness and act as strong selective forces that can drive the evolution of resistance traits. Previously, we showed that *Drosophila melanogaster* evolved behavioral immunity to *Gamasodes queenslandicus* mites during artificial

selection. Here, we reveal that selection for mite resistance led to transcriptional changes in metabolic pathways. Mite-resistant flies also showed reduced starvation resistance and greater depletion of nutrient reserves. These lines exhibited elevated nighttime activity, decreased sleep, and higher oxygen consumption. Across *D. melanogaster* lines with variable sleep durations, reduced sleep was positively associated with increased mite resistance. Restricting activity in resistant flies during parasite exposure diminished their resistance advantage compared to controls. Together, these findings suggest that resistance to ectoparasites involves increased nighttime activity and metabolic investment, which comes at a cost to starvation resilience.

Poster # 7A

Withdrawn

Poster # 7B

Long-term stability of urinary and kidney protein biomarkers for diabetic kidney disease

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The NIH promotes the use of large clinical trials biorepositories to accelerate the discovery of biomarkers for diabetic kidney disease (DKD). Access to such repositories could significantly advance research on the molecular pathways connecting diabetes to cardiovascular and kidney disease, enhancing both retrospective and prospective studies. However, a major limitation is that little is known about the stability of proteins in samples stored for several years. Most published reports evaluate protein integrity for only a week up to one year, and in some cases, in the absence of protease inhibitors and with uncontrolled storage conditions, leaving considerable uncertainty regarding the long-term reliability of biobanked samples for retrospective research. To address this, we evaluated the stability of key DKD biomarkers in human urine and murine kidney lysate samples collected 10-15 years ago by our group, stabilized with protease inhibitors, and stored continuously at –80 °C. We were particularly interested in the recovery of urinary neprilysin (NEP) and angiotensin-converting enzyme 2 (ACE2), which we propose as early biomarkers of DKD. Using western blot, ELISA and enzyme activity, our analysis confirmed that NEP, ACE2 and albumin remained readily detectable, demonstrating that our protocol efficiently maintained protein integrity for over a decade. Significantly, recovery of proteins from urine and kidney lysates in which baseline levels are inherently low underscores the value of optimized preservation approaches to ensure maximization of the utility of biobanked samples. Confirming the stability of NEP and ACE2 for over a decade validates the use of long-stored specimens from repositories such as those provided by NIDDK and NHLBI. This finding opens significant opportunities to identify and study these novel urinary markers of DKD without the immediate need for new, large-scale clinical studies, thereby not only accelerating research on the link between diabetes and its complications but also reducing cost.

Poster # 8A

A rapid, non-destructive, specific method for intervertebral disc imaging with KI-enhanced micro-CT

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Intervertebral disc (IVD) degeneration (IDD) is the leading cause of low back pain, a condition that affects one in four adults over any three-month period and nearly 40 million members of the workforce each year. Radiographic evidence is seen in 40% of adults over 40, rising to nearly 90% by age 80. The economic impact of IDD is substantial, with low back and neck pain accounting for $134.5 billion in healthcare costs annually, more than any other medical condition. Early degeneration of the nucleus pulposus (NP) is a key diagnostic marker of IDD but is frequently overlooked on standard Magnetic Resonance Imaging. Micro-computed tomography (micro-CT) produces detailed three-dimensional (3D) images of bone, yet its application to soft tissue has been limited by inadequate contrast agents. In this study, we tested potassium iodide (KI) as a contrast agent for visualization of IVDs in multiple preclinical animal models. Spines and tails from mice, rats, rabbits, and sheep were incubated in 25% KI for allotted times and imaged using micro-CT at 10 um resolution. IDD was modeled by annular puncture of

caudal IVDs in 12-week-old mice (n=10) with sham controls, and age-related changes were evaluated in 18 to 21-month-old mice (n=5). Findings were validated in rabbit and sheep IVDs (n=5) and compared to histology. KI staining allowed for strong X-ray attenuation and reproducible 3D measurements of IVD height and volume across species. Punctured IVDs demonstrated a significant reduction in NP area, height, and volume (p=0.014), and aged spines displayed degeneration parallel to histological results. KI was able to be rinsed out of the sample post-scan, preserving samples for subsequent immunostaining and histology. These results position KI as a simple, rapid (<1hr), reversible, and histology-compatible approach for micro-CT-based IVD imaging, highlighting its translational potential to both preclinical and clinical evaluation of IDD.

Poster # 8B

Determining changes in gene expression from microgravity through qRT-PCR

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The effects of microgravity and their impacts on the human body continue to be an important area of research as the process of advancing space exploration continues forward. Skeletal muscles play a substantial role in human health and are greatly impacted by the effects of microgravity. Sialic acid is known to play a crucial role in muscle function and is involved in some muscle loss disorders such as GNE Myopathy. This study aims to determine one possible mechanism of muscle atrophy when exposed to microgravity during spaceflight. The study aims to determine if exposure to microgravity, simulated by hind limb unloading in Wistar rats, reduces sialic acid in skeletal muscles, and therefore plays a role in the muscle atrophy experienced by astronauts. To assess muscle sialylation in these rats, qRT-PCR was used to measure the gene expression of several sialidase and sialyltransferase enzymes which regulate sialylation. Although this project is still in progress, we have been able to troubleshoot and refine our protocols greatly and are looking forward to continuing this research in the future.

Poster # 9A

Purines dynamically mediate astrocyte

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In neuroinflammation, astrocytes can adapt to a reactive state, undergoing morphological and molecular changes that result in altered cytokine production, receptor expression, and neurochemical release. Purines have come to the forefront as biomarkers of interest due to their role in the modulation of major neurotransmitters. Specifically, nucleoside derivatives, adenosine and guanosine, have increased in recognition due to their neuroprotective and immunomodulatory roles in the central nervous system (CNS). While adenosine has been extensively studied under pathological conditions, astrocytes have been identified as a primary source of extracellular adenosine during injury; the role of guanosine remains underexplored. Despite evidence showing that exogenous guanosine reduces neuroinflammatory damage, the mechanisms by which guanosine modulates astrocyte function during inflammation remain poorly defined. In this study, we investigate how guanosine influences astrocyte reactivity by engaging with purinergic receptors and activating the PI3K/AKT signaling pathway, leading to downstream changes in cytokine production, receptor regulation, and astrocyte phenotype. We utilized primary astrocyte cell culture treated with lipopolysaccharide (LPS) to induce a reactive astrocyte phenotype. Immunocytochemistry and flow cytometry were used to capture changes in astrocyte reactivity and surface receptor expression. ELISA assays quantified proinflammatory and anti-inflammatory cytokine release from these cells. Additionally, western blotting was used to assess expression levels of adenosine receptors (A1R and A2AR), equilibrate nucleoside transporters (ENT1 and ENT2), and PI3K/AKT pathway components. The use of selective PI3K/AKT inhibitors provided mechanistic insight into guanosine's signaling actions. Collectively, this approach aims to uncover novel pathways by which guanosine modulates astrocyte behavior during neuroinflammation, potentially revealing new therapeutics.

Poster # 9B

Engineering bacteria for a sustained release of mycosporine-like amino acid, shinorine, for gut and neurodegenerative disorders

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Shinorine, a UV-absorbing mycosporine-like amino acid, serves as a promising candidate for antioxidant and photoprotective applications. However, scalable production and delivery methods remain limited. Our recent work focuses on engineering Escherichia coli strains for shinorine biosynthesis, incorporating shinorine into outer membrane vesicles (OMVs). These vesicles may serve as vehicles for oral administration, enabling targeted access to tissues with the aim of harnessing shinorine's antioxidant properties. Notably, animal studies revealed that orally or systemically administered shinorine was detectable in serum and brain tissue suggesting both gut-blood axis and blood–brain barrier permeability. Additionally, in vitro studies on murine N2a neuronal cells revealed the potential for the use of shinorine to treat neurodegenerative disorders. Collectively, these findings highlight shinorine as a bioactive compound of interest for translational applications and the potential of engineered bacterial platforms and OMVs in developing next-generation therapeutics.

Poster # 10A

Exploring the effect of cortisol on antibody production

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Antibody production is a fundamental component of adaptive immunity. Production of antibodies is regulated by class switch recombination (CSR) and the 3' regulatory region (3' IgHRR) of the immunoglobulin heavy chain (IgH) gene. CSR enables B cells to transition from secreting IgM to producing other isotypes such as IgG, IgA, and IgE. Each antibody isotype has specialized immune function. Mouse studies support an essential role of the 3'IgHRR in CSR, and emerging evidence suggests that human-specific genetic variations within the 3'IgHRR may influence antibody production and potentially individual susceptibility to external factors. Hormonal factors (e.g., estrogen and cortisol) and environmental toxicants (e.g., dioxins) also modulate antibody production. However, gaps remain in understanding the precise molecular mechanisms underlying these effects, particularly regarding how the 3'IgHRR integrates environmental and hormonal signals to regulate IgH expression. This study aims to investigate how cortisol, dioxins, and combined exposures impact IgH gene regulation and antibody production in a human B-cell model.

Poster # 10B

Circadian disruption by artificial light at night alters activity and male mating in the tsetse fly *Glossina morsitans morsitan*

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Urbanization has transformed ecosystems worldwide, introducing new forms of sensory pollution that directly affect organisms. Among these, artificial light at night (ALAN) has steadily increased and is expected to continue rising, becoming a pervasive anthropogenic stimulus. As an unnatural light source, ALAN disrupts the natural light–dark cues essential for regulating biological processes. The tsetse fly *Glossina morsitans morsitans*, the primary vector of African trypanosomiasis, relies strongly on environmental light cues to regulate its daily and circadian rhythms and behaviors. Under a normal 12:12 light–dark cycle, male *Glossina* display the expected U-shaped daily rhythm of activity, with peaks at dawn and dusk. However, when exposed to ALAN, this bimodal activity pattern was disrupted, suggesting that their behavioral rhythms depend heavily on natural light cues during the night. To further investigate the effects of ALAN, we developed a male competition assay where ALAN-exposed and control males were paired with a virgin female. We measured mating latency, number of attempts, and duration of each attempt. Our results indicate that ALAN exposure alters circadian rhythms in ways that likely reduce mating performance and competitiveness. This work provides insight into how anthropogenic light pollution can influence vector behavior at multiple developmental stages, with potential consequences for both tsetse ecology and disease transmission.

Poster # 11A

Gut microbiome and type 1 diabetes: a possible link

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Type 1 diabetes (T1D) is a genetic disorder in which the immune system is triggered to attack and destroy insulin-producing pancreatic β-cells. Development of T1D requires a mutation in the human leukocyte antigen (HLA) gene complex, which is responsible for coding the major histocompatibility complex (MHC) receptors on antigen presenting cells. However, not all genetically predisposed individuals end up developing the disease, indicating T1D is triggered by external factors. Studies have indicated a link between human gut microbiota and T1D progression but have failed to link any specific microbial population to T1D development. Additionally, a correlation has been observed between T1D progression and a "leaky" gut syndrome, indicating that the thickness of the mucosal lining in the intestine potentially plays an important role in the gut microbiota's ability to trigger disease development. Research in our group is focused on finding a link between distinct gut microbe populations and their spatial arrangement as a result of mucosal thickness. Fluorescence in situ hybridization (FISH) combined with a lectin mucosal stain is used to visualize the bacteria in murine intestines. In FISH, a short sequence of complementary DNA with a fluorescent probe on the 5' end is created for each type of bacteria to be visualized. Combining these methods allows one to better understand how bacterial mimics may be able to trigger development of T1D in genetically predisposed individuals. At this time there are no definite findings as research is still ongoing. This research was made possible, in part, using the Cincinnati Children's Bio-Imaging and Analysis facility [RRID: SCR_022628].

Poster # 11B

Characterization of Nrac, a nutritionally regulated adipose and cardiac-enriched microprotein

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Objective: Nrac (nutritionally regulated adipose and cardiac-enriched gene) is a microprotein encoded by the long noncoding RNA A530016L24Rik. It is highly expressed in the heart, brown adipose tissue (BAT), and white adipose tissue (WAT), with expression reduced by fasting and obesity. While its biological function is unknown, prior work suggested plasma membrane localization in white adipocytes. This study aimed to define the molecular function and localization of Nrac in adipocytes and the heart. Methods and Results: To assess subcellular localization, we used a cardiomyocyte-targeted MyoAAV to deliver HA-V5-Nrac or GFP-HA-V5 (control) to 8-week-old C57BL/6J mice (2×10^{12} vg/kg, retro-orbital injection). Two weeks later, cardiomyocytes were isolated for immunostaining, and heart tissue was cryoembedded, sectioned, and stained with Oil Red O. Nrac localized specifically to the sarcoplasmic reticulum (SR), and its overexpression increased intracellular lipid accumulation. To evaluate Nrac function in vivo, we generated Nrac knockout (KO) mice via CRISPR/Cas9. Tissue depot weights, serum triglycerides (TG), and histological analyses were compared between WT and KO mice. KO mice exhibited smaller visceral fat depots and reduced liver size. BAT and WAT histology revealed smaller lipid droplets and a shift toward more small adipocytes (<2400 μm^2) in KO mice. KO mice also had elevated serum TG and non-esterified fatty acids (NEFA), indicating altered lipid metabolism. RNA-sequencing of heart tissue revealed marked downregulation of genes involved in adipogenesis and fatty acid metabolism, alongside upregulation of SR stress-related genes. Conclusions: Nrac is an SR-localized microprotein enriched in the heart and adipose tissue. Loss of Nrac impairs adipogenesis, reduces lipid droplet size, alters systemic lipid metabolism, and induces transcriptional changes consistent with SR stress. These findings identify Nrac as a potential regulator of lipid storage and adipocyte biology, with implications for metabolic and cardiac function.

Poster # 12A

TRPV4-mediated mitochondrial dynamics: a novel mechanism regulating endothelial function and angiogenesis

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Transient receptor potential vanilloid type 4 (TRPV4) is a mechanosensitive ion channel involved in the regulation of endothelial cell (EC) functions, including proliferation, migration, and angiogenesis. However, the molecular

mechanism(s) underlying TRPV4-mediated regulation of EC function is fully unknown. In this study, we investigated whether TRPV4 channels influence endothelial function through modulation of mitochondrial dynamics. Confocal microscopy revealed a peri-nuclear localization of round mitochondria in normal endothelial cells (NEC), whereas elongated mitochondria diffused throughout the cytoplasm in TRPV4 knockout endothelial cells (KOEC). TEM further confirmed the presence of rounded mitochondria in NEC, in contrast to elongated mitochondria with distinct cristae in KOEC. Notably, FACS analysis revealed a significant increase in mitochondrial content in KOEC, which was accompanied by an elevated expression of PGC-1α, the master regulator of mitochondrial biogenesis. At the molecular level, western blot and qPCR analysis revealed an enhanced ratio of fusion to fission proteins (Optic Atrophy 1 (OPA1)/mitochondrial fission factor (MFF)) in KOEC compared to NEC. Furthermore, seahorse flux analysis demonstrated significantly higher basal oxygen consumption rate (OCR), maximal OCR, ATP-linked OCR, and spare capacity in KOEC relative to NEC, all of which were notably reduced upon treatment with the small molecule OPA1 inhibitor MYLS22. Importantly, MYLS22 normalized abnormal proliferation, migration, and angiogenesis by KOEC. Finally, MYLS22 treatment normalized tumor angiogenesis and reduced tumor growth in endothelial-specific TRPV4 knockout mice. These findings demonstrate that TRPV4 channels regulate angiogenesis by modulating mitochondrial dynamics through OPA1 and highlight endothelial TRPV4 as a novel therapeutic target for the regulation of mitochondrial function in EC.

Poster # 12B

FAK activation by M64HCl promotes osteoclastogenesis: a potential therapeutic strategy for high bone mass disorders

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Focal adhesion kinase (FAK) a non-receptor tyrosine kinase that orchestrates cellular processes including adhesion, migration, and survival previously studied in epithelial repair and mesenchymal stem cell (MSC) lineage commitment. While FAK inhibition is known to impair osteoclast (OC) differentiation, the therapeutic potential of isolated FAK activation in promoting OC-mediated bone resorption remains unclear. Our study investigated the effect of M64HCl, a newly developed and selective FAK small molecule activator, on osteoclastogenesis and bone resorption using in vitro and in vivo approaches. Murine osteoclast-precursors (OCP) isolated from 6-8 week old wild-type C57BL/6J male and female mice (Strain #000664, Jackson Laboratories) were cultured with M-CSF and RANK-L in presence or absence of various doses of M64HCl (100-500 nM). FAK activation significantly increased OC differentiation, confirmed by enhanced TRAP activity and staining, increased OC size and number, and upregulation of osteoclast-related markers including CTSK, Calcitonin Receptor, and OC-STAMP. Functionally, M64HCl-treated OCs exhibited greater bone resorption on dentin slices, quantified by Toluidine blue staining and ImageJ analysis. In vivo, C57BL/6J mice, male 6-8 weeks old, housed and maintained at Northeast Ohio Medical University (NEOMED) at facility accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC), under controlled conditions (21°C, 12-hour light-dark cycle). All procedures approved by Institutional Animal Care and Use Committee (IACUC) at NEOMED. Localized delivery of M64HCl via collagen sponges using calvarial bone resorption model showed increased TRAP+ OCs and OC-mediated bone resorption. Our results demonstrate targeted activation of FAK by M64HCL potently enhances OC differentiation and function, establishing M64HCl as promising therapeutic approach for managing rare bone diseases characterized by increased bone mass.

Poster # 13A

Decoding fibroblast heterogeneity in severe fibrotic lung disease

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Introduction: Idiopathic pulmonary fibrosis (IPF) is a fatal fibrotic lung disease marked by aberrant activation of fibroblasts that results in their impaired clearance, and excessive production and deposition of extracellular matrix (ECM) proteins. Wilms' Tumor 1 (WT1) is a transcription factor that is selectively expressed in mesothelial cells and is essential in lung development. In a recent study, we demonstrated upregulation of WT1 in fibroblasts and its pathogenic role in fibroblast activation in IPF and a mouse model of TGFα-induced pulmonary fibrosis. However, the mechanisms by which WT1 contributes to fibroblast accumulation and ECM production remain unexplored. Methods: To identify heterogeneity in WT1-positive fibroblasts, we performed single-nucleus RNA sequencing (snRNA-seq) analysis of distal lung tissue samples from 18 IPF and 11 healthy controls. To investigate the effects of WT1 on fibroblast survival and ECM production, we performed knockdown and overexpression of WT1 in fibroblasts from IPF and healthy lungs. We assessed changes in the pro-apoptotic and anti-apoptotic gene expression using RT-PCR and western blot analysis. We quantified the number of fibroblasts undergoing apoptosis using TUNEL assays. In vivo, we assessed the effects of WT1 overexpression in fibroblasts using PDGFRαCreERT mice during bleomycin-induced pulmonary fibrosis. Results: Our snRNA-seq analysis revealed increased proportions of mesenchymal, epithelial, and endothelial cells compared to scRNA-seq, highlighting the effectiveness of the single-nuclei method to isolate single cells from intact tissue. Within these lineages, we identified 28 distinct cell subpopulations. Among mesenchymal cells, we identified seven fibroblast subtypes, including alveolar-fibroblasts, adventitial fibroblasts, mesothelial cells, pericytes, myofibroblasts, SMCs, and WT1-positive fibroblasts. RNA-ISH validated the selective accumulation of novel WT1-positive myofibroblasts in distal fibrotic lesions of IPF. Notably, the knockdown or overexpression of WT1 suggests that it functions as a positive regulator of proliferation, survival, and ECM production. Importantly, fibroblast-specific over-expression of WT1 is sufficient to augment bleomycin-induced pulmonary fibrosis in vivo. Conclusion: Our new findings uncover a pathogenic role for WT1 in fibroblast activation and ECM production in IPF.

Poster # 13B

Comparative effects of canagliflozin and pioglitazone on urinary ACE2 shedding and renal injury in diabetic mice

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Diabetes is a leading cause of chronic kidney disease (CKD) and progression to end-stage renal disease. Previous studies showed elevated urinary angiotensin-converting enzyme 2 (ACE2) and neprilysin (NEP) in diabetic db/db mice, which was attenuated by normalizing hyperglycemia and glycosuria with the PPAR- γ agonist, rosiglitazone and physical exercise training. Sodium-glucose co-transporter 2 (SGLT2) inhibitors, such as canagliflozin, lower blood glucose by inhibiting renal glucose reabsorption and induce glycosuria. The study compared the effects of canagliflozin and the PPAR-γ agonist pioglitazone on urinary and renal ACE2, and ADAM17, along with albuminuria and renal injury markers such as neutrophil gelatinase-associated lipocalin (NGAL), arginase-II, and sirtuin-1 (SIRT1). Six-week-old db/db and lean control mice were treated with chow supplemented with canagliflozin or pioglitazone (20 mg/kg/day) for 15 weeks. Metabolic and renal parameters were measured weekly, and urine was collected for evaluating glycosuria, protein expression and enzyme activity. Diabetic db/db mice exhibited augmented hyperglycemia, increased renal ADAM17, Arginase II and decreased Sirt1. In addition, they showed increased urinary ACE2, and NGAL levels. Both treatments significantly reduced blood glucose ($p<0.001$) in db/db mice. Canagliflozin induced glycosuria in diabetic and lean control mice and paradoxically increased urinary ACE2 and albuminuria. However, pioglitazone decreased renal ADAM17 and attenuated urinary ACE2 and albuminuria. Both treatments increased renal Sirt1, decreased arginase-II and attenuated urinary NGAL. In conclusion, the findings suggest that canagliflozin-induced glycosuria may contribute to increased albuminuria and urinary ACE2 shedding, possibly linked to elevated ADAM17 activity. Conversely, pioglitazone demonstrated a more favorable renal profile, with reduced albuminuria and ACE2 shedding. Both treatments conferred renoprotective effects, potentially driven by upregulation of renal SIRT1 and downregulation of NGAL and arginase-II.

Poster # 14A

Investigating NDM-4 antibiotic resistance mechanisms through structural analysis of NDM variants

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The global occurrence of β-lactamase-producing bacteria and their resistance to multiple antibiotics has become a significant public health concern. To develop effective strategies to overcome these infections, it is crucial to gain a comprehensive understanding of the mechanisms underlying antibiotic resistance in these bacteria. My research aims to investigate the mechanisms of antibiotic resistance in metallo-β-lactamase NDM-4. NDM-4 hydrolyzes β-lactam antibiotics very rapidly, which makes it hard to capture a stable, non-hydrolyzed complex for structural study. Because of this, I use engineered mono-zinc variants NDM-X and NDM-X2 that show slower hydrolysis. These variants help me form more stable enzyme–ligand complexes and increase the chance of obtaining crystals suitable for X-ray diffraction. My work combines protein purification, stability measurements, and enzymatic assays with crystallization screening. The goal is to obtain a crystal structure of NDM-X and NDM-X2 bound to non-hydrolyzed β-lactams. This structure will provide important insight into how mutations and zinc content change enzyme function, and it will support the design of inhibitors that may help fight antibiotic resistance. These structures will show how mutations and reduced zinc content change active-site geometry compared with NDM-4. Together with stability and activity data, the structures will give a clearer view of the molecular basis of antibiotic resistance in this enzyme family and will support the design of inhibitors that could help fight infections caused by NDM-producing bacteria.

Poster # 14B

Airway inflammation and fear: elucidating brain nodes and cellular substrates

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Post-traumatic stress disorder (PTSD) is a prevalent, trauma-evoked mental disability affecting ~7% of civilians and ~20% of combat veterans. A hallmark of this disorder is failure to regulate fear memories due to deficits in fear extinction. Recent genetic and epidemiological studies demonstrate strong links between PTSD and severe allergic asthma. Key to this pathology is elevated lung production of interleukin-17A (IL-17A), a proinflammatory cytokine involved in severe airway inflammation (AI). Currently, cellular substrates underlying severe asthma-associated AI and PTSD-relevant fear are not known. Our lab has developed a murine model of severe house dust mite (HDM) induced allergic asthma effects on PTSD-relevant fear extinction. Interestingly, mice with severe AI (mixed T-helper cell (Th) 2/17) but not mild (Th2) AI exhibit deficits in fear extinction that are rescued by anti-IL17A antibodies. Central nodes that are receptive to severe AI/IL-17A and regulate fear extinction deficits are not well understood. Deficits in prefrontal cortex activity, particularly the infralimbic (IL) subdivision, are associated with compromised fear extinction in PTSD. In recent studies, we observed engagement of the subfornical organ (SFO) in severe AI mice. Importantly, the SFO directly projects to the IL, suggesting an important role of cellular substrates within these regions in translating severe AI effects on fear extinction. Based on previous data, we hypothesized that 1) blockade of SFO microglial IL-17A receptor will prevent extinction deficits in severe AI mice, and 2) IL neuronal activity will be temporally modulated in severe AI mice. For these studies, novel AAV-Cre vectors for microglial-specific targeting in IL-17RA$^{fl/fl}$ mice will be tested in the severe AI paradigm. *In vivo* fiber photometry studies will be conducted to determine real-time fluctuations in IL activity. Collectively, these studies will determine cellular substrates within the SFO and IL that are recruited by severe AI immune mediators to impact fear extinction.

Poster # 15A

Investigating foraging behavior via the insulin/IGF-1 pathway in *C. elegans*

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Foraging within animals can elicit a high risk, high reward response as conservative foraging strategies can result in

limited food acquisition while foraging can increase the possibility of encountering hazards. In humans, foraging is understood within the context of dietary behavior. *C. elegans* can be used to model foraging behavior, as they are genetically tractable, and share orthologs with humans for relevant pathways. In our study, foraging assays were conducted on animals of different genotypes. We used two strains; daf-2 mutant that lacks the insulin-like peptides that stimulate the sensation of "fullness", and a FOXO transcription factor mutant which affects the proception of "hunger". *C. elegans* were starved or left to feed for one hour. Worms of each strain were then placed in the center of a fructose ring and allowed to forage towards two diacyl dots for fifteen minutes. Worms inside the circle were counted. Wildtypes experienced low exiting during their fed state compared to their unfed state. CB1370 experienced high exiting overall regardless of the metabolic state. DR 27 showed reversed effects, with low exiting regardless of metabolic state. High exiting indicates the strain's lack of proception of "fullness" is constantly induced which would cause high exiting of the fructose ring to scavenge for nutrients. The decrease overall in exiting could be caused by the lack of perception of hunger in which the worms would not leave the ring to seek food. This work will improve our understanding of the genetic and physiological mechanisms underlying complex feeding behaviors.

Poster # 15B

Adipose-specific overexpression of NDUFV2 attenuates cardiometabolic comorbidities in females in a "2-hit" mouse model of HFpEF

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Background: The prevalence of heart failure with preserved ejection fraction (HFpEF) has surged in parallel with epidemic of obesity, constituting fifty percent of all heart failure cases. A panel of genetically diverse mouse strains, termed the Hybrid Mouse Diversity Panel (HMDP), has revealed sex-biases in the progression of HFpEF as well as identifying the potential female-specific protective role of the adipose gene, NDUFV2. Our previous work with this gene has demonstrated its sex-specific regulation of adipose mitochondrial function, such that its overexpression in the adipose tissue resulted in a female-specific protection against obesity. The objective of this study was to assess the sex-specific effects of adipose NDUFV2 overexpression on whole-heart cardiac and mitochondrial function in a '2-Hit' mouse model of HFpEF. We hypothesize that adipose NDUFV2 overexpression will reduce diastolic dysfunction and prevent metabolic comorbidities in female mice, along with improving heart mitochondrial function. Results: Our studies show that by the end of study, female NDUFV2 mice had significantly reduced body mass, as well as reduced heart and lung weights normalized to tibia length, compared to female GFP mice. Left ventricular ejection fraction remained unchanged between sexes or groups. Doppler E/A ratio was significantly decreased in female NDUFV2 mice compared to female GFP mice. Fatty acid oxidation capacity in heart mitochondria was significantly reduced in both female and male NDUFV2 groups compared to GFP groups, while the respiration capacities of complexes I, II, and IV were significantly elevated only in the female NDUFV2 group compared to GFP females. Conclusion: We report that adipose NDUFV2 overexpression mitigated diastolic dysfunction in a '2-Hit' mouse model of HFpEF only in females, potentially due to improved mitochondrial respiration capacities. These effects were coupled with a female-specific protection against HFpEF comorbidities.

Poster # 16A

Chronic ethanol exposure triggers multi-organ dysfunction via gut-liver axis perturbation

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Background: Chronic ethanol (EtOH) consumption is a major contributor to multi-organ pathology, yet its systemic effects remain incompletely understood. Methods: We employed a physiologically relevant long-term mouse model (20% EtOH in drinking water for 60 weeks) to examine the integrated consequences of chronic EtOH exposure. RESULTS: Mice consuming EtOH (0.4–0.5 mL/day) for 60 weeks exhibited >30% reductions in chow and fluid intake, resulting in a 12% decrease in caloric intake versus controls ($P \leq 0.001$). Body mass remained comparable until week 52, after which EtOH mice weighed less due to reductions in both lean and fat mass ($P \leq 0.001$). Functional testing revealed impaired grip strength (−11%) and treadmill endurance (−17%) ($P \leq 0.012$), with no change in motor coordination

(P = 0.203). EtOH altered gut microbiota composition, reducing Lactobacillus and Muribaculaceae while enriching Turicibacter and Clostridium at genus level, accompanied by significant short-chain fatty acid depletion (P ≤ 0.05). Gut permeability markers (LPS, zonulin) and liver enzymes (ALT, AST) were elevated, alongside increased total cholesterol and >60% upregulation of hepatic TNFα and IL-6 (P ≤ 0.044). EtOH induced dyslipidemia and glucose intolerance (P ≤ 0.022), while white adipose tissue exhibited minimal transcriptomic changes despite elevated free fatty acids. Conclusions: Chronic EtOH consumption disrupts energy balance, barrier integrity, and hepatic metabolism, driving inflammation and metabolic dysfunction. These findings highlight the gut-liver axis as a potential mediator of EtOH-induced pathology and identify the gut microbiome as a therapeutic target.

Poster # 16B

The quantitative assessment of computational simulations involving vulnerabilities in miniature excitatory postsynaptic current detection

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Cognitive processes such as learning and memory are mediated through synaptic plasticity, or a change in the strength of synaptic communication. Miniature excitatory postsynaptic currents (mEPSCs) are electrical signals in response to the spontaneous release of a single vesicle of glutamate within mouse cortical pyramidal neurons, representing the fundamental units of communication. mEPSC amplitudes within a neuron increase following prolonged activity blockade, a process known as homeostatic synaptic plasticity. The magnitude of the effect is observed utilizing quantitative analyses. In the raw data ratio plot, all mEPSC amplitudes from control and experimental records are sorted in descending order, and the ratio of each pair of events is calculated and graphed against the control amplitude. The rank order plot involves sorting equivalent quantiles of the control and experimental mEPSC amplitudes, plotting these against each other, and fitting with a linear regression line. A previous study of homeostatic plasticity using the rank order plot concluded a uniform effect, but we found clear deviation from uniformity with the raw data ratio plot. We hypothesize that the random nature of mEPSC amplitudes (considering no two records will have identical events), coupled with the difficulty in detecting the smaller mEPSCs due to the signal-to-noise ratio, causes a distortion of the effect in that range of the data. This distortion will obscure the true effect in the raw data ratio plot, but will cause less distortion in the linear regression slope in the rank order plot, making the latter a better approach when the deviation from uniformity is solely due to experimental limitations. To produce a known uniform effect, we altered the membrane potential, a manipulation that changes the driving force, and employed computational simulations imitating expected distortions. From the aforementioned methods, we can determine which quantitative approach fits best.

Poster # 17A

Evaluation of saposin C-dioleoylphosphatidylserine nanovesicles for drug delivery to the placenta

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Placental insufficiency affects over 10% of all pregnancies and is a leading cause of fetal growth restriction as well as maternal and neonatal morbidity/mortality. Current in-utero therapies aimed at improving fetal growth have generally failed to fully address the issue without causing additional damage, and some have even led to significant negative off-target effects in the mother and developing fetus. This study aims to explore the potential of Saposin C-Dioleoylphosphatidylserine (sapC-DOPS) nanovesicles for the targeted delivery of therapeutics to the placenta, leveraging the unique selective external expression of the target phosphatidylserine on the cell membrane during the stage of development of the syncytiotrophoblast layer. To evaluate their ability to target the placenta, SapC-DOPS nanovesicles tagged with the fluorescent dye CellVue Maroon were injected intra-amniotically into in vivo mice models at gestational days E15-18. IVIS imaging, when analyzed with ImageJ and GraphPad, depicted significantly higher fluorescence in treated placentas compared to controls, confirming successful localization of nanovesicles to syncytiotrophoblast placental tissue. Hemotoxylin and Eosin staining analysis depicted no structural

abnormalities or adverse effects on placental architecture observed following intra-amniotic administration of the sapC-DOPS nanovesicles thus far. While this study has not yet concluded, these preliminary findings are optimistic and support the potential of sapC-DOPS nanovesicles to serve as a safer and more effective method for therapeutic delivery during pregnancy - providing a promising foundation for further research into improving outcomes in placental insufficiency cases.

Poster # 17B

Diabetes mellitus impairs regenerative fibroblast activation

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Diabetes mellitus (DM) is a metabolic disorder commonly known as Type 1 (DM1) and Type 2 (DM2) Diabetes. Around the world, nearly 1 in every 10 people suffer from DM. DM greatly hinders organ repair and has been identified as an independent risk factor for the development of idiopathic pulmonary fibrosis (IPF), and those impacted by this comorbidity tend to experience worse clinical outcomes. DM1 is characterized by insulin deficiency while DM2 is characterized by insulin resistance. Both forms result in patients exhibiting chronic hyperglycemia and metabolic stress. DM and IPF patients display chronic accumulation of extracellular adenosine. In humans, chronic adenosine promotes fibrotic remodeling, while in mice it impairs fibrosis resolution. Since IPF is marked by chronic adenosine accumulation, our rationale is to use the partial pneumonectomy model of lung regeneration in a genetic background where a human surfactant mutation is a risk factor for IPF. Lipo-, myo-, matrix fibroblasts (FB) are three distinct subtypes of PDGFRa+ FB with specialized functions for maintaining and repairing healthy lungs. Preliminary *in vitro* data reveal treatments with high glucose or adenosine reduces matrix-FB marker expression and augments a shift towards fibrotic matrix FB phenotypes. The pathological relationship between metabolic dysfunction and lung fibrosis has not been investigated closely. To further explore the way metabolic pathways shape FB phenotypes, we will test the hypothesis that DM-induced adenosine signaling disrupts regenerative PDGFRα+ FB function and epithelial repair, driving fibrotic remodeling following an acute injury. Using established mouse models of Type 1 and Type 2 diabetes and *in vitro* human and murine alveolar organoid co-cultures, we will define how adenosine receptor subtypes drive alveolar fibrosis. Assessing the potential of adenosine receptor antagonists to promote regenerative over fibrotic injury repair will provide new therapeutic targets to ameliorate clinical outcomes of those with DM and IPF.

Poster # 18A

Perioperative fluid conservation guidelines did not negatively impact early postoperative clinical outcomes during the nationwide IV fluid shortage due to Hurricane Helene

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A severe, nationwide IV fluid (IVF) shortage occurred in Fall 2024 due to production facility damage from Hurricane Helene. This shortage resulted in significantly decreased IVF delivery, necessitating significant conservation efforts across our healthcare system. In our hospital, strict perioperative IVF guidelines were implemented to reduce holding room, intraoperative, and postoperative fluid administration. It is not known how these guidelines impacted clinical outcomes early after surgery. This study seeks to understand postoperative complications due to this fluid restriction.

Poster # 18B

Neurokinin signaling promotes proper conduction and restricts cardiomyocyte number in the zebrafish heart

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Innervation of the heart can affect its function and growth and is often impaired with congenital heart defects (CHDs). Signaling through Substance P (SP), a neuropeptide which is released from the vagus nerve and acts on the neurokinin-1 receptor (NK_1R) in the cardiac plexus, can mediate heart rate, blood pressure, cardiac output, as well as aid in cardiac regeneration. However, the requirements for SP/ NK_1R signaling within

the developing heart remain poorly understood. Here, we inhibited SP/ NK_1R signaling in zebrafish larva using treatments of pharmacological NK_1R antagonists from 72 to 120 hours post-fertilization (hpf), which is when vagal innervation has been reported to begin in zebrafish larva. Surprisingly, we found that quantifying cardiomyocytes using a *myl7:nls-Kaede* transgenic line showed that NK_1R inhibition at 72 hpf produced a surplus of atrial cardiomyocytes, an effect which was recapitulated in larva with CRISPR/Cas9-mediated knockdown (KD) of *tacr1a*, a NK_1R we found is expressed within the larval zebrafish atrium with hybridization chain reaction (HCR) *in situ*. Additionally, using a *myl7:gCaMP7* transgenic line, we found that the inhibition of NK_1R in zebrafish larva caused repolarization defects in the ventricle by 120 hpf. Altogether, our study shows that neurokinin signaling may act to limit atrial cardiomyocyte proliferation and control ventricular repolarization with larval zebrafish hearts.

Poster # 19A

Dry conditions shift mosquito behavior and blood feeding

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Mosquitoes are considered the deadliest animal on the planet, vectoring diseases that result in over 600,000 human deaths annually. In addition to their reproductive function, female mosquitoes can utilize blood meals for survival, water content regulation, and protection under dehydrating conditions. During dry periods, these mosquitoes increase their blood feeding, likely utilizing the additional bloodmeals for rehydration and nutritional supplementation to survive dehydration bouts. Given sufficient opportunities to refeed on a host, even within a single gonotrophic cycle, mosquitoes may offset the reproductive deficit caused by dehydration. This secondary blood feeding approximately doubled biting rates under dry conditions, allowing mosquitoes to survive prolonged dry periods, nearly twenty days, without rehydration from water sources. Interestingly, the behavior of these dehydrated mosquitoes also consisted of increased activity, decreased sleep, and an early return to CO2 sensing. The ability of mosquitoes to survive these adverse conditions comes at the cost of increased blood feeding, resulting in predicted increases to disease transmission, especially during dry conditions. These results continue to advance our understanding of the interactions between mosquitoes, dry conditions, and their contributions to vectorial capacity and disease transmission dynamics.

Poster # 19B

The kissing bug likely has a single functional eye photoreceptor

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Kissing bugs are nocturnal blood-sucking hemipteran insects, serving as the vector of Chagas disease in the Americas. Vision is a key sensory modality required for many aspects of insect behaviors, but little is known about kissing bug visual systems. Therefore, an in-depth examination of the vision of kissing bugs is required. Here, we used transcriptomics, phylogenetics, and electrophysiological (extracellular electroretinography (ERG) analyses to identify and characterize the opsins and related visual processes in the compound eyes for *Rhodnous prolixus*. RNA-seq of the eyes and phylogenetic analysis confirmed three visual opsin genes, one of which is highly expressed in the eyes and belongs the blue-green sensitive class of opsins. To investigate the spectral sensitivity of opsins in the eyes, we recorded ERGs from adult R. prolixus compound eyes, and assessed the photoreceptor response to three monochromatic light stimuli (365nm, 460nm, and 605nm). We found the highest response in the blue (480 nm) region. Furthermore, we assessed the wavelength sensitivity of the opsins with photoreceptor bleaching experiments with UV (365nm), blue (460nm), and orange (605nm) light stimuli and these specific wavelengths attenuated the entire ERG response, suggesting a single functional opsin. Together, our results indicate that three visual opsins are expressed in the R. prolixus compound eye,

however, only one blue-green opsin is responsible for a majority of the response to light stimuli. Knowing the spectral classes of photoreceptors in kissing bugs is critical to understanding their vision and could provide novel targets to alter the behavior of these pests.

Poster # 20A

Identifying a novel protein protecting against atherosclerosis and vascular dysfunction

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Atherosclerosis is a chronic inflammatory condition of the arteries and the leader of mortality in developed countries. Atherosclerosis begins with EC activation, a key step in the progression of atherosclerosis which is characterized by the expression of adhesion molecules and thus monocyte recruitment to the inflamed EC. Monocytes will be then differentiated into macrophages which in turn will engulf the ox-LDL turning into resident foam cells, a hallmark of atherosclerosis. Recently, using a humanized transgenic mouse model, our lab discovered that Fat-specific Protein 27 (FSP27) protects against endothelial dysfunction. We hypothesized that Endothelial-specific FSP27 may play a critical role in protection against plaque formation. To test our hypothesis, we generated mice expressing human FSP27 transgene on the background of ApoE-/- mice (E-FSP27tg-Apoe-/-). Our results show that there was almost no plaque development in the aorta of the E-FSP27tg-Apoe-/- mice compared to the significant atheroma development in the aorta, carotid, and subclavian arteries of ApoE-/- mice fed the western diet for 5 weeks. Our in vitro studies in HUVECs show decreased vascular oxidative stress and inflammation in HUVEC upon adenoviral-mediated FSP27 overexpression expression. Studies are underway to analyze the mechanistic role of FSP27 in protection against plaque deposits in the atherosclerotic arteries of mice. Overall, our study identifies a novel role of endothelial-specific FSP27 in the pathogenesis of atherosclerosis.

Poster # 20B

Age-progressive and sex-dependent bone phenotype in mice lacking Atp13a2

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ATPase cation transporting 13A2 (ATP13A2) contributes to the homeostasis of metal ions and is important in regulating the proper function of lysosomes. Previous work has demonstrated that deletion or loss of function of the ATP13A2 gene is associated with improper organelle function and cell death. This study focused on investigating the bone phenotype in the long bones of Atp13a2 knockout mice. Femoral bones were collected from 3- and 18-month-old WT and KO mice and scanned using micro-CT. 3D reconstruction of the scan was done using the 3D Avizo software, and bone data was collected using the CTAn software. The subchondral bone of the 3-month WT female had significantly more bone volume/tissue volume, trabecular thickness, trabecular number, and lower trabecular separation than the KO group. There were no significant differences in the above values between the 18-month female group. This trend was not observed in the 3-month and 18-month male WT and KO groups. Bone mineral density was higher in the 3-month WT female group than in the 3-month female KO and the 18-month female WT group. We also analyzed the bone below the epiphyseal plate. Data from this region showed no statistical difference between the 3-month male WT and KO samples or between the 18-month female WT and KO samples. However, the 18-month male KO group had significantly higher trabecular number than the 18-month male WT group. For the 3-month female group, there were significant differences, which followed the same trend as seen in the subchondral region. This study is the first to report bone phenotype in Atp13a2 KO in mice. These results suggest that Atp13a2 may influence trabecular bone structure in a sex and age-dependent manner. Further studies are needed to investigate the mechanisms underlying this and to further explore the relationship between Atp13a2, bone health, and joint health.

Poster # 21A

Withdrawn

Poster # 21B

Neurovascular LAT1 signaling in the DRG as a driver of neuropathic pain

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Neuropathic pain is a chronic and often treatment-resistant condition that arises after injury to the nervous system and is estimated to affect approximately 1/5 individuals worldwide. The dorsal root ganglia (DRG), which house the cell bodies of primary afferent neurons, are a key site of maladaptive plasticity in neuropathic pain. Therapeutics are limited and often include opioids, which carry significant risks, including dependency and the potential to further sensitize sensory neurons, exacerbating pain over time. The L-type amino acid transporter (LAT1) has been implicated in various cellular functions, including nutrient sensing, mTOR signaling, and the cellular uptake of gabapentinoids. While LAT1 has been extensively studied in cancer models, few studies have assessed its role in sensory neurons of the DRG in the context of pain. However, its contribution to sensory processing in the DRG remains unclear. Using RNAscope and publicly available single-cell RNAseq data, we found that Slc7a5 (LAT1) is predominantly expressed in endothelial cells (ECs) within the DRG, with minimal neuronal expression. Interestingly, small-diameter DRG neurons located near blood vessels exhibited higher LAT1 signal than those farther away, suggesting possible endothelial-to-neuronal LAT1 paracrine signaling. Our lab has shown that in spared nerve injury mice, LAT1 protein is upregulated in both the spinal cord and DRG. Functionally, in vivo administration of the LAT1 inhibitor JPH203 reduced pain behaviors in SNI. In vitro, treatment of mouse and human DRG neurons with JPH203 decreased neuronal excitability and multi-firing in whole-cell patch clamp recordings, and reduced Ca2+ dynamics in Ca2+ imaging experiments. Together, these findings support a model in which EC-derived LAT1 participates in neurovascular signaling within the DRG, modulating sensory neuron excitability and potentially influencing chronic pain perception.

Poster # 22A

Lipin1 restoration mitigates cardiomyopathy progression in Duchenne muscular dystrophy

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Cardiomyopathy and heart failure are primary causes of mortality in Duchenne Muscular Dystrophy (DMD). The absence of dystrophin disrupts cardiomyocyte sarcolemmal stability, triggering chronic inflammation, cellular necrosis, dystrophin-glycoprotein complex disruption, and progressive myocardial fibrosis, leading to dilated cardiomyopathy. Lipin1 has recently emerged as a crucial regulator of sarcolemmal integrity in skeletal muscle; however, its role in dystrophic cardiac tissue remains unclear. Using a transgenic mdx mouse model with restored lipin1 expression in the heart (mdx:lipin1Tg/0), we demonstrate that lipin1 restoration at six months improves sarcolemmal integrity, reduces macrophage infiltration, attenuates myocardial fibrosis, and improves cardiac function. These findings identify lipin1 as a critical modulator of cardiac pathology in DMD and highlight its therapeutic potential in managing DMD-associated cardiomyopathy.

Poster # 22B

Oxidative stress induces mitochondrial DNA leakage in chondrocytes

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Mitochondrial dysfunction is a hallmark of cellular damage. Mitochondrial injury can cause leakage of mtDNA from the organelles, which in turn activates intracellular receptors and triggers inflammatory responses. Osteoarthritis (OA), the most common degenerative joint disease, affects more than 32 million Americans over the age of 55. Because OA is associated with a high degree of chronic, sterile inflammation in the joint, mitochondrial dysfunction and mtDNA leakage represent potential therapeutic targets. In this study, we hypothesize that exposure of chondrocytes to proinflammatory cytokines or oxidative stressors induces mitochondrial dysfunction and promotes mtDNA

release into the cytoplasm. Furthermore, we hypothesize that attenuating mtDNA damage with mitoTEMPO, a mitochondria-targeted antioxidant, will reduce both mtDNA damage and leakage. HTB94 human chondrosarcoma cells were cultured in DMEM and transfected with mitoDsRed, a plasmid encoding a red fluorescent protein targeted to mitochondria. Cells were then treated with DMSO (control), IL-1β, Rotenone (a mitochondrial electron transport chain complex I inhibitor), or tert-Butyl hydroperoxide (TBHP), in the presence or absence of mitoTEMPO. After treatment, cells were fixed and stained with DAPI and dsDNA antibodies to assess mtDNA leakage. Confocal microscopy revealed higher levels of mtDNA leakage in treated cells compared to controls. Notably, mitoTEMPO treatment reduced mtDNA leakage, suggesting that ROS-mediated mtDNA damage drives its release. Cells were also stained with anti-8-hydroxy-2'-deoxyguanosine (8-OHdG), a marker of oxidative DNA damage. This analysis demonstrated that mitoTEMPO attenuated ROS-induced mtDNA damage. Further studies are needed to determine how leaked mtDNA interacts with intracellular receptors such as cGAS or other pattern recognition receptors.

Poster # 23A

Cardiomyocyte-specific TRPV4 deletion attenuates adverse cardiac remodeling via modulation of protein kinase G signaling

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Left ventricular hypertrophy is an adaptive response to volume stress or pressure overload that can ultimately lead to contractile dysfunction and heart failure. Previously, we demonstrated that global or endothelial-specific deletion of transient receptor potential vanilloid 4 (TRPV4) channels protects the heart from adverse remodeling following myocardial infarction (MI) or pressure-overload (TAC), through inhibition of fibroblast differentiation or increased microvasculature, respectively. However, the specific role of the cardiomyocyte TRPV4 in cardiac remodeling remains unclear. To investigate this, we generated cardiomyocyte specific-TRPV4 knockout mice (TRPV4MKO) and subjected them to Isoproterenol (ISO; 30mg/kg/day) treatment for 14 days. Echocardiography analysis revealed that cardiac function is preserved in TRPV4MKO mice compared to TRPV4lox/lox mice. Further, we found that cardiac hypertrophy and collagen deposition decreased in TRPV4MKO compared to TRPV4lox/lox mice, post-ISO treatment. Importantly, single-nucleus RNA sequencing revealed significant downregulation of Protein kinase G1 (PKG1) in the hearts of hypertrophic cardiomyopathy patients compared to healthy controls. Mechanistically, TRPV4 inhibition increased PKG1 expression levels and prevented ISO-induced hypertrophy in AC16 human cardiomyocytes. Finally, pharmacological inhibition of PKG1 using KT5823 exacerbated hypertrophy in AC16 cells in response to ISO. Taken together, our results suggest that cardiomyocyte-specific deletion of TRPV4 mitigates adverse cardiac remodeling via downregulating PKG1 and identifying the TRPV4/PKG1 signaling as a potential therapeutic target for heart failure. Keywords: Cardiac hypertrophy, Cardiac remodeling, Isoproterenol, Protein Kinase G1, TRPV4.

Poster # 23B

Queuosine derived from the microbiome influences the physiology of mosquito larvae through altered tyrosine metabolism

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Transfer RNAs (tRNAs) are central to protein synthesis and represent an underexplored aspect of vector biology. Chemical modifications to tRNA support their function through modulating the speed and fidelity of translation. One such modification, queuosine (Q), is sourced from the diet and gut bacteria in eukaryotes and has been proposed as an important micronutrient for animal health. In this study, we investigated the role of Q in mosquito larval development and behavior. Larvae reared with bacteria lacking Q showed altered levels of tyrosine and dopamine, leading to behavioral abnormalities and defects in cuticle formation. Predation assays revealed that Q-deficient larvae were less capable of evading capture by predatory beetle larvae. These findings underscore the broad physiological and behavioral consequences of microbially-derived Q and suggest that this modification is critical for mosquito larvae to achieve optimal development.

Poster # 24A

Study of age- and sex-related changes in the tail vertebrae of Atp13a2 knockout mouse

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Introduction: Atp13a2 is a lysosomal ATPase essential for lysosomal and mitochondrial homeostasis. Loss of Atp13a2 function disrupts lysosomal polyamine regulation, leading to a buildup of polyamines, increased lysosomal pH, oxidative stress, and reduced autophagy, which has been linked to many neurological disorders. We hypothesize that loss of Atp13a2 leads to reduced lysosomal function, altering osteoclast and osteoblast activity subsequently reduces bone remodeling. In this study, we investigated bone phenotype in young and old Atp13a2 knockout mice using their tail vertebrae. Methods: Mouse tissue was collected from young (3-month) and old (18-month) male and female mice (n=7 per group). Micro-computed tomography (micro-CT) was used to determine bone phenotype. Avizo software was used for 3-D visualization and intervertebral disc height measurement. CTAn software was used to analyze bone volume/tissue volume, trabecular thickness, trabecular number, trabecular separation, and bone mineral density. Statistical significance between the two groups was calculated using a two-tailed, unpaired t-test. Results: The young KO males and females had a higher BV/TV%, trabecular thickness, trabecular number, and bone mineral density. The WT young females had a higher trabecular separation than the KO group. Both the males and females in the old KO group had a higher BV/TV%, trabecular number, and bone mineral density. The old WT groups had a higher trabecular separation for both males and females. The trabecular number was significantly decreased in the old female WT group compared to the corresponding young group. Bone mineral density was significantly increased in both the old male WT and KO groups compared to the corresponding young male group. Discussion: Atp13a2-deficient mice displayed a bone phenotype that varied with age and sex. Loss of Atp13a2 function can lead to increased bone density in male mouse tail vertebrae. Significance: This study enhances our understanding of the role of Atp13a2 in bone health.

Poster # 24B

TRPV4 mechanotransduction mediates TGF-β2–induced endothelial-to-mesenchymal transition (EndMT) via Rho/Snail pathway

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Endothelial-to-mesenchymal transition (EndMT) is a critical cellular differentiation process implicated in embryonic development and cardiovascular diseases including atherosclerosis and cardiac fibrosis. Although soluble factors such as TGF-β are major mediators of EndMT, mechanical forces such as substrate stiffness, stretch and shear stress also play equally important role in EndMT. However, the mechanotransduction mechanisms in EndMT are not well known. Here, we investigated the role of a mechanosensitive ion channel, TRPV4 in EndMT. First, we found that TGF-β2 is a more potent inducer than TGF-β1 in inducing EndMT i.e. differentiation of human microvascular endothelial cells (HMEC-1) into mesenchymal phenotype as measured by increased expression of alpha smooth muscle actin (α-SMA) and reduction in CD31and VE-cadherin. Further, we found that a specific antagonist of TRPV4, GSK2 significantly inhibited TGF-β2 induced EndMT. Notably, TGF-β2 treatment enhanced TRPV4 protein expression and TRPV4 mediated calcium influx in response to a specific agonist of TRPV4, GSK1 which was attenuated by a TRPV4 antagonist, GSK2. Mechanistically, we found that TGF-β2-induced Rho (RhoGTP) activation, expression of transcription factors (TFs), Snail, Slug, Twist-1, SIP-1 and ZEB-1. Importantly, TRPV4 inhibition with GSK2 attenuated TGF-β2-induced Rho activation and Snail expression but no other TFs. These results indicate that TRPV4 channels mediate TGF-β2 induced EndMT via Rho/Snail pathway. Funding: NIH R01 HL148585; AHA TPA-971237

Poster # 25A

Distinct regulation of apolipoprotein j in pathological and physiological skeletal muscle conditions

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Background: Apolipoprotein J (APOJ), also known as clusterin, is a ubiquitously expressed glycoprotein implicated in diverse pathological processes, including Alzheimer's disease, cancer, and tissue repair; however, its role in skeletal muscle remains poorly understood. This study investigated APOJ expression in distinct myopathic conditions and in response to physiological stress induced by exercise. Methods: Four murine models of muscle pathology and their respective controls were examined: age-related sarcopenia (AGED), chronic alcohol-induced myopathy (CAM), Duchenne muscular dystrophy (DMD), and limb-girdle muscular dystrophy (LGMD). Tibialis anterior muscles were harvested and analyzed for APOJ content via Western blotting. In a separate experiment, healthy wild-type mice were subjected to either a single bout or repeated bouts of eccentric contractions and euthanized one week after the final contraction to assess APOJ responsiveness to contraction-induced injury and training. Results: APOJ levels were significantly elevated across all myopathic conditions compared with controls ($P \leq 0.018$), with increases of approximately 30% in CAM and greater than 168% in AGED, DMD, and LGMD groups. In contrast, no significant changes in APOJ expression were observed following either single or repeated eccentric contractions ($P = 0.982$). Conclusions: These findings suggest that APOJ upregulation is a conserved feature of diverse myopathic states associated with muscle atrophy and weakness, despite their distinct etiologies. Conversely, the absence of APOJ modulation following eccentric contraction-induced injury or adaptation indicates that APOJ may play a more prominent role in pathological dysfunction rather than physiological remodeling.

Poster # 25B

The role of the CD44 receptor in post-traumatic and age-related osteoarthritis

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Osteoarthritis (OA) is a debilitating joint disease. Our laboratory is investigating Gpnmb, also known as osteoactivin, as a potential therapeutic for OA. Unpublished data from our laboratory show that mice ubiquitously overexpressing Gpnmb experience less severe cartilage and subchondral bone changes follow induction of post-traumatic (PT) OA via destabilization of the medial meniscus (DMM) surgery. Intra-articular injection of Gpnmb also prevented damage following DMM. CD44 is a known anti-inflammatory receptor of Gpnmb. CD44 signaling has been well reported in joint homeostasis and OA biology. We therefore seek to investigate the role of CD44 in PT and age-related OA. For the PT model, male CD44-/- mice and controls (C57BL/6, B6) were randomized to sham or DMM groups. Surgery was performed at 10 weeks on the right knee and animals were sacrificed at 20 weeks. For the age-related model, male CD44-/- and B6 animals were aged to ~52 weeks and sacrificed. Right knees were assessed with thionin staining, and micro-computed topography (µCT) analysis. In the PT-OA study, cartilage changes showed damage following DMM for both CD44-/- and B6 animals, however, further investigation is required to delineate responses between phenotypes. There was, however, a phenotype in the subchondral bone. µCT analysis showed significant tibial subchondral bone sclerosis in CD44-/- DMM versus CD44-/- sham animals, which were absent in B6 DMM versus sham animals. In the age-related study, cartilage assessment is underway, however significant subchondral bone differences were seen. µCT analysis showed tibial subchondral bone sclerosis in aged CD44-/- versus aged B6 animals. Our data suggest that CD44-/- animals experience more severe subchondral bone sclerosis in both PT and age-related models of OA. Overall, this indicates that the CD44 receptor plays a major role in the bone changes associated with PT and age-related OA.

Poster # 26A

Gpnmb overexpression delays progression of post-traumatic and age-related osteoarthritis

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Glycoprotein nonmetastatic melanoma protein B (Gpnmb), also known as osteoactivin, is a transmembrane glycoprotein with known anti-inflammatory properties. However, in the context of osteoarthritis (OA), Gpnmb's potential anti-inflammatory effect on cartilage and subchondral bone remodeling has not been elucidated. We seek to assess the effects of the induction of post-traumatic OA via destabilization of the medial meniscus (DMM) surgery, and the effects of age, on mice that ubiquitously overexpress Gpnmb ($Gpnmb^{TG}$). For the post-traumatic OA study, male $Gpnmb^{TG}$ mice and control C57BL/6 animals (B6) were randomized to sham or DMM groups. Animals at 10 weeks of age underwent surgery on the right knee and were sacrificed at 20 weeks of age. For the age-related OA study, male $Gpnmb^{TG}$ and B6 animals were aged to approximately 52 weeks and sacrificed. For both studies, right knees were assessed via general histological survey with thionin staining, micro-computed topography (µCT) analysis, and tartrate resistant acid phosphatase staining for osteoclast (OC) assessment. Further analysis and female animal assessment is currently underway. Following the induction of post-traumatic OA, both groups experienced cartilage damage following DMM, however, $Gpnmb^{TG}$ animals experienced decreased cartilage damaged as assessed via OARSI scoring and fewer osteophytes. µCT analysis showed tibial subchondral bone sclerosis for B6 DMM animals, while $Gpnmb^{TG}$ DMM animals did not experience subchondral bone sclerosis. Subchondral OC number and OC surface/bone surface showed an increase in B6 DMM versus B6 sham animals, while $Gpnmb^{TG}$ sham and DMM animals showed no difference. For the age-related study, thionin staining of right knee joints showed very mild age-related cartilage damage with no differences between B6 and $Gpnmb^{TG}$ animals in OARSI or osteophyte scores. However, $Gpnmb^{TG}$ animals had significantly greater minimum articular and total cartilage thickness. Overall, our data support the claim that Gpnmb overexpression is protective against post-traumatic and age-related OA.

Poster # 26B

Osteoactivin/Gpnmb, a novel therapeutic for post-traumatic osteoarthritis

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Osteoarthritis (OA) is a degenerative disease characterized by cartilage destruction, synovitis, and osteophyte formation and is the most common disease of the joint. Our laboratory is interested in investigating osteoactivin, also known as glycoprotein nonmetastatic melanoma protein B (Gpnmb), an anti-inflammatory glycoprotein, as a potential therapeutic in post-traumatic OA (PT-OA) mouse model, utilizing intra-articular recombinant Gpnmb (rGpnmb) and Gpnmb related-peptide (pGpnmb) treatment. C57BL/6 male mice underwent destabilization of medial meniscus (DMM) surgery of the right knee at 10 weeks of age. Treatment groups included sham, DMM with PBS injection, DMM with rGpnmb injection and DMM with pGpnmb injection. pGpnmb is a synthetic 18-amino acid peptide comprised of a portion of the C-terminus domain of Gpnmb. Injections were performed at 6 weeks post-DMM and animals were sacrificed at 14 weeks post-DMM. Knees were sectioned and underwent histological and histomorphometric analyses using Safarin-O and fast green staining, or tartrate resistant acid phosphatase (TRAP) staining. Intra-articular injection of rGpnmb or pGpnmb led to significantly less severe OA compared to those treated with PBS as shown via decreased OARSI and osteophyte scores. Animals treated with rGpnmb or pGpnmb had increased minimum cartilage thickness, and increased chondrocyte number compared to PBS treated animals. Histological BV/TV assessment showed increased subchondral BV/TV in PBS, rGpnmb and pGpnmb treated animals compared to sham operated animals, as Gpnmb is a known negative regulator of osteoclastogenesis. Trabecular histological BV/TV analysis showed increased BV/TV in animals treated with

pGpnmb in comparison to sham operated animals. Subchondral OC number and OC surface/bone surface trended upward with PBS treatment and did not for rGpnmb or pGpnmb treated animals. With no disease modifying treatment options for PT-OA available, the chondroprotective and subchondral bone remodeling protective effects of rGpnmb and pGpnmb show positive potential for their use as therapeutics for OA.

Poster # 27A

Drying habitats increase mite parasitism of their fly hosts

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Dehydrated environments are common settings for parasite-host interactions, and dehydration stress is well-documented in many species to influence parasitic behavior. Drosophila fruit flies are an example of such a system, frequently interacting with ectoparasitic mites in decomposing organic matter that is prone to drying as these habitats deteriorate. Here, we present two fly-mite systems that were examined to assess if increased mite parasitism occurred for Drosophila under dry conditions. Flies artificially selected for behavioral resistance to mites also had an increase in mite parasitism with the increasing dryness of surrounding media. Through water balance and activity assays, mites in dry conditions were confirmed to be dehydrated, becoming increasingly active, and there was an increase in mite parasitism. These results suggest the importance of drying conditions, and therefore the dehydration of mites, as a key factor in the intensity of mite infestations for fruit flies. This increase in parasitism may offset nutritional deficiencies of the local conditions and enable migration to more optimal environments.

Poster # 27B

Bioamine disruption leads to memory deficits in the whip spider *Phrynus marginemaculatus*

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Amblypygi (whip spiders) are an order of arthropods (Subphylum: *Chelicerata*, Class: *Arachnida*) that navigate primarily by their keen olfactory abilities. Experiments in the laboratory reveal that the species *Phrynus marginemaculatus* form both short and long-term memories for odors associated with access to a shelter. While bioamine function and location in the whip spider remains completely unexplored, comparative anatomy indicates that their olfactory memory likely depends on serotonin and dopamine signaling in a brain region relevant to olfactory input. Hence, if serotonin or dopamine activity is pharmacologically disrupted within the whip spider brain, their performance in an associative olfactory learning task should be significantly impaired. Subjects (n = 52) were trained on an olfactory memory paradigm, injected with 0.9% physiological saline, the serotonin receptor antagonist methiothepin mesylate (MET), or the dopamine receptor antagonist SCH-23390, and tested for memory retention 24 hours afterward. Controls injected with saline performed above chance (serotonin control: N = 10, p = 0.006, dopamine control: N = 10, p = 0.039), while treated groups performed at chance (MET: N = 10, p = 0.375, SCH-23390: N = 10, p = 0.892). There was a significant difference in performance between the treated and control groups on test day (serotonin groups: p = 0.048, dopamine groups: p = 0.016). Additionally, there were no significant differences in locomotion between the treatments and control groups on test day ($p > 0.05$). Taken together, these results indicate that these serotonin and dopamine antagonists impair olfactory memory consolidation without impairing locomotion in *Phrynus marginemaculatus*.

Poster # 28A

The effects of cocaine on sialyltranaferase levels in rat skeletal muscle

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Cocaine is a highly addictive drug that is rapidly becoming more popular and has been shown to cause

skeletal muscle damage with no treatment. There is currently no research about the effects cocaine has on sialic acid, a sugar that is found on the terminal end of sugar chains and is attached to skeletal muscle cells. Sialic acid plays a crucial role in stability, regeneration, and cell-to-cell recognition in skeletal muscles and has been linked to muscle atrophy when cells lack it. This study aimed to investigate the effects of cocaine on sialylation by investigating the enzyme sialyltransferase, which is responsible for adding sialic acid to skeletal muscle. We compared rats that self-administered cocaine to rats that self-administered saline. The rats' soleus and gastrocnemius were then used to perform a Western Blot to study the protein sialyltransferase levels. The primary antibody, ST6GALNAC4, was used to bind to the sialyltransferase enzyme, and the Goat Anti-Rabbit, a secondary antibody, was used to fluorescently tag the primary. The membrane with the antibodies was then imaged and quantified using ImageJ. Although the fluorescent intensity was slightly higher in the rats who had been administered cocaine, there was no significant difference between the sialyltransferase concentration in cocaine and saline rats. This study shows that more research needs to be done involving the effects of cocaine and its negative impacts on skeletal muscle.

Poster # 28B

Sex differences in endocannabinoid regulation of stress-cocaine interactions in rats

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Stress plays a vital role in substance use disorders (SUD), but its underlying neurobiological mechanisms have yet to be understood. Therefore, understanding the impact of stress on SUD is critical and can be examined using rats and a cocaine self-administration (SA) paradigm paired with an electric foot shock stressor that induces enhanced cocaine-taking and -seeking behavior within rats. This enhancement is likely influenced by a signaling pathway implicated in both reward and stress, such as the endocannabinoid (eCB) system. We hypothesize that eCB signaling is recruited by stress in mesocorticolimbic brain regions to regulate cocaine SA and cocaine-seeking behavior in male and female rats. Rats undergo cocaine SA in 4x30 minute blocks with 4x5 minute drug-free blocks, wherein intermittent electric foot shock was administered. Rats then underwent extinction training followed by cocaine-primed reinstatement testing. Foot shock significantly increased cocaine SA in both sexes. Systemic cannabinoid receptor 1 (CB1R) antagonist attenuates cocaine SA in both sexes with a history of stress. In male rats this was localized to the NAc shell and VTA. Additional rats were used to examine eCB regulation of cocaine-evoked dopamine via in vivo fiber photometry measurement of the dopamine biosensor, dLight 1.3b, in the NAc shell. Females were found to have higher sensitivity to CB1R and 2-AG regulation of cocaine-evoked dopamine than males. For cocaineseeking behavior, intra-PrL CB1R antagonist administration attenuates cocaine-primed reinstatement only in rats with a history of stress. These data suggest repeated stress recruits CB1R signaling in mesocorticolimbic brain regions to regulate cocaine SA and cocaine-seeking behavior. Females may be more sensitive to eCB regulation of cocaine-related behaviors, but further study is needed. Understanding the relationship between stress and cocaine-related behaviors is crucial and helps identify eCB signaling as a potential therapeutic target for cocaine use disorder.

Poster # 29A

Sex differences and the role of plasma extracellular vesicles in HFpEF pathology

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Background: Heart failure with preserved ejection fraction (HFpEF) accounts for ~50% of all heart failure, also the leading cause of morbidity and mortality in the US population. The pathophysiology of HFpEF is not well understood due to its multiple biological phenotypes contributing to heterogenous clinical syndrome. HFpEF is strongly associated with obesity and is higher in women, thus the sex-specific adipose-heart crosstalk especially via adipose derived extracellular vesicles (EV) is gaining much attention. Approach: We used C57BL/6J female and male mice, fed with high fat diet and L-NAME for a period of 8 or 16 weeks to induce HFpEF. Next, we investigated the sex differences in HFpEF phenotypes, heart mitochondria functions followed by isolation of plasma EV and their effect on iPSC-derived cardiomyocytes (iPSC-CMs) mitochondrial functions.

Results and conclusions: We first confirmed HFpEF is more pronounced in females than males with higher E/A and E/E' ratios, higher LV mass and lung mass. We also noticed females having higher fatty acid oxidation capacity in both 8 and 16 weeks of HFpEF compared to males. In HFpEF, the individual mitochondrial electron transport chain (ETC) activities are comparable in both sexes except for a significant decrease in complex IV activity in females at 16 weeks HFpEF in comparison with 16 weeks HFpEF males. Next, our nanoparticle tracking analysis (NTA) found that chow-fed female animals' plasma-EV are more diversified in their size compared to chow-fed males. However, this sex-specific EV size diversity was lost in HFpEF. Upon HFpEF, the EV count is increased in males compared to females. Strikingly, the plasma EV carries mitochondrial ETC subunits (mitochondrial complexes II, IV and V) in both sexes. Further, the iPSC-CMs treated with chow-fed female EV improved the mitochondrial functions. Currently, we aim to elucidate the sex-specific role of plasma EV in adipose-heart communications and HFpEF pathology.

Poster # 29B

The expanded version of the RNA binding protein PABPN1 is functionally insufficient and causes a dominant-negative RNA export defect in a cellular model of OPMD

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Polyadenylate binding protein nuclear 1 (PABPN1) is a primarily nuclear localized RNA binding protein involved in multiple early and late steps in RNA processing. The PABPN1 sequence contains an N-terminal ten alanine tract which has no known function. Small expansions of the polyalanine tract lead to the late onset oculopharyngeal muscular dystrophy (OPMD). OPMD is characterized by craniofacial and proximal limb muscle weakness and causes drooping eyelids, trouble swallowing, and loss of mobility. The mechanisms of OPMD remain poorly understood, and no pharmacologic therapies are available. Nuclear aggregates formed by expanded PABPN1 have been implicated in OPMD pathology, however aggregates are only seen in ~5% of muscle nuclei. We aim to define the protein binding partners of wild type and expanded PABPN1 using proximity labeling. Toward this aim, we constructed a PABPN1-TurboID fusion construct. Depletion of PABPN1 produces a defect in the export of poly(A) RNA, and we took advantage of this phenotype to assess the functional consequences of alanine expansion using oligo-DT FISH. WT PABPN1-TurboID functionally rescued RNA export in the presence of native PABPN1 depletion while expanded PABPN1 did not. As OPMD causes muscle weakness in mature myotubes, and expanded PABPN1 was insufficient to rescue RNA export, we expressed WT and expanded PABPN1-TurboID in mature myotubes under near native and overexpression conditions. Under both conditions expanded PABPN1-TurboID caused a dominant negative accumulation of poly(A) RNA in the nucleus and reduced cytoplasmic RNA. When we expressed expanded PABPN1-TurboID and took advantage of its labeling properties we found that it interacted with components of the nuclear export machinery less than wild type PABPN1-TurboID. Our future studies will focus on the mechanism of RNA export disruption in OPMD pathology. Our findings will expand the knowledge of PABPN1 function and provide additional insight into the mechanisms that ca

Poster # 30A

Inhibition of cardiomyocyte GLUT1 ameliorates KLF5 activation and diabetic cardiomyopathy

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Introduction: Cardiomyocytes primarily rely on fatty acid oxidation (FAO) for ATP synthesis. Paradoxically, despite increased FA utilization in diabetes, humans and mice develop diabetic cardiomyopathy (DbCM). We previously identified that KLF5 drives DbCM by inducing oxidative stress and lipotoxicity. Our present study explores the involvement of cardiac glucose metabolism in DbCM. Methods and Results: We induced Type 1 and Type 2 diabetes (T1D, T2D) in wild-type mice (streptozotocin and high-fat diet, respectively). Consistent with prior findings, cardiac KLF5 expression was elevated at 12 weeks post-T1D and 10 months post-T2D. Surprisingly early (4 weeks) and late (12 weeks) T1D cardiac gene expression analysis revealed higher PDK4 expression at the late stage, coinciding with oxidative

stress and severe cardiomyopathy. Seahorse analysis demonstrated enhanced mitochondrial glucose utilization in early T1D, which was attenuated in late T1D, while metabolomic analysis indicated higher myocardial glucose content. Given that GLUT4 translocation is impaired in diabetes, we examined if GLUT1 is involved in DbCM. Cardiomyocyte-specific GLUT1-/- mice were protected from DbCM in both T1D and T2D and so were they with pharmacological GLUT1 inhibition (STF31). Cardioprotection was associated with reduced cardiac glucose uptake (PET/CT), decreased KLF5 expression and its downstream targets involved in oxidative stress and ceramide biosynthesis, and lower oxidative stress (DHE staining). Cardiac metabolomic analysis revealed increased antioxidant metabolites (tyrosine, serine), while lipidomics showed no significant changes in toxic lipids. Notably, GLUT1 inhibition suppressed total protein O-GlcNAcylation, a major post-translational modification in diabetes. In AC16 cells, GLUT1 overexpression aggravated glucose-stimulated O-GlcNAcylation and OGT expression, whereas GLUT1 inhibition attenuated pyruvate and FAO genes (*Pdk4, Cpt1ß, Cd36*), restoring metabolic homeostasis. Conclusion: In diabetes, GLUT1 is essential in mediating activation of a firstly-described GLUT1–KLF5–dependent gluco-lipotoxicity axis that promotes DbCM, thus identifying GLUT1 as a promising therapeutic target

Poster # 30B

Investigating radiation sensitivity of proton therapy-treated HNSCC murine cells

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The conventional standard of care for Head and Neck Squamous Cell Cancer (HNSCC) is surgery followed by conventional photon (XRT) radiation and chemotherapy. Despite treatment advancements, the recurrence rate for HNSCC is high. Additionally, XRT can cause toxic side-effects to surrounding healthy tissue, decreasing the quality of life for patients. An alternate form of radiation therapy is proton therapy which utilizes protons rather than photons. Proton therapy offers advantages such as mitigating radiation-induced toxicity offering a more tissue-sparing approach due to the Spread-out Bragg Peak (SOBP). However little is known about radiation therapy resistance patterns to previously proton irradiated tumors. The goal of this project is to compare the radio-sensitivity of a secondary dose of XRT radiation on previously XRT and proton irradiated HNSCC tumor cells. We hypothesize that tumors previously treated with XRT (XRT-experienced tumors) will exhibit reduced resistance to reirradiation compared to those treated with proton therapy. Murine Oral Carcinoma (MOC-1) tumor xenografts were irradiated with equivalent doses of proton vs XRT, compared to non-irradiated tumor. Tumors were harvested to create radio-experienced cell lines in monoculture. To test radio-sensitivity, an APH assay was used to test cell growth, a clonogenic assay tested colony formation capability, and immunofluorescence staining of γ-H2AX to indicate DNA damage. Preliminary results have found proliferation to decrease in XRT and proton-experienced MOC-1cells but clonogenic capabilities to increase in previously proton irradiated cells compared to XRT and control cells. Although proton- and XRT- experienced cells accumulate less DNA damage immediately after irradiation, DNA repair appears to be impaired compared to control tumor cells. In conclusion, although PT and XRT increase cell survival after reirradiation, cellular mechanisms such as DNA repair and proliferation are decreased.

Poster # 31A

Disengaging hypoxia inducible factors 1 alpha (HIF-1α) regulation from hypoxia

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Hypoxia is a key factor in ischemia contributing to heart failure/stroke. β-adrenergic receptors (βARs) are key regulators of cardiac function, and their dysfunction underlies heart failure. Our previous study showed that acute hypoxia activates Phosphoinositide 3-kinase γ (PI3Kγ) in the endosomes impairing βARs resensitization leading to cardiac dysfunction and HIF-1α stabilization. However, acute hypoxia in PI3Kγ knock out (KO) mice resulted in preserved cardiac function and βAR signaling. Notably, HIF-1α did not accumulate in PI3Kγ KO mice despite hypoxia, showing novel regulation of HIF-1α by PI3Kγ. To investigate the role of PI3Kγ in HIF-1α regulation, we generated transgenic (Tg) mice with cardiomyocyte-specific expression of PI3Kγ under α-MHC promoter (PI3Kγ-WT). Immunoblotting of cardiac lysates revealed significant accumulation of HIF-1α in the

PI3Kγ WT Tg at baseline, while it was absent in the PI3Kγ KO and Non-Tg (NTg) controls. Similarly, overexpression of PI3Kγ-WT in HEK 293 cells leads to stabilization of HIF-1α even in normoxia while was minimal in the parental HEK 293 cells. Treatment of cells expressing PI3Kγ-WT with PI3K inhibitor wortmannin or overexpression of inactive PI3Kγ (deletion in the ATP binding site, PI3Kγ-inact) leads to loss in HIF-1α stabilization in normoxia showing that stabilization HIF-1α is kinase-dependent mechanism. These findings establish PI3Kγ as a novel regulator of HIF-1α that could bypass hypoxia-mediated regulation of HIF-1α to mediate unique transcriptional response underlying the anti-apoptotic role of PI3Kγ. Our cellular and cardiac studies show that PI3Kγ regulates HIF-1α stabilization through Von Hippel-Lindau (VHL), a key ubiquitin ligase mediating HIF-1α degradation and mechanisms of VHL regulation by PI3Kγ will be discussed in our presentation. Understanding the mechanisms of HIF-1α stabilization by PI3Kγ will provide insights on accelerating acute adaptive signaling in response to myocardial infarction/stroke.

Poster # 31B

Microglia-selective expression of APOE2 improves remyelination even in the presence of CNS APOE4

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Demyelination occurs with aging and is exacerbated in neurodegenerative diseases. During demyelination, microglia upregulate expression of apolipoprotein E (APOE), the gene encoding for the brain's primary lipid transport protein (ApoE). Compared to the E3 and E2 allele of APOE, the E4 allele increases risk for Alzheimer's disease and is associated with an increased severity and progression of multiple sclerosis. Previous work shows that mice expressing E2 exhibit improved microglial function and remyelination compared to mice expressing E4. However, whether microglial-derived APOE is responsible for driving these differences following demyelination, and whether microglia-selective expression of E2 is sufficient to provide protection, is unknown. We sought to determine if a microglia-specific replacement of the E4 allele with E2 can rescue myelin loss and promote remyelination, even in the presence of continued E4 CNS expression. E4 to E2 allelic "switch" mice (4s2M) and Cre-negative controls (4s2-) received tamoxifen at 6-weeks to induce a microglia-selective transition from expression of E4 to E2 (Tmem119-CreERT2). At 8-weeks, mice were given either lysophosphatidylcholine (LPC) corpus callosum injections (euthanized 10 d.p.i) or cuprizone (CPZ) diet for 5 weeks before sacrifice (demyelination) or return to standard chow for 1 week (remyelination). Histological assessment of myelination, gliosis, lipid droplets, and lipidomics were performed on brain tissue. We found that microglial E2 replacement decreased astrogliosis following LPC-demyelination, improved remyelination, lowered microgliosis and astrocytic lipid droplet load following CPZ-remyelination with subtle alterations to the CNS lipid profile. Our results indicate that microglia-specific E2 expression, in the presence of continued E4 expression, may provide protection against myelin loss via cell and non-cell autonomous mechanisms.

Poster # 32A

Atp13a2 deficiency triggers chondrocyte inflammation and exacerbates spontaneous osteoarthritis severity in an aging mouse model

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Introduction: Osteoarthritis (OA) is a chronic, degenerative joint disease characterized by the loss of joint cartilage and bone remodeling leading to joint pain, stiffness, and reduced mobility. Lysosomes are essential for cellular homeostasis and survival, as they break down and recycle unwanted cellular molecules and defective organelles. Atp13a2, a transmembrane lysosomal transporter protein, regulates the homeostasis of inorganic cations and polyamines. Based on these factors, we hypothesize that the loss of lysosomal function in chondrocytes induces inflammation that promotes OA pathogenesis with age. Methods: Knee samples were harvested from young (3-month) and old (18-month) mice. Micro-CT was used to examine bone-related changes, and histology was performed to determine the damage to cartilage and other joint tissues. Immunostaining was performed to assess the expression of inflammatory markers (IL-6, IL-1B, TNFa).

Results: Our analyses revealed a significant phenotypic difference between the bone of young WT and Atp13a2 KO female mice. Furthermore, old Atp13a2 KO mice exhibited a high degree of cartilage degeneration, as indicated by an increased OARSI score. LysoSensor staining revealed lower lysosomal function and reduced chondrocyte density in old Atp13a2 KO mice compared to age-matched WT littermates. Consistently, micro-CT imaging showed a higher number of osteophytes in the knee joints of old Atp13a2 KO mice compared to age-matched WT littermates. Immunostaining further showed high inflammation in Atp13a2 KO mice. Taken together, these results indicate that Atp13a2 deletion decreased lysosomal function, increased cell death, and exacerbated OA pathogenesis with age. Discussion: Mice deficient in Atp13a2 displayed a bone phenotype that progressed with age and varied by sex. These findings further demonstrated that the loss of Atp13a2 function triggered inflammation in chondrocytes and increased osteoarthritis severity in aging mice. Significance: Overall, the present study enhances our understanding of the role of the lysosome and its association with chondrocyte death in OA.

Poster # 32B

Next-generation 3D-printed scaffolds enhance auricular cartilage regeneration in pediatric microtia

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Introduction: Microtia is a congenital malformation characterized by the absence or underdevelopment of the external ear, often accompanied by auditory canal atresia and hearing impairment. Current reconstructive options are limited by donor tissue availability and variable cosmetic outcomes, driving the need for regenerative solutions. This study investigates plasma-enhanced 3D-printed scaffolds as a novel platform to promote chondrogenesis in auricular cartilage engineering. Methods: Auricular chondrocytes were isolated from five pediatric microtia patients under IRB approval (Akron Children's Hospital/NEOMED). Cells were seeded onto selective laser sintered (SLS) polyethylene (PE) scaffolds with or without plasma surface modification. Scaffold performance was assessed by (i) biocompatibility (MTT assays, 24–72 h), (ii) chondrogenic gene expression (qPCR: COL2A1, SOX9, Aggrecan), and (iii) extracellular matrix (ECM) deposition (Alcian Blue staining, 7–14 days). Results: Plasma-modified scaffolds significantly enhanced chondrocyte viability and proliferation compared with untreated controls. qPCR demonstrated strong upregulation of SOX9 and Aggrecan, coupled with downregulation of catabolic and inflammatory markers (MMP13, ADAMTS4, IL-1β), reflecting a favorable microenvironment for cartilage formation. Histological analysis confirmed robust glycosaminoglycan (GAG) deposition in plasma-treated groups, underscoring improved matrix synthesis and scaffold integration. Discussion: Plasma-treated SLS PE scaffolds—particularly SLS PE + RxG and SLS PE + RxC—demonstrated superior bioactivity, highlighting the critical role of surface modification in supporting auricular chondrocyte function. These findings position plasma-enhanced scaffolds as promising candidates for clinical translation in microtia reconstruction, offering a reproducible and patient-specific approach to cartilage tissue engineering.

Poster # 33A

Characterizing the mechanism of norepinephrine transporter in secondary lymphoid organ.

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Norepinephrine (NE) clearance at neuroimmune synapses is critical for regulating immune function in lymphoid organs like the mesenteric lymph node (MLN). Sympathetic nerves release NE to modulate immune cells, and its rapid removal is essential for controlling local immune responses. This clearance is primarily mediated by plasma membrane transporters from the SLC family, which use a sodium electrochemical gradient. Key monoamine transporters include the dopamine transporter (DAT), norepinephrine transporter (NET), serotonin transporter (SERT), and organic cation transporters (OCTs). We investigated the roles of these transporters in NE clearance using fast-scan cyclic voltammetry (FSCV) in ex vivo MLN slices. This technique allowed us to measure spontaneous NE transients with high temporal resolution. By pharmacologically inhibiting specific transporters—DAT with GBR12909, SERT with fluoxetine, and OCTs with verapamil—we observed significant changes in NE signaling kinetics. The results showed that blocking each transporter distinctly altered the NE peak amplitude, clearance rate, and event

frequency. This suggests that multiple transporters work together to regulate the availability of NE in the MLN on a rapid timescale. Further RT-PCR and immunoblotting assays confirmed the expression of these transport proteins. Our findings identify a cooperative mechanism for NE clearance at the neuroimmune interface. Understanding how these transporters terminate noradrenergic signaling is crucial for comprehending how sympathetic inputs shape adaptive immunity. This work highlights transporter-mediated clearance as a promising new target for future immunomodulatory therapies.

Poster # 33B

Egg viability is improved by tick burrowing into moist soil

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Ticks are important vectors of human and veterinary pathogens, and environmental factors strongly influence their survival off-host. One key but understudied factor is how soil microclimates, particularly soil moisture and relative humidity, shape the burrowing, oviposition, and reproductive success of gravid females. In this study, we examined the effects of soil moisture gradients, relative humidity, and chemosensory interference through Haller's organ disruption and DEET exposure on gravid tick reproductive behavior. Our findings show that gravid females actively seek favorable moisture conditions when selecting oviposition sites. In dry environments (10–33% RH), they burrowed and oviposited deeper, whereas in humid conditions (75–93% RH), they remained closer to the surface. This indicates that under desiccating conditions, gravid ticks move deeper into the soil to protect eggs from water loss, while in humid soils, shallow burrowing is sufficient. Soil moisture analysis confirmed that egg viability was lowest in dry soil and increased steadily with moisture, peaking at full saturation (100%). Thus, while females respond behaviorally to dryness by burrowing deeper, reproductive success ultimately depends on water availability for eggs. Sensory capacity proved critical in this process: ticks with intact Haller's organs located suitable depths, but sensory disruption or DEET exposure caused shallow oviposition regardless of humidity, thereby reducing reproductive success. These results demonstrate that gravid tick reproduction is shaped by abiotic factors (soil moisture and humidity) and biotic factors (sensory capacity) to ensure egg viability. Targeting these behaviors through habitat modification or sensory interference may provide ecologically sustainable strategies for tick control.

Poster # 34A

miR-146a overexpression protects and stabilizes the muscle environment in Duchenne muscular dystrophy

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Duchenne Muscular Dystrophy (DMD) is an X-linked genetic disease caused by mutations in the dystrophin gene, resulting in severe muscle weakness, degeneration, and early death. Abnormal phenotypes seen in DMD muscle include inflammation, fibrosis, and dysregulated metabolism. Literature suggests microRNA-146a (miR-146a) targets each of these phenotypes: inflammation via nuclear factor-kappa B, fibrosis via transforming growth factor-beta, and metabolism via peroxisome proliferator-activated receptor (Ppar)-alpha, Ppar-gamma, and peroxisome proliferator-activated receptor gamma coactivator 1-alpha. We therefore hypothesize that overexpression of miR-146a will reduce muscle inflammation and fibrosis in dystrophic mice and improve muscle metabolic defects, resulting in a stabilized muscle environment. We generated a cohort of dystrophin-deficient (mdx4cv) mice overexpressing miR-146a (mdx4cv;miR-146aKI/WT) and analyzed muscle histology at 3 and 7 months of age compared to mdx4cv mice. Data show reductions in inflammation (macrophages) and regenerating myofibers (embryonic myosin heavy chain expression) in skeletal muscle of mdx4cv;miR-146aKI/WT mice at 3 months of age and reduced cumulative muscle damage in the diaphragm muscle of mdx4cv;miR-146aKI/WT mice by 7 months of age. We performed spatial transcriptomics on diaphragm muscles of 7-month-old dystrophic mice and demonstrated that genes responsible for inflammation are downregulated with miR-146a overexpression, whereas driver genes for pathways involved in muscle function and oxidative phosphorylation (metabolism) are upregulated.

Collectively, our data show an exciting potential for miR-146a as a therapeutic to protect muscle from deleterious downstream effects of dystrophin-deficiency.

Poster # 34B

Absence of chloride intracellular channels (CLICs) offers resistance to hypoxia via differential regulation ERK and AKT pathways

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Ion channels are key regulators of cellular excitability, ion homeostasis, and signal transduction and hence are integral to the cellular response to hypoxia. Ion channel modulation under low oxygen conditions affects cell excitability and survival. Chloride intracellular channels (CLICs) are a unique class of chloride channels localized in the intracellular organelles. Given the known involvement of CLICs in redox regulation and their expression changes in hypoxia, we examined hypoxic responses of Drosophila melanogaster CLIC mutants that only possess one CLIC homolog. We applied hypoxia stress to the null mutant animals of and observed that CLIC mutant animals were resistant compared to their wild-type counterparts. Acute hypoxic stress followed by re-oxygenation did not decrease the cardiac function of mutant animals, unlike the wild types. We investigated the mechanistic reasons for this protection and found that loss of CLICs results in decreased mRNA, total protein, and phosphorylated form of ERK protein. We also observed that the CLIC mutants retained the organized structure of the fibers, while the wild types appeared haphazard. We have also found protective signaling pathways such as AKT are up-regulated as read by phosphorylation of AKT protein, an effect which went away when the AKT pathway was blocked via rapamycin. Taken together, we hypothesize that CLIC plays a role in inducing fibrosis and down-regulating survival proteins in hypoxic stress. Hence, blocking CLICs might be beneficial to prevent damage to the hearts during hypoxic scenarios, and would help overall survival.

Poster # 35A

Withdrawn

Poster # 35B

Exploring the efficacy of pantoprazole-based approaches for cancer treatment

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Cancer remains as a leading cause of mortality within the United States and is thought to continue to rise as time goes on. While there are many currently available chemotherapies for treatment, a main challenge in cancer treatment remains resistance in many cancer subtypes and severe side effects. This has led researchers to turn towards drug repurposing to turn to clinically approved drugs to not only provide a more cost-effective option for patients but also speed up the drug development process. While many commercially available medications have been explored, this study focuses on repurposing pantoprazole. Pantoprazole is currently used as a proton pump inhibitor that irreversibly binds to a pump to stop gastric acid secretion within the stomach. It is used often in gastroesophageal reflux disease, erosive esophagitis and for the prevention of stomach ulcers. Many have also found it to have a chemotherapeutic effect when used alone and in conjugation with current chemotherapies in a multitude of cancers. In a review of multiple trials, this study found that pantoprazole has promising effects specifically in breast cancer and glioblastoma patients. While many research studies were preliminary, they showed hopeful results that pantoprazole works on certain gene mutations such as fatty acid synthase in breast cancer and glioma-stem cells. One phase I clinical trial was done on solid tumors in castration-resistant prostate cancer along with doxorubicin therapy to determine the recommended dosage for phase II. While further clinical trials need to be executed, the goal of the current project is to explore the efficacy of pantoprazole's and pantoprazole-based approaches in cell culture systems as well as in preclinical and clinical settings against diverse cancer types, which support that drug repurposing is an avenue researchers should consider to make more effective and cost-conscious therapies.

Poster # 36A

Interaction between human APOE polymorphisms and sex differences in hippocampal mitochondrial functions in lean and obese mice

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Alzheimer's disease (AD) is a neurodegenerative disease that affects 6.5 million Americans aged 65 or older. Of the 6.5 million Americans with AD, 4.2 million of them are female, demonstrating that the female sex is at higher risk for AD than the male sex. One genetic risk factor for AD is APOE genotype. Apolipoprotein E (APOE) has three predominant alleles in humans: APOE2, APOE3, and APOE4. Individuals that are homozygous for APOE4 have up to a 15-fold increase in AD risk compared to APOE3 homozygous individuals. A third, modifiable risk factor for AD is diet. A high fat, "Western" style diet has been shown to be associated with AD. 12-week-old human APOE3 and APOE4 knock-in mice of both sexes were fed a standard chow or Western diet for 16 additional weeks (total 6 months old) to investigate the effects of diet, sex, and APOE genotype. Hippocampus were separated from the brains and processed for mitochondrial frozen respirometry and immunoblotting. When fed a chow diet, there were no differences in respiration capacities between the APOE3 and APOE4 genotypes within the sexes. However, chow-fed females of both genotypes displayed significantly decreased mitochondrial complex I- and IV- dependent respiration capacities in the hippocampus compared to chow-fed males. When fed a Western diet, APOE4 males displayed significantly decreased mitochondrial complex I- and IV-dependent respiration capacities as well as significant reduction in all electron transport chain complex proteins compared to APOE3 males. Our findings suggest that female APOE4 KI mice exhibit reduced mitochondrial function under chow-fed conditions compared to male APOE4 KI mice. A Western diet leads to mitochondrial maladaptation in male and female APOE4 KI mice, however mitochondrial dynamics differ between the sexes, demonstrating different responses of mitochondria to stress. Further research is needed to examine which mitochondrial response to stress is beneficial or detrimental.

Poster # 36B

Modulation of fear behavior and neuroimmune alterations in a model of allergic asthma in female mice

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Accumulating evidence suggests that chronically elevated inflammatory load may be a potential risk factor for PTSD. Allergic asthma is a common inflammatory condition known to cause airway inflammation (AI) and compromised mental health. Evidence supports a strong association of severe asthma with PTSD although underlying mechanisms are unknown. To address this knowledge gap in our lab developed a model of house-dust-mite (HDM) exposure effects on fear conditioning and extinction in male mice, reporting compromised fear extinction in mice with severe neutrophilic AI. As women have a higher prevalence of PTSD as well as immune/inflammatory conditions, it is now important to determine effects of AI in females. Accordingly, in the current study female mice were exposed to HDM +/-anti-C5aR1 antibody to elicit mild versus severe AI. Consistent with our male study, fear extinction-specific effects were observed in females suggesting a vulnerability of extinction-regulatory mechanisms to severe AI. However, contrary to males severe AI females exhibited active rearing behavior and low freezing during extinction suggesting divergent defensive coping. Preliminary mapping of regional delta FosB showed increased neuronal activation in subregions of the bed nucleus of stria terminalis (BNST) in severe AI mice, an effect absent in males. Our data indicates potential engagement of discrete fear circuits in severe AI effects on extinction. Current studies are exploring immune alterations in the lung (T cells) and brain (microglia) in females, hypothesizing increased lung neutrophilic response and microglial alterations within BBB-devoid circumventricular nodes. Collectively, these data indicate sex-specific behavioral effects of severe-airway inflammation, suggesting potential divergence at the cell-circuit level. Our studies provide valuable insights on the association between lung inflammation and mental health pertinent to increased susceptibility observed in females.

Poster # 37A

Exploring the allocation of copper to mitochondria during myoblast differentiation

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Copper (Cu) is required for various biological processes, including cellular respiration. One of its critical roles is serving as a cofactor in cytochrome c oxidase (COX), the terminal enzyme in the mitochondrial electron transport chain. Assembly of the COX complex requires several accessory proteins, including SCO1/2, COX11, COA6, COX19, and COX17. The mitochondrial matrix stores copper used for COX assembly, and it is transported into the mitochondrial matrix via SLC25A3. Interestingly, SLC25A3 also facilitates the transport of inorganic phosphate. Loss of SLC25A3 function results in reduced COX activity, and mutations in the SLC25A3 gene have been linked to skeletal and cardiac myopathies, emphasizing the importance of mitochondrial copper homeostasis in muscle function. The specific role of SLC25A3 in copper transport during skeletal muscle development remains underexplored, especially concerning mitochondrial copper loading during myoblast differentiation. Differentiation is a copper-dependent process, and copper distribution within the cell varies with differentiation stage. Early in differentiation, copper is primarily directed to ATP7A, which supplies copper to lysyl oxidase (LOX), a secreted enzyme critical for extracellular matrix remodeling and myocyte fusion. In later stages, copper levels increase while ATP7A expression decreases, suggesting a shift in copper utilization toward mitochondrial processes like COX assembly. We hypothesized that mitochondrial copper delivery becomes essential in late differentiation. Supporting this, levels of COX proteins and copper assembly factors rise, and COX activity increases. SLC25A3 deficiency with mild copper chelation reduced COX and myotube width, though differentiation proceeded. However, SLC25A3 loss in mature myotubes impaired survival. Similar results were seen with COX inhibition or COX17 deletion. These findings suggest mitochondrial copper import via SLC25A3 is required for mature myotube function.

Poster # 37B

Exploring the responses of therapeutic outcomes and adverse effects of aurora kinase inhibitors in diverse human malignancies

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Aurora kinases (AURKA, AURKB, and AURKC) are a group of threonine/serine kinases that regulate mitotic events such as segregation of chromosomes, cytokinesis, and spindle assembly. Circumstances resulting in increased activity and/or expression levels of these kinases are most commonly seen across different cancers and are connected to progression of tumors, resistance to therapies, and poor clinical outcomes. Due to this, Aurora kinase inhibitors (AKIs) are actively being used as anticancer agents and have over 50 compounds tested in many clinical trials. AKIs tend to display a wide-range of antitumor activities in specific hematologic malignancies such as multiple myeloma and acute myeloid leukemia as well as solid tumors, including ovarian, breast, and non-small cell lung cancer. The responses in a clinical setting tend to vary and show to be stronger when combined with standard radiotherapy, chemotherapy or other targeted agents. AURKA inhibition in certain situations can lead to the suppression of centrosome amplification, an increase in tumor cell apoptosis and reduced oncogenic signaling. Whereas AURKB can hinder chromosomal condensation and cytokinesis, while also causing mitotic catastrophe. However, resistance mechanisms such as compensatory signaling, mutations in the kinase domain and efflux can properly cap the effectiveness. Harmful effects keep continuing to be a major obstacle to clinical utility. Hematological toxicities (anemia, thrombocytopenia and neutropenia), gastrointestinal toxicities (diarrhea, nausea and mucositis), hypertension and fatigue, are more frequently seen toxicities. However, pan-Aurora inhibitors tend to have a marginally larger toxicity when compared to selective agents. The more limited therapeutic range shows the need for dose optimization and use of biomarkers for patient stratification. The goal of the current project is to compare the therapeutic outcomes and adverse effects of AKIs across diverse human malignancies with the objective of identifying selective inhibitors for combinations to improve AKIs long-term efficacy while decreasing adverse effects.

Poster # 38A

Loss of FSP27 impairs cognitive function via disruption of neuro-metabolic pathways

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Fat-Specific Protein 27 (FSP27), originally identified for its role in adipocyte lipid metabolism and energy homeostasis, plays a key role in regulating lipolysis and maintaining insulin sensitivity. Beyond adipose tissue, emerging studies have uncovered its involvement in hepatic and skeletal muscle function. More recently, FSP27 has also been implicated in maintaining vascular health through its influence on endothelial signaling. Despite growing insights into FSP27's systemic functions, its involvement in the central nervous system and cognitive regulation has remained unexplored. In this study, we present the first evidence that FSP27 is a critical regulator of cognitive function. Utilizing a global FSP27 knockout (Fsp27-/-) mouse model, we demonstrate that FSP27 deficiency results in significant impairments in learning, memory retention, and spatial awareness. To elucidate the underlying molecular mechanisms, genome-wide transcriptome profiling of brain tissue from Fsp27-/- mice was performed, revealing significant ($P<0.05$) alterations in gene expression related to neurocognition and metabolic pathways. Notably, FSP27 deletion was associated with genomic instability (P=0.05), downregulation of genes essential for axonal transport (NES=-1.91, FDR q-value=0.21), neuronal plasticity, and brain development (NES=-1.91, FDR q-value=0.28), along with signatures of disrupted systemic metabolism and elevated stress responses (NES=1.81, FDR q-value=0.20) in the brain, the processes tightly linked to cognitive dysfunction. Collectively, these findings establish FSP27 as a molecular node connecting metabolic regulation with cognitive health and identify it as a promising target for therapeutic intervention in neurodegenerative and cognitive disorders.

Poster # 38B

How female sex affects mitochondria in Alzheimer's disease

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Alzheimer's disease (AD) is a neurodegenerative disease that affects more than 6.5 million Americans annually, with approximately 4.2 million of them being female, highlighting the increased risk of AD in women. Mitochondrial maladaptation is a hallmark of AD pathology, characterized by decreased respiration, reduced levels of mitochondrial proteins and altered mitochondrial dynamics. Our goal in this project is to investigate how female sex affects mitochondria in a mouse model of Alzheimer's disease. To answer this question, we used the 5xFAD (on a C57BL/6J background) mouse model, which carries two transgenes (APP and PSEN1) with five AD-causing mutations. Brains were harvested at 2, 4 and 6 months of age, and hippocampi were isolated for further analysis. Mitochondrial function was assessed using frozen mitochondrial respirometry, protein levels were evaluated through immunoblotting, and AD progression was examined through staining. Our preliminary results indicate that 2-month-old females exhibit reduced levels of mitochondrial proteins compared to their male counterparts. The findings from this project will guide future research on mitochondrial involvement in AD.

Poster # 39A

Role of growth hormone in post-traumatic osteoarthritis

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Growth hormone (GH) regulates skeletal growth, cartilage metabolism, and subchondral bone remodeling; however, its local versus systemic contributions to osteoarthritis (OA) remain unresolved. Our previous work demonstrated that bovine GH transgenic mice develop severe age-related OA, whereas germline GH receptor knockout (GHR-/-) and GH

antagonist mice are protected. To further dissect GH action in OA, we employed both cartilage-specific and systemic GHR knockout models in a post-traumatic OA (PTOA) context. Noninvasive anterior cruciate ligament rupture was induced at 10–13 weeks of age, followed by weekly assessment of knee hyperalgesia for 8 weeks and endpoint analyses of cartilage, subchondral bone, and osteophytes by histology and micro-CT. Cartilage-specific GHR deletion conferred a sex-dependent effect: female GHR-CartKO mice exhibited significantly higher knee hyperalgesia thresholds and reduced osteophyte formation after injury compared with wild-type controls, whereas no protection was observed in males. In systemic GHR-/- mice, both sexes showed reduced hyperalgesia and diminished osteophyte formation, along with attenuated OA pathology. These findings indicate that GH signaling contributes to OA progression through mechanisms that may involve both local joint effects and systemic actions, with cartilage-specific GHR deletion yielding sex-specific benefits and systemic deficiency conferring broader protection. Overall, our study underscores the physiological role of GH signaling in joint homeostasis and OA pathogenesis and highlights its potential as a therapeutic target in musculoskeletal disease.

Poster # 39B

The effects of systemic gene therapy with AAV-lipin1 on model Duchenne muscular dystrophy skeletal muscle

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Duchenne muscular dystrophy (DMD) is a genetic recessive disorder caused by loss of functional dystrophin protein, leading to progressive muscle degeneration and weakness. While gene therapy using adeno-associated virus (AAV) to restore dystrophin expression is a promising approach, the large size of the dystrophin gene presents significant delivery challenges, highlighting the need for alternative therapeutic strategies. Past studies show that Lipin-1, a protein critical for muscle health and membrane integrity, is reduced in DMD patients and mdx models of DMD. Moreover, restoring Lipin-1 expression in transgenic mdx mice that lack dystrophin resulted in marked improvement in molecular, histological, and functional symptoms of the disease. To evaluate the therapeutic potential of systemic Lipin-1 gene delivery, we administered MyoAAV-Lipin1 to mdx mice and assessed muscle histology and function post-treatment. In gastrocnemius muscle, Picrosirius Red staining showed a large decrease in collagen deposition and H&E staining supported improved tissue morphology in MyoAAV3-Lipin1–treated mdx mice. Furthermore, the systemic gene therapy provided protection against eccentric contraction–induced injury in gastrocnemius muscle using an in-situ approach. The Lipin1-treated mdx mice retained 48.9% of their initial force during repeated eccentric contractions, compared to 26.1% in mdx. We also include an initial examination of ex vivo eccentric force production in fast-twitch extensor digitorum longus (EDL) in MyoAAV-treated D2-mdx mice, a more severe mouse model of DMD. Overall, our results suggest that systemic Lipin-1 delivery via AAV can lower fibrosis and protect muscles from contraction-induced injury. This makes gene therapy with Lipin-1 a promising treatment for DMD that may be employed in combination with glucocorticoids and possibly other gene therapy approaches.

Poster # 40A

Metabolomic profiling uncovers a sex-specific bone phenotype in a pre-clinical model of non-syndromic-autosomal recessive intellectual disability

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Intellectual disability (ID) affects 1–3% of the global population, with a U.S. pediatric prevalence of 2.2% between 2019 and 2021. While X-linked causes of ID are well characterized, many autosomal-recessive forms remain poorly understood. Non-syndromic autosomal-recessive ID (NS-ARID) due to TRAPPC9 mutations is associated with microcephaly, obesity, and skeletal abnormalities. Recent reports suggest skeletal and dental features may be part of the phenotype, though mechanisms linking TRAPPC9 to bone biology are unknown. Notably, TRAPPC9 knockout (KO) mice exhibit sex-specific behavioral differences, raising the possibility of dimorphic effects on skeletal homeostasis. To address this, we examined the skeletal phenotype of TRAPPC9 KO

mice in a sex-dependent manner. Male and female KO and wild-type mice were analyzed at 6–8 and 30–35 weeks using micro-CT, chemical isotope labeling LC-MS, gene expression, and osteoclast differentiation assays. Our findings revealed clear sexual dimorphism. Young KO mice of both sexes showed no differences in bone volume fraction (BV/TV) compared to controls. With age, however, KO females exhibited increased BV/TV, whereas KO males displayed reduced BV/TV. Metabolomic profiling of bones from aged mice identified alterations in key metabolites, including elevated Taurine in KO females but not males. Taurine is known to suppress osteoclastogenesis and enhance osteoblastogenesis. Consistently, KO females showed reduced TRAP and OC-STAMP expression in bone, indicating suppressed osteoclast activity. Paradoxically, in vitro assays demonstrated increased osteoclast formation from bone marrow precursors in both sexes, suggesting a disconnect between precursor potential and in vivo function.

Poster # 40B

Regional variability of lipid content in normal versus diabetic hearts and coronary microvessels

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Type 2 Diabetes (T2D) is both a metabolic and cardiovascular disease characterized by hyperglycemia and insulin resistance. Elevated circulating fatty acids (FA) in T2D are associated with myocardial injury, including fibrosis, apoptosis, reduced contractility, and left ventricular dysfunction. A hallmark of diabetic myocardium is a shift toward FA metabolism and increased lipid deposition, even in patients with preserved function, suggesting metabolic remodeling precedes structural decline. Lipid droplets (LDs) are essential for lipid storage and homeostasis, buffering cells against FA excess, but in non-adipose tissues such as the heart, their accumulation can contribute to lipotoxicity. Based on prior transcriptomics data showing enrichment of adipogenesis pathways in diabetic myocardium and coronary microvasculature (CRM), we hypothesized that lipid deposition would be increased in CRM, perivascular, and myocardial regions of T2D db/db mice compared to controls, with further increases in fasted db/db animals. Hearts from non-diabetic and db/db mice (n=5–6 per group), including fasted and non-fasted cohorts (n=2–3 per group), were perfusion-fixed at 17 weeks. Tissue was stained with BODIPY to visualize neutral lipid droplets, imaged at 40x, and analyzed with ImageJ. We observed significantly greater BODIPY staining in db/db myocardium ($p=0.0036$) and perivascular regions ($p=0.0320$) compared to controls. In contrast, CRMs showed minimal lipid accumulation and no significant group differences, despite expression of lipid-handling proteins such as PLINs. A trend toward increased lipid deposition in fasting db/db mice was observed but not statistically significant, likely due to small sample size. These results suggest that while myocardial and perivascular lipid accumulation is a key feature of diabetic hearts, CRMs may possess protective mechanisms against lipid overload, potentially mediated by PLIN-associated pathways.

Poster # 41A

Repurposing aurora kinase A and B inhibitors to enhance immunotherapy in non-small cell lung cancer

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Lung cancer remains a leading cause of cancer-related mortality worldwide, with limited treatment options for patients resistant to standard therapies. Immune checkpoint inhibitors (ICIs) targeting programmed death-1 (PD-1)/PD-ligand1 (PD-L1) and cytotoxic T-lymphocyte antigen 4 (CTLA-4) have revolutionized cancer therapy but are hindered by immune evasion mechanisms within the tumor microenvironment (TME). Aurora kinases (AURKA and AURKB) are the key regulators of cell cycle progression, which have emerged as promising therapeutic targets due to their dual roles in tumor proliferation and immune modulation. AURKA inhibition enhances anti-tumor immunity by reducing immunosuppressive factors such as transforming growth factor beta (TGF-β) and interleukin 10 (IL-10), lowering PD-L1 expression, and increasing MHC-I-mediated antigen presentation. Preclinical and clinical studies demonstrate that combining AURKA inhibitors with ICIs leads to significant tumor regression and enhanced T cell response. AURKB inhibition reprograms the TME by downregulating PD-L1, reducing immunosuppressive cytokines, and improving T cell-mediated immune responses. Preclinical and clinical studies demonstrate that AURKB inhibitors enhance immune responses and sensitize tumors to immune checkpoint blockade,

resulting in tumor regression and improved survival outcomes when combined with ICIs compared to monotherapy. This review will provide a concise overview of the biology of Aurora kinases and their oncogenic roles, as demonstrated in preclinical and clinical studies on lung cancer. Ongoing clinical trials are investigating their combination with immune checkpoint inhibitors (ICIs) to evaluate efficacy and identify biomarkers for patient selection. This dual-targeting approach presents a promising strategy to overcome immune resistance and enhance treatment outcomes in lung cancer.

Poster # 41B

Protein glutathionylation is essential in acute myeloid leukemia through OxPhos regulation

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Acute Myeloid Leukemia (AML) is an aggressive blood cancer that affects both peripheral blood and bone marrow. Its low five-year survival rate is primarily due to high rates of relapse, driven by a rare subset of treatment-resistant cells known as leukemia stem cells (LSCs). LSCs are highly dependent on oxidative phosphorylation (OxPhos) to maintain their survival. However, direct inhibition of OxPhos has shown significant toxicity in clinical trials. To overcome this, our research investigates alternative regulatory mechanisms that control OxPhos in LSCs, aiming to uncover safer targeted therapeutic options. In our lab, we found that OxPhos in LSCs is modulated by a reversible protein modification called glutathionylation, where glutathione is temporarily conjugated to cysteines that have been oxidized by reactive oxygen species generated by some cellular processes and AML therapies. This modification protects proteins from damage, aiding LSCs to survive during treatment. Since glutathionylation typically impairs protein function, its reversal—deglutathionylation—is essential once oxidative stress is resolved. This process is in part mediated by a family of enzymes called glutaredoxins. Our preliminary data shows that the mitochondrially localized glutaredoxin 2 (GLRX2), is overexpressed in LSCs compared to hematopoietic stem and progenitor cells (HSPCs). When we depleted GLRX2, energy production and viability in leukemia cells was impaired, while HSPCs were spared, indicating a specific vulnerability in AML. To further understand GLRX2's role, we conducted RNA-sequencing on GLRX2-depleted AML cells. The analysis revealed that GLRX2 is essential for the proper splicing of RPTOR, a key mediator of the mTOR signaling pathway, which regulates cellular metabolism. This connection between GLRX2 and RPTOR had not previously been reported in AML. Our findings uncover a novel metabolic dependency in LSCs and offer a potential therapeutic target that will spare HSPCs

Poster # 42A

An initial evaluation of body protective compound 157 (BPC-157) a peptide, as treatment for musculoskeletal pain

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Musculoskeletal injury and pain remains a common and challenging condition to manage, often requiring medications that carry risks of delayed healing, dependency, overdose, or other side effects. BPC-157, a stable gastric pentadecapeptide with regenerative and anti-inflammatory properties, has emerged as a potential non-opioid option for musculoskeletal healing and pain. In this Pilot study, patients with musculoskeletal injuries were treated with BPC-157 to evaluate its analgesic effects. Pain intensity was measured using patient-reported numeric rating scales (NRS) over several weeks following treatment. Patients received BPC-157 (500 µg) via subcutaneous injection daily for ten days. Results showed a relevant reduction in self-reported pain scores over time, with most patients experiencing substantial improvement at 2 week intervals and 3 weeks after treatment, despite no significant improvement during the first week. Across all patients, no adverse effects were reported during the treatment with BPC-157. These findings suggest that BPC-157 may offer a safe and effective therapeutic alternative for the treatment of musculoskeletal pain. Further controlled trials are required to confirm these outcomes and to evaluate the duration of treatment and relief in musculoskeletal injuries.

Poster # 42B

Does zinc deficiency promote renal inflammation?

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Background: Renal inflammation is a crucial factor in the progression of Chronic Kidney Disease (CKD), significantly contributing to kidney damage and dysfunction. Individuals with CKD often exhibit low serum zinc (Zn) levels. Our preclinical models demonstrated that Zn deficiency promotes kidney damage. Since renal inflammation is implicated in kidney damage, this project seeks to investigate if Zn deficiency promotes renal inflammation. Experimental Design: To investigate if disrupted Zn homeostasis induces renal inflammation, male mice were administered a Zn adequate- or Zn deficient-diet for six weeks. Kidney damage was examined by assessing glomerular (morphological) and tubular (urinary KIM1) changes. Renal inflammation was evaluated by measuring the expression of a proinflammatory cytokine (urinary IL6) and presence of renal macrophages (CD68+, F4/80+, and CD206+). Results: Compared to Zn adequate mice, glomerular histological changes were observed in Zn deficient mice, including loss of endothelial cells, increased urinary space, and mesangial cell expansion. Also, KIM1 and IL6 expressions were elevated with Zn deficiency. Consistently, increased abundance of renal macrophages was observed in Zn deficient mice. Summary: These data demonstrate that Zn deficiency-induced renal damage is accompanied by renal inflammation. Taken together, these novel findings highlight renal inflammation as a possible driving factor in the progressive kidney damage and dysfunction associated with CKD. Funding: NIDDK R01 DK-133698

Poster # 43A

Role of PKLR overexpression and knockdown in cholesterol biosynthesis

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Background: Coronary artery disease is the leading cause of death in the United States and can stem from having abnormal plasma lipid levels. Cholesterol, the most important sterol in mammals, is essential for cellular function and membrane structure. The liver plays an essential role in maintaining cholesterol homeostasis by regulating its synthesis, storage, transport through lipoproteins and reuptake. Disruptions in circulating cholesterol levels are major contributors to atherosclerosis. Our previous studies identified PKLR (liver pyruvate kinase) as a potential causal gene involved in lipid imbalances. In the present study, we plan to explore this relationship further to establish PKLR as a causal gene for elevated plasma cholesterol levels leading to atherosclerosis. Approach: We used PKLR loss-of-function and gain-of-function strategies in mice, AML12 (mouse hepatocyte cell line) and/or HUH7 cells (human hepatoma cell line) and cholesterol levels and cholesterol homeostasis-related genes were measured. Results: We first demonstrated that PKLR overexpression in mice increased plasma cholesterol levels, accompanied by an upregulation of liver Srebf2 and Pcsk9 gene expression, both key regulators of cholesterol homeostasis. In contrast, PKLR silencing ameliorated them. Next, we demonstrated that PKLR overexpression in hepatocytes led to a marked accumulation of lipid droplets, primarily due to increased cellular cholesterol levels. In addition, PKLR overexpression increased Srebf2 and Pcsk9 gene expression, as well as PCSK9 protein levels in these hepatocytes. Follow-up studies demonstrated that PKLR modulates SREBP2 signaling through mitochondrial ROS (mtROS) generation. We report that scavenging mtROS reversed the PKLR overexpression phenotypes. Lastly, studies in atherogenic mice further revealed that PKLR silencing reduced both total and LDL cholesterol levels. Conclusions: These findings suggest that PKLR plays a critical role in cholesterol metabolism and plays a causative role for hypercholesterolemia. Our results provide new insights into the molecular mechanism linking PKLR to aberrant plasma cholesterol levels and cardiovascular risk.

Poster # 43B

Characterizing the functional properties of a malarial parasite homolog of the iron transporter DMT1

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Malaria is a life-threatening infectious disease caused by *Plasmodium* species. We have identified a *Plasmodium falciparum* homolog of human divalent metal-ion transporter-1 (hDMT1), so named PfDMT1, that is required for blood-stage growth and iron metabolism [*Proc Natl Acad Sci USA* **121**, e2411631121; 2024]. How the parasite acquires iron from the acidified food vacuole (containing hemoglobin) is unknown. hDMT1 is a H^+-coupled transporter that transports iron from acidified environments into the cytoplasm, e.g. from the recycling endosomes in red blood cell precursors. We tested the hypothesis that PfDMT1 is a H^+-coupled iron transporter. We expressed PfDMT1–GFP and hDMT1–GFP fusion proteins in RNA-injected *Xenopus* oocytes and used a radiotracer assay to examine iron-transport activity. Whereas we observed strong fluorescence at the perimeter of oocytes expressing hDMT1–GFP and robust $^{55}Fe^{2+}$ uptake at pH 5.5, we observed very faint fluorescence in oocytes expressing PfDMT1–GFP and little or no iron-transport activity. Expression of PfDMT1 stimulated $^{55}Fe^{2+}$ uptake at pH 4.5 but the activity was not sufficient for detailed characterization. We have generated PfDMT1-hDMT1 chimeric constructs in an attempt to obtain robust expression in the oocyte and activity and test only specific regions of PfDMT1 substituted into the hDMT1, namely: (i) PfDMT1 TM1–12, (ii) TM1 and TM6, (iii) 6 residues in the metal-binding pocket in TM6. By measuring $^{55}Fe^{2+}$ uptake and Fe^{2+}-evoked currents (two-microelectrode voltage clamp) we will compare the properties of PfDMT1 and hDMT1, specifically with regard to: (i) $K_{0.5}$ for $^{55}Fe^{2+}$, (ii) metal-ion selectivity, (iii) voltage dependence, and (iv) H^+ coupling. We expect the results of this comparative analysis will provide insight into the structure and function of PfDMT1, and aid in the development of new approaches for treating or preventing malaria.

Poster # 44A

Comparative analysis of diphenylbutylpiperidine class of compounds for cancer treatment: evidence from single vs. combination approaches

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Ongoing challenges in oncology treatment have prompted growing interest in research on repurposed drugs that can target shared cancer cell mechanisms. Despite initial therapeutic success, cancer cells often acquire resistance, leading to treatment failure. Among repurposed drugs, antipsychotics have gained prominence due to their multiple mechanisms extending beyond dopaminergic signaling. These drugs influence diverse cellular processes, including apoptosis, organelle function, metabolism, and oncogenic cascades, making them potentially useful for complex, treatment-resistant cancers. Within this group, the diphenylbutylpiperidine (DPBP) antipsychotics penfluridol and fluspirilene have shown emerging anticancer potential. The goal of the current project is to highlight the underlying mechanisms of these agents as well as discuss DPBP-based combination approaches exhibiting additive or synergistic effects for cancer treatment. Overall, the comparative analysis reveals that both penfluridol and fluspirilene target critical cancer pathways through overlapping and distinct mechanisms, highlighting their potential as candidates for combination therapies with conventional treatments. These findings support the repurposing of DPBP antipsychotics as part of combination oncology therapies, warranting further preclinical and translational studies to advance their clinical potential.

Poster # 44B

Hemochromatosis, hepcidin, ferritin, and transferrin in cancer: mechanistic insights and clinical implications

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Hemochromatosis has been studied as a pluripotent disease with mutations in iron-regulatory genes such as HFE, which primarily induce hereditary hemochromatosis (HH), and is increasingly implicated in cancer pathogenesis beyond liver cancer. Notably, the hepcidin-ferroportin axis is central to this phenomenon

where dysregulated iron homeostasis alters iron availability because of the increased production of reactive oxygen species (ROS) and modification of the tumor microenvironment. Oncogenic transformation, tumor progression, and metastasis are facilitated by aberrant regulation of key iron-binding proteins such as hepcidin, transferrin, transferrin receptors (TfR1/TfR2), and ferritin that regulate oxidative DNA damage, immune evasion, and resistance to ferroptosis. This review consolidates recent advancements in the mechanistic understanding of iron dysregulation in diverse cancers, with a particular focus on the roles of beta2-microglobulin, inflammatory signaling, and epigenetic reprogramming in hemochromatosis-linked oncogenesis. We also summarize experimental and clinical evidence linking HH with cancer phenotypes, highlighting the mechanistic relevance of hepcidin, ferritin, and transferrin in tumor initiation, progression, and therapy resistance. Furthermore, emerging therapeutic strategies targeting iron metabolism, such as iron chelators, hepcidin mimetics and inhibitors, transferrin receptor-directed drug delivery, and ferroptosis-based interventions, are also emphasized. These studies indicate the exciting possibilities of exploring iron modulators as promising approaches for precision oncology, particularly in tumors driven by iron addiction and hemochromatosis-related molecular alterations.

Poster # 45A

Immune checkpoint inhibitor cardiotoxicity screening: using a single test to diagnose a condition

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Immune checkpoint inhibitors (ICIs), such as Ipilimumab and Nivolumab (Ipi3/Nivo1) enhance the host anti-tumor immune response but may increase the risk of autoimmune reactions, such as myocarditis. This case demonstrates biologically active brain natriuretic peptide (BNP), *N*-terminal prohormone BNP (NT-proBNP), and troponin can be utilized as useful, but potentially discordant, biomarkers. A 59-year-old Caucasian male with an history of metastatic melanoma to the lungs, brain, and spine presented with severe headaches and persistent fatigue. They were first diagnosed with stage IA (T1bN0Mx) malignant melanoma of the right lower back which metastasized to a IIB (T4aNxMx) right chest wall nodular melanoma. MRI later revealed brain metastases escalating treatment to Ipilimumab and Nivolumab (Ipi3/Nivo1). Patient then developed Grade 4 hepatitis with an AST 395 U/L (13-39 U/L) and ALP 1097 U/L (7-53 U/L). Ipi3/Nivo1 was discontinued to begin prednisone (1 mg/kg) and mycophenolate mofetil (500 mg BID). Additionally, BNP was 748 pg/mL (normal range 0–100 pg/mL) and troponin was 5 ng/L (0–20 ng/L), prompting further evaluation of cardiac function. The patient had no history of heart conditions or taking BNP altering medications such as Entresto (sacubitril and valsartan). Echocardiogram revealed normal cardiac output estimated at 60–65%, no signs of pericardial effusion or pericarditis. NT-proBNP was 71 (0–210 pg/mL). BNP levels eventually returned to normal at 17 pg/mL (0–100 pg/mL). In screening for cardiovascular toxicity for patients treated with Ipi3/Nivo1, NT-proBNP, troponin, and BNP are sensitive markers of myocardial damage associated with autoimmune consequences of ICIs. Treating practitioners should not take a single abnormal value, specifically of BNP and NT-proBNP, as an indication a patient has potentially fatal myocarditis as values can be elevated in inflammation and hepatic diseases. Nevertheless, vigilance for cardiovascular symptoms must be maintained when using ICIs. True toxicities must be ruled out to avoid premature cessation of beneficial cancer treatment.

Poster # 45B

Adipocyte subpopulations regulate growth hormone action

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Growth hormone (GH) has pleiotropic effects in adipose tissue, as it stimulates lipolysis, inhibits lipogenesis, and induces proliferation and adipogenesis. In our previous publication, we found a subpopulation of adipocytes, termed Type 2 adipocytes are highly responsive to GH, with greater GH-induced lipolysis. Furthermore, we demonstrated that inhibiting GH-induced lipolysis from this subpopulation was sufficient to reduce GH-induced glucose intolerance. In this study, we extend on these findings by assessing the effect of ablating GH receptor (GHR) expression specifically in Type 2 adipocytes (Type2Ad-GHRKO mice). This will inhibit all GH-mediated effects in these adipocytes. We find that Type2Ad-GHRKO mice have increased fat mass, reduced lean

mass, and reduced overall body weight as compared to littermate controls. Interestingly, female, but not male Type2Ad-GHRKO showed reduced GH-mediated glucose and insulin resistance. Furthermore, Type2Ad-GHRKO female mice exhibited less fat mass loss than controls after six weeks of daily i.p. injection with GH (6 µg/g BW) while no differences were observed in male mice. Histological examination of Type2Ad-GHRKO adipose tissue revealed a biphasic distribution of adipocytes with a marked increase in Type 2 adipocyte cell size. Notably, these differences in adipocyte size were not observed upon inhibition of GH-induced lipolysis, suggesting that GH signaling may control adipocyte size through other mechanisms. Taken together, these results indicate that in a sex dependent manner, GH signaling in Type 2 adipocytes critically regulates physiological and metabolic effects.

Poster # 46A

Investigating how CHIP autoubiquitination shapes its interaction with Hsp70

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Protein quality control is vital for maintaining protein homeostasis by balancing synthesis, folding, and degradation. Disruption of this process leads to the accumulation of misfolded proteins, which contribute to neurodegenerative and systemic diseases such as Alzheimer's, Parkinson's, Huntington's, and cancer. Ubiquitination, a post-translational modification, regulates protein fate by attaching ubiquitin molecules to lysine residues of target proteins. Polyubiquitination (≥ 4 ubiquitins) typically marks proteins for proteasomal degradation, while monoubiquitination influences protein stability, localization, DNA repair, histone regulation, and protein–protein interactions. This study explores how ubiquitination-induced modifications in CHIP (C-terminus of Hsc70- interacting protein) affect its interaction with Hsp70, thereby clarifying the regulatory role of CHIP autoubiquitination in protein quality control. Prior studies identified nine lysine residues as autoubiquitination sites on CHIP. To dissect site-specific effects, CHIP mutants will be generated with eight lysine residues mutated to arginine, leaving a single lysine available for modification. These constructs will be incubated with an E1/E2/ubiquitin/ATP/Mg^{2+} system to produce singly ubiquitinated CHIP species. Two ubiquitin constructs will be used: a lysine-free "K-zero" ubiquitin to generate monoubiquitinated CHIP and wild-type ubiquitin to allow polyubiquitin chain formation. Ubiquitination will be confirmed by Western blotting, and binding affinities of CHIP variants for Hsp70 will be evaluated using bio-layer interferometry. We anticipate that CHIP autoubiquitination alters its affinity for Hsp70, with distinct effects between mono- and polyubiquitinated forms. These findings will provide mechanistic insights into chaperone-mediated protein quality control and advance understanding of pathways underlying protein misfolding diseases.

Poster # 46B

Ultrasound pressure fields visualized by fast object-oriented C++ ultrasound simulator (FOCUS)

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Deep Vein Thrombosis (DVT) is the formation of blood clots in the deep veins, most commonly in the legs. If a thrombus dislodges, it can lead to a pulmonary embolism, which can be life threatening. Patients with high risk DVT or those with significant acute symptoms require more rapid treatment. Histotripsy is a non-invasive technique that uses focused ultrasound pressure waves to mechanically ablate soft tissue and is being investigated as a treatment for DVT. The current duration of treatment is approximately 20 minutes, which is longer than clinically desirable. Increasing the volume of the focal zone of the therapeutic ultrasound may reduce treatment time. To design an effective transducer, an accurate model of the ultrasound pressure field is required. The goal of this study was to compare in silico simulations using the Fast Object-Oriented C++ Ultrasound Simulator (FOCUS) with an analytical model of ultrasound propagation to assess whether FOCUS may be suitable for future transducer design studies. Using both the simulator and the model, the pressure field is generated by a single rectangular element measuring 3.5 mm by 14 mm. Both approaches produced similar pressure fields with minor variations. FOCUS generated higher amplitudes and greater spatial variation than the analytical model. Both models identified focal zones at approximately 5 mm in the axial direction. These findings support future investigations using FOCUS to design advanced transducers that have increasing focal volume in order to reduce histotripsy treatment times for DVT. Funding: NIH R01 HL144443

Poster # 47A

UTCOMLS third-year subject exam and clerkship performance: benchmarking against national data

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Evaluating curricular effectiveness is challenging in undergraduate medical education (UME), particularly during the preclinical years. National Board of Medical Examiners (NBME) subject exams provide a standardized measure of medical knowledge, allowing assessment of curricular changes and areas for improvement [*Adv Med Educ Pract* **9**, 599–604; 2018]. This study reviewed NBME subject exam reports from 2017–2025. Data were organized by clinical skill category (Diagnosis, Foundation, General Principles, Prevention, Management). For each clerkship and skill, the percentage of correct responses was calculated. The University of Toledo College of Medicine & Life Sciences (UTCOMLS) performance was compared to national averages using one-sample z-tests for proportions. Data were analyzed using Microsoft Excel. Surgery, family medicine, obstetrics and gynecology (OB/GYN), and psychiatry exams demonstrated the most significant differences between UTCOMLS and national performance, while internal medicine, pediatrics, neurology, and emergency medicine aligned closely with national averages. UTCOMLS students consistently outperformed national averages in OB/GYN. In family medicine, national averages for Management exceeded UTCOMLS scores in 2024-2025 ($p<0.01$). Diagnosis skill showed the most significant differences across clerkships. Findings suggest strengths in OB/GYN education and opportunities for improvement in family medicine. Limitations include using data from a single institution and relying on exam performance to demonstrate curricular effectiveness. NBME subject exam analysis highlights both strengths and gaps in the UTCOMLS curriculum, guiding targeted improvements in medical education.

Poster # 47B

Cardiomyocyte KLF5 inhibits miR-30-5p family in ischemic cardiomyopathy via stimulation of 3 circular RNAs

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Introduction: Our lab previously demonstrated the cardiotoxic effect of the Krüppel-like factor (KLF) 5 in ischemic cardiomyopathy (ICM) in humans and mice. Investigation of the underlying mechanisms revealed that KLF5 suppresses all 5 members of the cardioprotective miR-30 family. Hypothesis: KLF5 inhibits all miR-30 family members in ICM by inducing non-coding RNA molecules with miRNA sponging activity. Methods and results: MiRNA array analysis in cardiac RNA of cardiomyocyte-specific KLF5 knockout mice (CM-KLF5-/-) revealed higher expression of all five members of the cardioprotective miR-30-5p family, which is linked to improved survival of heart failure patients. Accordingly, higher cardiac KLF5 expression in patients with ICM, mice with Myocardial Infarction (MI) and CM-specific KLF5 transgenic mice (αMHC-rtTA-KLF5) suppressed the expression of all five miR-30s. In contrast, miR-30-3p and pri-miRs remained unchanged, suggesting regulation at the post-transcriptional level. CircRNA microarray analysis in cardiac RNA from CM-KLF5-/- mice with MI and CM-rtTA-KLF5 identified 147 circRNAs that were upregulated with KLF5 induction and downregulated with KLF5 inhibition. In silico analysis for the lead circRNAs with miR-30-5p Response Elements and qRT-PCR validation showed that KLF5 induces the expression of 3 splice variant circRNAs (circPRDM5ex4-10, circPRDM5ex7-12, circPRDM5ex7-13) that are conserved between mice and humans. All 3 splice variant circRNAs are derived from the Prdm5 gene, which is also induced transcriptionally by KLF5. Individual and combined transfections of all three circRNAs revealed that each circPRDM5 suppressed all 5 miR-30s with stronger inhibition when combined. Notably, all three

circRNAs were upregulated in HF patients that do not respond to mechanical unloading, highlighting their cardiotoxic potential. Conclusions: CM KLF5 activation in humans and mice with ICM stimulates the expression of Prdm5 and three splice variant circRNAs from

Poster # 48A

Stress induced RNA decay in cardiac hypertrophy

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Increasing evidence has demonstrated that post-transcriptional regulation plays an important role in maintaining cell homeostasis during pathological remodeling, such as modification, alternative splicing, and degradation. While most of current literature explores the role of transcriptional regulation during cardiac hypertrophic response, the role of targeted mRNA degradation remains unknown. Using a BRIC-Seq in normal and hypertrophic cardiomyocytes we found a global shift in RNA stability between the two conditions. In addition, GO analysis have identified that the mRNA with altered half-life is involved in cardiac hypertrophy, inflammation and metabolic processes without any impact on classic nonsense mediated decay (NMD) targets, suggesting a previously uncharacterized cardiac hypertrophic stress induced transcriptome remodeling at the level of mRNA degradation. Among the known factors involved in mRNA degradation, we found only Upf1 (Up-frameshift protein 1), but not other Upf family members, is significantly induced in hypertrophic cardiomyocytes and failing mouse hearts, suggesting the observed changes in RNA stability during pathological stress may be an Upf1-dependent but NMD-independent mechanism. Using in vitro cultured cardiomyocytes, we have identified that loss of Upf1 expression led to cardiac hypertrophy. In vivo, we further demonstrated loss of Upf1 exacerbates myocardial infarction induced cardiac pathogenesis using AAV9 mediated shUpf1 inactivation. Mechanistically, we have validated that Upf1 interacts directly with RBFox1, a cardiac enriched RNA binding protein, using targeted co-IP analysis and proximity ligation assay, and this interaction is disrupted upon hypertrophy stimulation. In summary, we have identified a global shift of mRNA stability in stressed myocytes regulated by Upf1-RBFox1 complex, targeted manipulation of the stress regulated mRNA stability could potentially provide new therapeutic targets for cardiac disease.

Poster # 48B

APOE4 protects against metabolic dysfunction-associated steatotic liver disease (MASLD) by increasing mitochondria

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Apolipoprotein E ε4 (APOE4) allele is the strongest genetic risk factor for Alzheimer's disease. On the flip side, several genetic and population studies identified that APOE4 protects against metabolic dysfunction associated steatotic liver disease (MASLD). Though lipid droplet (LD) accumulation drives both diseases, the presence of APOE4 increases LD accumulation in microglia and astrocytes, while it decreases the LD accumulation in liver. This infers, APOE4 protein has diversified functions in lipid homeostasis. To investigate the mechanistic insights of APOE4 protection against MASLD, we used both in vivo and in vitro models in the present study. Human APOE3 and APOE4 are overexpressed in cell culture models, while human APOE knock-in (KI) mice, homozygous for APOE3 or APOE4 are used for in vivo studies. The KI mice were fed a western diet to induce MASLD. We first confirmed APOE4 KI mice showed reduction in liver weights, and hepatic lipid content. We next found that this reduction is due to decrease in large droplet macro-vesicular steatosis and increase in small-droplet macro-vesicular steatosis in APOE4 KI mice compared to APOE3 KI mice. Additionally, the mitochondrial fatty acid oxidation and pyruvate oxidation capacities were comparable between APOE3 and APOE4 isolated liver mitochondria. Nevertheless, we observed APOE4 KI mice have increased mitochondrial number, elevated citrate synthase activity and increased individual respiration capacities. We next isolated hepatic mitochondrial subpopulations and found that peridroplet mitochondria (PDM) content are lower, while unbound cytoplasmic mitochondria (CM) content are increased in APOE4 KI mice. Also, this increased the respiration capacities of hepatic CM and decreased the

respiration capacities of PDM in APOE4 KI mice. Altogether our study will lead to new insights into the cellular and molecular mechanisms by which APOE4 increases overall mitochondrial number followed by a differential regulation of hep

Poster # 49A

Ventricular and sex-specific remodeling of GLUT1 in a mouse model of HFpEF

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Background: Heart failure with preserved ejection fraction (HFpEF) accounts for over 50% of HF cases. A hallmark of HF is altered cardiac energetics, marked by a shift from fatty acid to glucose utilization. Glucose uptake is regulated by transporters, with GLUT1 abundant in fetal hearts and GLUT4 in adults. Interestingly, studies report ventricle-specific GLUT1 changes, with increased GLUT1 protein in the right ventricle (RV) in one study and decreased GLUT1 mRNA in the left ventricle (LV) in another. These findings highlight poorly understood ventricular-specific glucose remodeling in HF. Notably, females are more prone to HFpEF, emphasizing need for studies on sex- and ventricle-specific metabolic remodeling. Objective: This study investigates sex- and ventricle-specific regulation of GLUT1 and metabolic regulators PDK4 and CPT1B in a high-fat diet (HFD) + L-NAME–induced HFpEF mouse model. Methods: Male (C57BL/6JN) and female (C57BL/6J) mice were subjected to a HFD with L-NAME treatment for 5-weeks (early) and 12-weeks (late) to induce HFpEF. Diastolic dysfunction was evaluated by echocardiography, with body weight and blood pressure monitored to confirm progression. RV and LV tissues were then collected for analyses. Results: In male HFpEF mice, we observed ventricle-specific regulation of GLUT1, with either increased protein expression or unchanged mRNA levels in the RV, but a decrease in both mRNA and protein levels in the LV at 5 and 12-weeks, consistent with previous human findings. In contrast, female HFpEF exhibited a uniform reduction in GLUT1 expression (mRNA and protein) across RV and LV at 12-weeks, indicating sex-dependent regulation. Notably, PDK4 and CPT1B expression were consistently upregulated across both sexes and ventricles at 12-weeks, indicating metabolic shift toward enhanced fatty acid utilization.

Poster # 49B

Topical imipramine and amitriptyline block experimental ultraviolet B radiation-induced erythema in rosacea subjects

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Background: Rosacea is a common chronic inflammatory condition often associated with photosensitivity. Previous studies by our group and others have demonstrated that Ultraviolet B (UVB) light exacerbates skin inflammation through the release of subcellular particles such as microvesicle particles (MVPs). The enzyme acid sphingomyelinase (aSMase) is a key driver for MVP generation, and functional inhibitors of aSMase (FIASMs), including the tricyclic antidepressants amitriptyline and imipramine, have been shown to block MVP release. Our study evaluated whether topical FIASMs reduce UVB-induced erythema in subjects with rosacea. Methods: In a single-center, double-blinded, placebo-controlled clinical trial, rosacea patients and controls received either 4% topical amitriptyline or imipramine on one facial side and vehicle on the contralateral side. Participants were exposed to a low-fluence (300 J/m²) of artificial UVB light. Erythema, pain, and itch were measured at baseline, 30 minutes after applying topical medication, and 10, 60, 120 minutes, and 24 hours post-UVB administration. Based on initial findings with 26 subjects, the trial was escalated to evaluate 10% formulations for enhanced efficacy, with ongoing enrollment. Results: At the 4% concentration, both amitriptyline and imipramine produced a statistically significant reduction in UVB-induced erythema compared to vehicle (one-tailed t-test, $p< 0.05$). The 10% concentration is currently under investigation, with preliminary data from ten subjects suggesting tolerability and the potential for greater erythema reduction (two-tailed t-test, $p<0.005$). No adverse events/safety concerns were observed.

Poster # 50A

Unraveling fibroblast and lung cell heterogeneity in fibrotic lesions through single-nucleus RNA sequencing

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Rationale: Idiopathic pulmonary fibrosis (IPF) is a progressive, fatal fibrotic lung disease manifested by myofibroblast accumulation and extensive collagen deposition in the distal lung regions. scRNA-seq has improved insights into cellular heterogeneity and dysregulated gene expression in IPF but often underrepresents mesenchymal and other fragile distal cells. To overcome this, we applied snRNA-seq, enabling comprehensive profiling of mesenchymal and other cell populations in distal fibrotic and healthy lungs. Methods: We employed snRNA-seq to profile nuclei isolated from the distal right lower lung lobe from 18 IPF and 11 normal donor lung samples. Following batch correction, quality control, and doublet exclusion, data analysis and clustering were performed using Seurat (v4.3.0). Clusters were categorized into four primary populations: mesenchymal (COL1A2), epithelial (EPCAM), endothelial (CLDN5), and immune (PTPRC) cells. Further sub-clustering was done manually using established cell type markers. Differentially expressed genes (DEGs) were identified using Seurat's 'FindAllMarkers' & 'FindMarkers' for cell types and across disease respectively. Results: We obtained a total of 108775 nuclei profiles, comprising 36586 and 72189 nuclei from healthy and IPF lungs respectively. Four primary cell lineages: mesenchymal, endothelial, epithelial, and immune cells were identified and their increased proportions compared to scRNA-seq, highlighting the effectiveness of single-nuclei method to isolate single cells from intact tissue. Within these lineages, we identified 28 distinct cell subpopulations. Among mesenchymal cells, we identified seven fibroblast subtypes, including alveolar-fibroblasts, adventitial-fibroblasts, myofibroblasts, mesothelial, SMCs, pericytes, and WT1-positive fibroblasts. Gene enrichment analysis of DEGs from WT1-positive fibroblasts revealed elevated profibrotic pathways linked to impaired fibroblast clearance and enhanced ECM production.

Poster # 50B

Phospholamban R14del cardiomyopathy develops independent of PLN aggregation through SR–mitochondrial disruption

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Objective: The phospholamban (PLN) Arg14 deletion (R14del) is a pathogenic mutation that causes dilated and arrhythmogenic cardiomyopathy, but the mechanisms driving early disease remain unresolved. Models have implicated toxic PLN aggregation, SERCA2a dysregulation, and mitochondrial defects. Clarifying which defects arise earliest is essential to guide therapy development. We sought to define PLN localization, SR–mitochondrial interactions, and metabolic remodeling in a humanized knock-in PLN-R14del mouse to resolve conflicting models of pathogenesis. Methods and Results: Subcellular fractionation of wild-type and heterozygous PLN-R14del hearts was performed by differential ultracentrifugation to isolate pure mitochondrial, mitochondrial-associated membrane (MAM), sarcoplasmic reticulum (SR), and other membrane compartments. Western blotting showed PLN remained correctly localized to the SR without high-molecular-weight aggregates in any fraction. Notably, MFN2 expression was reduced in MAM fractions, suggesting impaired SR–mitochondrial tethering. Complementary studies revealed structural and metabolic abnormalities in PLN-R14del hearts, including disrupted SR organization, mitochondrial swelling with cristae loss, and altered cardiac triglyceride handling, despite preserved electron transport chain integrity. These findings collectively demonstrate that mitochondrial dysfunction occurs in parallel with SR remodeling, rather than as a secondary response to PLN aggregation. Conclusions: Humanized PLN-R14del mice develop mitochondrial and metabolic defects early in disease without evidence of PLN mislocalization or aggregation. This work identifies SR–mitochondrial uncoupling as a central, aggregation-independent

mechanism of disease and challenges prevailing models focused solely on toxic PLN aggregates. Because DWORF, a SERCA-activating microprotein, reduces PLN aggregates and improves cardiac function in other PLN-R14del models, this aggregate-free system provides a critical platform to test whether DWORF can still confer therapeutic benefit.

Poster # 51A

The effect of genotypic mutations on NCCR-Driven BK polyomavirus gene expression

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BK Polyomavirus (BKPyV) has the highest mutation rate among dsDNA viruses resulting in a high degree of variability, particularly within the non-coding control region (NCCR), the site of transcriptional control. Previously, we identified 23 genotype-associated polymorphisms within the NCCR and showed that BKPyV strains of different genotypes have distinct NCCRs. Other studies have shown that mutating transcription factor binding sites crucial for regulation of viral transcription significantly alters the viral gene expression profile; hence we investigated the effect of genotypic variation on NCCR-driven viral gene expression. NCCRs from clinical BKPyV strains representative of genotypes Ia, Ib1, III, and IV were inserted into a dual-fluorescent reporter plasmid that allows for simultaneous measurement of early and late viral gene expression. HEK293TT cells were transfected and 48 hours later, gene expression was assessed qualitatively via visualization on a fluorescent microscope and quantitatively via flow cytometry in which mean fluorescent intensity was normalized to control strain Dunlop. There were observable genotypic differences regarding gene expression. Genotype Ib1 presented with the highest normalized early gene expression (58.3±37.2%) while genotype Ia presented with the lowest (38.5±37.2%). While there were no significant differences in early gene expression between genotypes, Dunlop, which exhibits a rearranged NCCR architecture, had significantly higher early gene expression than archetype Ia, Ib1, and IV strains. These results suggest that NCCR architecture significantly influences early promoter activation, which is supported by previous literature. Additionally, we found that Ib1 presented with the highest normalized late gene expression (430.4±154.0%) which was significantly higher than that of genotype IV which presented with the lowest normalized late gene expression (225.5±75.1%; $P > 0.001$) suggesting that genotype-specific mutations influence viral promoter activation and further, levels of gene expression.

Poster # 51B

Retinal pathways to the midbrain: characterizing olivary pretectal nucleus circuits in light-driven physiology

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Artificial light exerts dual influence on brain physiology. On one hand, irregular light cycles contribute to circadian disruption, a common feature of neurological and psychiatric disorders; on the other, light therapy has shown beneficial effects in some of these conditions. Light is detected by the retina and transmitted to brain regions that serve diverse physiological roles. In addition to its well-known role in image-forming vision, the retina–suprachiasmatic nucleus pathway is established as the master regulator of circadian rhythms. However, other retina-brain circuits remain far less understood. Defining how these pathways shape distinct brain circuits is key for understanding the broader influence of light on brain function, particularly in pathological contexts. One such region is the olivary pretectal nucleus (OPN), a bilateral midbrain structure classically associated with the pupillary light reflex (PLR). The OPN receives dense input from intrinsically photosensitive retinal ganglion cells (ipRGCs) and projects to multiple downstream targets, positioning it as a potential hub for integrating light signals beyond pupil control. Yet, the anatomical organization and molecular identity of OPN neurons remain poorly characterized. In this project, we combined viral tracing, genetic tools, and molecular profiling to define OPN inputs and neuronal subtypes.

RNAscope analyses revealed distinct populations, including galanin- and foxb1-expressing neurons, consistent with emerging transcriptomic data. Using viral strategies, we mapped ipRGC innervation to different OPN neuronal populations. Finally, to assess functional responsiveness, we manipulated retinal inputs with chemogenetic approaches and quantified cFos activation across OPN subtypes. Together, these studies provide the first integrated anatomical and molecular characterization of OPN circuitry, extending its role beyond pupillary control and laying the foundation for understanding how retinal projections influence broader aspects of brain physiology and pathology, and for optimizing light-based interventions in clinical settings.

Poster # 52A

The cross-link between mitochondrial DNA mutations in the polymerase gamma mutator mouse and the severity of traumatic osteoarthritis

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Mitochondria, often referred to as the “powerhouse of the cell,” contain their own DNA (mtDNA). Polymerase gamma (PolgA) is the sole enzyme responsible for mtDNA replication, making it essential for mitochondrial homeostasis. Mutations in PolgA impair proofreading, leading to the accumulation of mtDNA mutations, mitochondrial dysfunction, and premature aging. Osteoarthritis (OA) is the most common form of arthritis, most frequently affecting the knee joint. In 2020, 595 million people worldwide were diagnosed with OA (7.6% of the global population), representing a 132% increase since 1990. The aim of this study was to investigate the role of mtDNA mutations in OA progression using the PolgA$^{D257A/D257A}$ mutator mouse. All animal experiments were approved by the NEOMED IACUC. 12-week-old wild-type (WT) and PolgA mutant mice underwent destabilization of the medial meniscus (DMM) surgery to induce OA. Pain sensitivity was assessed using pressure application measurement (PAM) before surgery and biweekly thereafter. At 8 weeks post-surgery, knee joints were collected, fixed, and analyzed for bone remodeling, cartilage damage and inflammation. Bone parameters assessed included bone volume, trabecular number, trabecular thickness, trabecular separation, bone mineral density, osteophyte formation, and patellar thickness. Histological staining and OARSI scoring were performed to evaluate cartilage damage, while immunostaining was used to assess inflammation and oxidative DNA damage. Compared to WT mice, PolgA mutants exhibited lower pain thresholds, reduced bone density, fewer and thinner trabeculae, greater trabecular separation, and increased osteophyte formation. Histology revealed greater cartilage loss, reduced chondrocyte density, and enhanced subchondral bone remodeling in PolgA mutants. Immunostaining confirmed increased IL-6 expression and oxidative stress. OARSI scoring further demonstrated more severe OA in PolgA mice compared with WT. In conclusion, mitochondrial health is essential for maintaining joint integrity. Accumulation of mtDNA mutations accelerates OA progression through increased oxidative stress, inflammation, and tissue degeneration.

Poster # 52B

Using qPCR to detect *E. coli* in water samples

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Escherichia coli is a type of bacteria which lives within the intestines of warm-blooded animals and is often used as a biological marker to show fecal contamination within water. Numerous health issues can arise from drinking or swimming in water contaminated with E. coli, especially Shiga-toxin producing strains. Traditional methods used for detecting E. coli include culturing on differential and selective media. However, culturing is time-consuming and has low sample throughput. Alternatively, traditional PCR can be used to quickly identify bacterial species by detecting specific subsets of genes. Quantitative PCR (qPCR) is a more sensitive version of PCR, which can also provide an accurate quantification of bacteria present in the sample. In this project, regular and SYBR Green qPCR have been used to verify primers and test for the CydA, lacY, and yDiv genes, which are present in all E. coli strains. Additionally, primers for Stx1 and Stx2 were designed and tested to differentiate Shiga-toxin producing E. coli (STEC) from control strains. Next, we will design TaqMan probes for a more sensitive qPCR assay with the goal of eventually testing environmental water samples for STEC.

Poster # 53A

Evaluating the efficacy of a 3D-printed partial occlusion device (POD) in rat femoral artery microsurgical anastomosis revision

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Introduction: Successful vascular anastomosis is essential in microsurgery, as improper management can lead to leakage and revision. Cotton-tip (Q-Tip) applicators are commonly used for temporary occlusion in revisions, though they carry risks of fiber shedding and particulate contamination. To address these limitations, the Partial Occlusion Device (POD) was developed as a novel alternative. Featuring a stable flat base, adjustable multi-level saddle system, and grooved handle compatible with standard microsurgical clamps, POD maintains occlusion while eliminating fiber-related risks to improve both safety and usability. Therefore, this study compares POD with Q-Tips in a rat model to appraise effects on revision performance, vascular integrity, and microsurgical efficacy. Methods: Approved by the Columbia University IACUC, POD devices were 3D-printed using biocompatible resin while Q-Tips were commercially sourced. Femoral artery end-to-end anastomosis revisions were performed in 4-month-old male Sprague-Dawley rats (POD=22; Q-Tip=13). Two hours post-revision, arteries were harvested, fixed, paraffin-embedded, sectioned, H&E stained, and light microscopy imaged. Histopathological scoring was performed by a board-certified pathologist, supplemented by observational review. Efficacy outcomes included patency, revision time, and surgeon feedback. Statistics were calculated in Microsoft Excel, with significance set at $p<0.05$. Results: POD revisions achieved a 90.9% 40-minute patency rate versus 100% with Q-Tips, with similar revision times (POD=4.00±2.15 min; Q-Tip=3.81±2.50 min; p=0.54). Histopathology revealed no significant differences across intimal (p=1.0), medial (p=0.70), adventitial (p=0.52), or combined (p=0.77) groups, for parameters that included factors like loss of endothelial cells and thrombus formation. Observationally, Q-Tip-treated vessels demonstrated a density-dependent increase in inflammatory cells. Microsurgeons reported improved visibility, manipulability, and stability with POD, devoid of fiber-related complications. Conclusion: POD offers a reusable, customizable, and fiber-free alternative for vessel anastomosis revision, demonstrating non-inferior efficacy, preserved vascular integrity, and favorable user feedback. Future studies are warranted to further optimize designs and assess long-term outcomes for advancing physiological nativity and microsurgery.

Poster # 53B

A 3D-cardiac organoid model to mimic myocardial infarction in a dish

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Introduction: During myocardial infarction (MI), an obstruction in the coronary artery causes a cessation of blood flow and the resulting ischemia triggers molecular changes in the different cardiac cell-types: cardiomyocytes (CMs), endothelial cells (ECs), and cardiac fibroblasts (CFs). To develop therapies for MI, delineating cell-specific molecular changes is critical, but is challenging in the complex in vivo system. In this regard, 3D-organoids can bridge this gap by recreating a trilineage cardiac tissue structure in vitro. Methods: We generated 3D-cardiac organoids using a combination of CMs, ECs, and CFs, derived from human induced pluripotent stem cells (hiPSCs). Each organoid was comprised of 10,000 cells (6,000 CMs, 2,000 ECs, and 2,000 CFs). The morphology of the organoids was assessed via phase-contrast and confocal microscopy. To model MI in vitro, we subjected the organoids to hypoxia (1% O_2) and evaluated their Ca^{2+} transients and LDH release. Results: The organoids attained their peak contractility within 3–5 days after formation. Immunostaining with cell-type-specific markers (CMs: troponin T; ECs: CD31; CFs: vimentin) showed the presence of CFs on the exterior and CMs and ECs in the interior of the organoids. ECs appeared to form a tube-network possibly modelling the cardiac vasculature. However, contrary to our expectations, we observed an increase in Ca^{2+} and a decrease in the LDH release in the organoids as compared to their normoxia controls. Conclusion: While the 3D-organoids can model the cardiac tissue structure accurately in vitro, further investigations will be required to optimize their use for modeling MI in a dish.

OPS 2025 Poster Plan

CARE/Crawley Building, 3230 Eden Avenue