Iowa Physiological Society

and

Midlands Society of Physiological Sciences

SCIENTIFIC SESSIONS 2020

Dear Colleagues,

It is our distinct pleasure to welcome you to the joint meeting of the Iowa Physiological Society and the Midlands Society of Physiological Sciences. Enclosed in this program booklet you will find the meeting schedule, all submitted abstracts, an index of 'video posters', and information from our exhibitors.

This is clearly a unique year in terms of what is going on in the world and the effect that it has had on science and scientific meetings. While everyone might be feeling a bit Zoomed out these days, from the perspective of meeting organizers we are quite pleased that we are still able to offer opportunities for trainees and faculty to present their work. We sincerely miss the opportunity for in person conversation and networking that we all enjoyed in meetings of the past, and we hope that in the future we will again be able to return to face to face interactions that are less fraught than they are now.

We'd like to express our appreciation to the constituents of both societies and our invited speakers for their enthusiastic participation as well as the support of our exhibitors and the American Physiological Society.

Sincerely,

Noah Marcus

Noah J. Marcus, Ph.D.
IPS President

Erika Boesen

Erika Boesen, Ph.D.
MSPS Meeting Coordinator

Dustin Slivka

Dustin Slivka, Ph.D.
MSPS President

Vanja Duric

Vanja Duric, Ph.D.
IPS President Elect

IPS/MSPS Scientific Sessions 2020 Exhibitors

charles river

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Invited Presentations

Keynote Speakers:

Dr. Andrew Lovering, *University of Oregon*

Title: Getting to the Heart of the Matter: The "Hole" Story of Environmental Physiology and Medicine?

Dr. Brent Ruby, *University of Montana*

Title: Normal Humans Demonstrating Big Physiology: Energy and Fluid Demand Extremes

Invited Speakers:

Dr. Rebekah Gundry, *University of Nebraska Medical Center*

Title: An Analytical Chemist's Approach to Cardiac Systems Physiology

Dr. Daniel Christian, *Des Moines University|Medicine and Health Sciences*

Title: Increased NMDA Receptor Function during Protracted Withdrawal from Chronic Intermittent Ethanol Exposure

Exhibitor Presentations:

Dr. Kristiina Aasa, *FujiFilm VisualSonics*

Title: Small Animal Cardiac Physiology with VisualSonics High-Frequency Ultrasound

Dr. Steve Festin, *Charles River*

Title: New at RMS 2020

Wyatt Kern, *Data Sciences International*

Title: Advance Your Research with DSI Preclinical Physiologic Monitoring

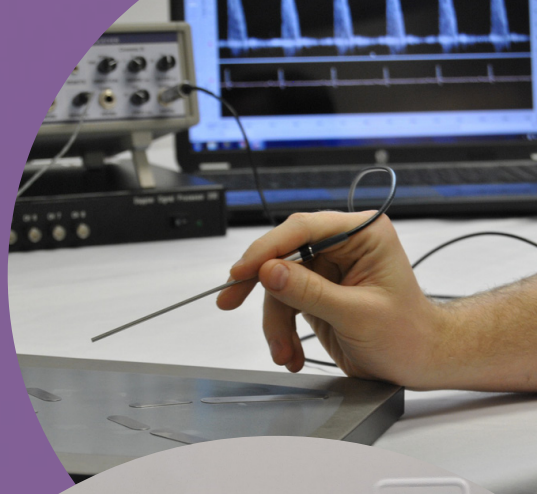
Dr. Shawn Sternisha, *Beckman Coulter*

Title: Mechanistic Origins of Activation in Glucokinase Variants Responsible for Hyperinsulinism

Dr. Gus Kalogeros, *Scintica Instrumentation*

Title: From whole animal imaging to cellular function: Choosing the right tools for your research

Linking scientists with precision tools for research



Imaging

- High Resolution 3D Ultrasound
- Optical Imaging
- PET/CT
- Compact MRI
- Laser Speckle Imaging
- PET Inserts

Physiology

- Oxgyen Perfusion & Tissue Vitality
- Anesthesia Equipment
- Blood Flow
- Stereotaxic Instrumentation
- Pressure & Wire Arteriograph
- Small Animal Telemetry
- Surgical Monitoring
- Blood Pressure Monitoring

Molecular

- Automated Colony Counter
- Hypoxia Chambers
- Cell Incubators
- Microtome & Cryostat
- Live Cell Imaging
- Cell Counter
- Gel Multimodal Imaging
- Gel Documentation

Scintica: Instrumentation

PRECLINICAL RESEARCH SOLUTIONS

Schedule, Friday October 30, 2020

12:30 PM - 01:00 PM | Zoom

Speaker Check-In (all presenters)

All Speakers are asked to arrive early to ensure all equipment/presentations are in proper working order

01:00 PM - 01:10 PM | Zoom

Welcome/Keynote Introduction (IPS President)

-  Noah J. Marcus, Ph.D.
  01:00 PM - 01:10 PM

01:10 PM - 02:00 PM | Zoom

Keynote Presentation

-  Andrew Lovering, Ph.D. **Getting to the Heart of the Matter: The "Hole" Story of Environmental Physiology and Medicine?**
  01:10 PM - 02:00 PM

02:00 PM - 02:10 PM

Questions/Discussion

-  Andrew Lovering, Ph.D. **Getting to the Heart of the Matter: The "Hole" Story of Environmental Physiology and Medicine?**
  02:00 PM - 02:10 PM

02:10 PM - 02:20 PM | Zoom

Abstract #26 Graduate Student Presentation

-  Kajal Kamra **Novel mechanism of neural control of breathing in Acute Lung Injury (ALI)**
  02:10 PM - 02:20 PM

02:20 PM - 02:25 PM

Questions/Discussion

-  Kajal Kamra **Novel mechanism of neural control of breathing in Acute Lung Injury (ALI)**
  02:20 PM - 02:25 PM

Schedule, Friday October 30, 2020

02:25 PM - 02:35 PM

Abstract #59 Graduate Student Presentation

-  Kelsey Schwartz — **Reproducibility of Laser Doppler Flowmetry and Laser Speckle Contrast Imaging During Whole-Body Cooling**
  02:25 PM - 02:35 PM

02:35 PM - 02:40 PM

Questions/Discussion

-  Kelsey Schwartz — **Reproducibility of Laser Doppler Flowmetry and Laser Speckle Contrast Imaging During Whole-Body Cooling**
  02:35 PM - 02:40 PM

02:40 PM - 02:50 PM | Zoom

Exhibitor Presentation (FUJIFILM VisualSonics)

-  Kristiina Aasa, Ph.D. — **Small Animal Cardiac Physiology with VisualSonics High-Frequency Ultrasound**
  02:40 PM - 02:50 PM

02:50 PM - 03:00 PM

Break

03:00 PM - 03:10 PM

Abstract #23 Graduate Student Presentation

-  Sumit Kar — **Hydrogen Sulfide Protects the Heart against Ferroptosis in Diabetic Cardiomyopathy**
  03:00 PM - 03:10 PM

03:10 PM - 03:15 PM

Questions/Discussion

-  Sumit Kar — **Hydrogen Sulfide Protects the Heart against Ferroptosis in Diabetic Cardiomyopathy**
  03:10 PM - 03:15 PM

Schedule, Friday October 30, 2020

03:15 PM - 03:25 PM

Abstract #43 Graduate Student Presentation

-  Patrick Walsh **Dysfunction of Renal Glucose Handling is Restored by Central Leptin Receptor Blockade in Model of Estrogen Deficiency.**
  03:15 PM - 03:25 PM

03:25 PM - 03:30 PM

Questions/Discussion

-  Patrick Walsh **Dysfunction of Renal Glucose Handling is Restored by Central Leptin Receptor Blockade in Model of Estrogen Deficiency.**
  03:25 PM - 03:30 PM

03:30 PM - 03:45 PM

Abstract #10 Post-Doctoral Scholar Presentation

-  Craig Workman, Ph.D. **Dorsolateral Prefrontal Cortex tDCS Does Not Immediately Affect Cerebral Blood Flow in People with Multiple Sclerosis**

03:50 PM - 04:05 PM

Abstract #58 Post-Doctoral Scholar Presentation

-  Maia Kelly, Ph.D. **Glycan signatures as mechanistic markers of beta cell injury in diabetes**
  03:50 PM - 04:05 PM

04:05 PM - 04:10 PM

Questions/Discussion

-  Maia Kelly, Ph.D. **Glycan signatures as mechanistic markers of beta cell injury in diabetes**
  04:05 PM - 04:10 PM

04:10 PM - 04:20 PM

Exhibitor Presentation (Charles River)

-  Steve Festin, Ph.D. **New at RMS 2020**
  04:10 PM - 04:20 PM

Schedule, Saturday October 31, 2020

04:20 PM - 04:45 PM

Day 1 Awards/Closing

-  Noah J. Marcus, Ph.D.
  04:20 PM - 04:30 PM
-  Dustin Slivka, Ph.D.
  04:30 PM - 04:40 PM

30 OCTOBER Friday | 31 OCTOBER Saturday

08:00 AM - 08:30 AM | Zoom

Speaker Check-In (all presenters)

All Speakers are asked to arrive early to ensure all equipment/presentations are in proper working order

08:30 AM - 08:35 AM | Zoom

Welcome (MSPS President)

-  Dustin Slivka, Ph.D.
  08:30 AM - 08:35 AM

08:35 AM - 08:55 AM | Zoom

Invited Presentation (MSPS)

-  Rebekah Gundry, Ph.D.
  08:35 AM - 08:55 AM
  An Analytical Chemist's Approach to Cardiac Systems Physiology

08:55 AM - 09:00 AM | Zoom

Questions/Discussion

-  Rebekah Gundry, Ph.D.
  08:55 AM - 09:00 AM
  An Analytical Chemist's Approach to Cardiac Systems Physiology

Schedule, Saturday October 31, 2020

09:00 AM - 09:20 AM | Zoom

Invited Presenter (IPS)

-  Daniel Christian, Ph.D. **Increased NMDA Receptor Function during Protracted Withdrawal from Chronic Intermittent Ethanol Exposure**
  09:00 AM - 09:20 AM

09:20 AM - 09:25 AM | Zoom

Questions/Discussion

-  Daniel Christian, Ph.D. **Increased NMDA Receptor Function during Protracted Withdrawal from Chronic Intermittent Ethanol Exposure**
  09:20 AM - 09:25 AM

09:25 AM - 09:35 AM

Exhibitor Presentation (Data Sciences International)

-  Wyatt Kern **Advance Your Research With DSI Preclinical Physiologic Monitoring**
  09:25 AM - 09:35 AM

09:35 AM - 09:40 AM

Break

09:40 AM - 09:47 AM | Zoom

Abstract #21 Undergraduate Presenter

- Cody Anderson **Effects of Heated-Water-Based versus Land-Based Exercise Training on Vascular Function in Individuals with Peripheral Artery Disease**
  09:40 AM - 09:43 AM

09:47 AM - 09:50 AM | Zoom

Questions/Discussion

- Cody Anderson **Effects of Heated-Water-Based versus Land-Based Exercise Training on Vascular Function in Individuals with Peripheral Artery Disease**
  09:47 AM - 09:50 AM

Schedule, Saturday October 31, 2020

09:50 AM - 09:57 AM | Zoom

Abstract #28 Undergraduate Presenter

- Kayla Olstinski — **Protective Effects of Low-dose Metformin Treatment in a Mouse Model of Diabetic Kidney Disease**
  09:50 AM - 09:57 AM

09:57 AM - 10:00 AM | Zoom

Questions/Discussion

- Kayla Olstinski — **Protective Effects of Low-dose Metformin Treatment in a Mouse Model of Diabetic Kidney Disease**
  09:57 AM - 10:00 AM

10:00 AM - 10:07 AM | Zoom

Abstract #54 Undergraduate Presenter

- Madeleine Nelson — **Impact of Synthetic Cannabinoids on Cardiovascular Health.**
  10:00 AM - 10:07 AM

10:07 AM - 10:10 AM | Zoom

Questions/Discussion

- Madeleine Nelson — **Impact of Synthetic Cannabinoids on Cardiovascular Health.**
  10:07 AM - 10:10 AM

10:10 AM - 10:17 AM | Zoom

Abstract #52 Undergraduate Presenter

- Manar Yaseen — **Effects of Playing Breath-Controlled Instruments on Heart Rate and Mean Arterial Pressure**
  10:10 AM - 10:17 AM

10:17 AM - 10:20 AM | Zoom

Questions/Discussion

- Manar Yaseen — **Effects of Playing Breath-Controlled Instruments on Heart Rate and Mean Arterial Pressure**
  10:17 AM - 10:20 AM

Schedule, Saturday October 31, 2020

10:20 AM - 10:30 AM | Zoom

Exhibitor Presentation (Beckman Coulter)

-  Shawn Sternisha, Ph.D.
  Mechanistic Origins of Activation in Glucokinase Variants Responsible for Hyperinsulinism
  10:20 AM - 10:30 AM

10:30 AM - 10:40 AM

Break

10:40 AM - 11:30 AM | Zoom

Keynote Presentation

-  Brent Ruby, Ph.D., FACSM
  Normal Humans Demonstrating Big Physiology: Energy and Fluid Demand Extremes
  10:40 AM - 11:30 AM

11:30 AM - 11:40 AM

Questions/Discussion

-  Brent Ruby, Ph.D., FACSM
  Normal Humans Demonstrating Big Physiology: Energy and Fluid Demand Extremes
  11:30 AM - 11:40 AM

11:40 AM - 11:50 AM | Zoom

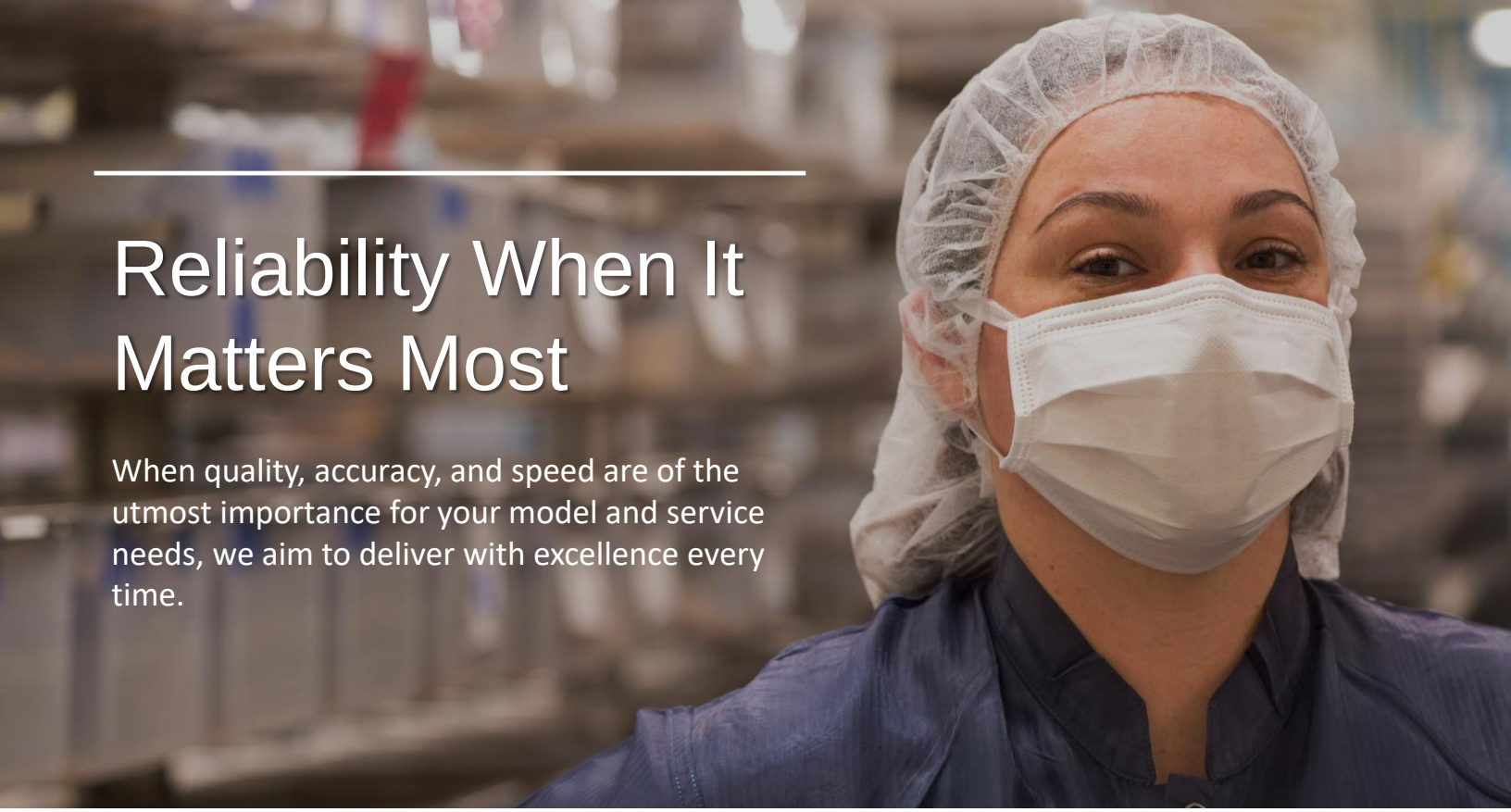
Exhibitor Presentation (Scintica Instrumentation)

-  Gus Kalogeros, Ph.D.
  From whole animal imaging to cellular function: Choosing the right tools for your research
  11:40 AM - 11:50 AM

11:50 AM - 12:00 PM | Zoom

Awards/Closing Remarks

-  Dustin Slivka, Ph.D.
  11:50 AM - 11:55 AM
-  Erika Boesen, Ph.D.
  11:55 AM - 12:00 PM



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Name: Richard Davis

Email: richard.davis@crl.com

Phone: 781-262-7090

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Avanti JXN-26 – The Avanti JXN-26 centrifuge delivers high-performance harvesting in therapeutic vaccine production workflows.

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- Fully automated sample prep and cell counting+viability
- Facilitates 21CFR part11-compliance support for vaccine production workflow

Vi-CELL MetaFLEX*† Bionanalyte Analyzer

- Monitor Cell Culture Parameters: pH, pO_2, pCO_2, glucose, lactate, and electrolytes
- Facilitates 21CFR part11-compliance support for vaccine production

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- Standard configurations ranging from 6- to 23-parameter detection

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- Automate DNA/RNA Extraction and NGS sample prep workflows
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Multisizer 4e* – Cell Volume, Counts, & Sizing

HIAC 9703+* – Characterize injectables for USP 789 & 797 methods

TOC Analyzer* – Water for Injection (WFI) Analysis (in-line & benchtop)

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CENT-7701FLY08.20

IPS/MSPS Scientific Sessions 'Video Posters'

Note: 1st line is hyperlinked to abstract, 2nd line is linked to video poster presentation

Undergraduate Students

Abstract #7 Luke Pavlat, Central College (hyperlinked to abstract)
"Sleep Changes Brought on by Covid-19 in Off-Season Division III College Student-Athletes"

Abstract #8 Erin Manion, Central College
"Sleep Quantity, Sleep Quality, Resting Heart Rate and Vertical Jump on Track and Field Athlete Recovery"

Abstract #18 Courtney Simon, Central College
"Changes in Aerobic Capacity Following Two Weeks of High Intensity Interval Training"

Abstract #39 Mackenzie Berschel, University of Iowa
"RNA Bulk Sequencing Analysis and Differential Gene Expression of Multiple Myeloma Susceptibility Strains: KaLwRij and CIH"

Graduate Students

Abstract #3 Safwan Elkhatib, University of Nebraska Medical Center
"Sympathetic splenic denervation ameliorates trauma-induced inflammatory and redox shifts in T-lymphocytes"

Abstract #6, Whitney Pavlat, Western Michigan University/Central College
"The Effects of Static Versus Dynamic Stretching on Power Output in College Aged Students"

Abstract #9, Alexandra Courtney Fietsam, University of Iowa
"Reduced glucose uptake heterogeneity after 3 mA tDCS in a woman with multiple sclerosis"

Abstract #11, Joe Weber, Central College
"The effects that sleep has on basketball game performance"

Abstract #13, Cassandra Moshfegh, University of Nebraska Medical Center
"Redox-Regulated Calprotectin Potentiates Psychological Trauma Induced Pro-Inflammatory T-Lymphocyte Differentiation"

Abstract #14, Sarah Schlichte, University of Nebraska Medical Center
"Chronic In Vivo Administration of MnTnBuOE-2-PyP5+ Does Not Decrease Hypertensive Blood Pressure"

Video Posters

Abstract #17, Kalie A. Savage, Des Moines University|Medicine and Health Sciences
"Effect of chronic intermittent hypoxia on inflammation and redox related gene expression in renal cortex"

Abstract #19, Mingqi Cai, University of South Dakota
"Soluble guanylate cyclase activation increases proteasome activities and facilitates degradation of misfolded proteins in cardiomyocytes"

Abstract #20, Linda Berg Luecke, University of Nebraska Medical Center
"CellSurfer Platform for semi-automated cell surface N-glycoprotein profiling of primary cells reveals chamber-specific cardiomyocyte surface maps"

Abstract #22, Luke Hamilton, University of Nebraska-Kearney
"Novel isoform of Curcumin (cis-trans Curcumin) binds to Adenosine Receptors A2A and A2B"

Abstract #24, Liz Pekas, University of Nebraska Omaha
"Dietary nitrate intake improves vascular function and walking capacity in patients with peripheral artery disease"

Abstract #27, Andrew Philipose, Des Moines University|Medicine and Health Sciences
"Renal Cortical KLF15 and KLF2 are downregulated in chronic heart failure"

Abstract #29, Samiksha Giri, University of South Dakota
"Defining molecular mechanism promoting neointimal hyperplasia by CSN8 hypomorphism."

Abstract #30, Liuqing Yang, University of South Dakota
"Ser14-Psmd11/Rpn6 phosphorylation is required for activation of the 26S proteasome by PKA"

Abstract #31, Pauline Xu, University of Nebraska Medical Center
"Pancreatic ductal adenocarcinoma highly expresses activin A: implications in adipose tissue and cancer cachexia"

Abstract #32, Mark McGlynn, University of Nebraska Omaha
"The acute effects of exercise and temperature on mtDNA copy number"

Abstract #33, Nathanael O'Reilly, University of Nebraska Omaha
"Effect of Local Cold Application during Exercise on Gene Expression Related to Mitochondrial Development"

Abstract #34, Monica Kwon, University of Nebraska Omaha
"Exercise in the Heat Blunts Improvements in Aerobic Capacity"

Video Posters

Abstract #36, Tyler Kambis, University of Nebraska Medical Center
"Transgenic overexpression of miR-133a mitigates metabolic remodeling by upregulating fatty acid metabolism in the diabetic heart"

Abstract #38, TeSean Wooden, University of Nebraska Omaha
"Combined anthocyanins and bromelain supplement improves endothelial function and skeletal muscle oxygenation status in healthy adults"

Abstract #40, Justin Sachs, Des Moines University|Medicine and Health Sciences
"16s metagenomic analysis of THC induced weight loss, a novel therapeutic approach?"

Abstract #44, Thomas Fusillo, Des Moines University|Medicine and Health Sciences
"Genetic Variants on the Calcineurin Homologous Protein Genes Associated with an Increase in Blood Pressure."

Abstract #45, Tiffany Chang, Des Moines University|Medicine and Health Sciences
"The Calcineurin Homologous Protein 2 Induces Acidification of Extracellular pH in Human Osteoblast Cells."

Abstract #46, Weilun Ai, University of Nebraska Medical Center
"Hepatocyte-Specific Thromboxane Prostanoid Receptor Deletion Alleviates Alcohol-Associated Liver Disease"

Abstract #47, Yi Luan, University of Nebraska Medical Center
"Activin A regulates white/brown adipose tissue switch in cancer cachexia mice"

Abstract #48, Yi Luan, University of Nebraska Medical Center
"Dispensability of cABL in oocyte death pathway by Cyclophosphamide"

Abstract #51, Allison Ash, Des Moines University|Medicine and Health Sciences
"Gene expression profiling of the limbic brain areas during chronic pain"

Abstract #53, Andrew Kang, Des Moines University|Medicine and Health Sciences
"Acute exercise mitigates pro-inflammatory responses in the hippocampus by downregulating the NF-kB pathway in rats"

Abstract #56, Corrine Monaco, University of Nebraska Medical Center
"Fibroblasts of the bovine corpus luteum activate downstream inflammatory signaling pathways and JNK/SAPK signaling"

Abstract #57, Megan Lewno, University of South Dakota
"Phenotypic Differences among Mice with induced Cardiomyocyte-restricted Ablation of Cops5, Cops8, or both"

Video Posters

Post-Doctoral and Faculty

Abstract #4, Terence Moriarty, University of Northern Iowa
"Exercise-Based Cardiac Rehabilitation Modulates Prefrontal Cortex Oxygenation during Submaximal Exercise Testing in Cardiovascular Disease Patients"

Abstract #5, David Pavlat, Central College
"Sleep Quantity, Quality and Resting Heart Rate in Division III Off-Season College Student-Athletes"

Abstract #12, Sarah Clayton, Des Moines University|Medicine and Health Sciences
"Attending the flipped classroom is not a flop when learning ECG interpretation skills"

Abstract #15, Aaron Bunker, Morningside College
"Increasing Academic Rigor in a Physiology Course and its Effect on Student Mastery of Course Objectives"

Abstract #16, David Senchina, Drake University
"Human PBMC In Vitro Cytokine and Proliferation Responses to Tinctures from Dried Echinacea laevigata Plant Material"

Abstract #25, Ryan Antony, University of South Dakota
"BDNF secretion from C2C12 cells is enhanced by methionine restriction"

Abstract #37, Santosh Yadav, University of Nebraska Medical Center
"Cytomegalovirus infection inhibits cell death mechanisms in cardiomyocytes"

Abstract #41, Vanja Duric, Des Moines University|Medicine and Health Sciences
"Role of Lipocalin-2 (Lcn2) in the limbic pain processing"

Abstract #49, Michael Huisman, Central College
"Movement Screens for the Division III Football Student-Athlete"

Abstract #55, Lie Gao, University of Nebraska Medical Center
"Exercise training protects myocardium against ischemia injury: A role of skeletal muscle Nrf2"

Vevo LAZR-X: Multi-modal In-vivo Imaging

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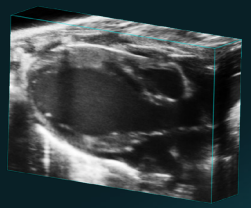
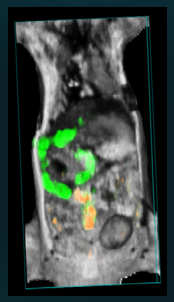
CARDIOLOGY



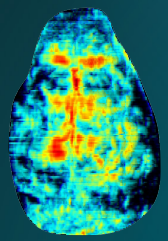
- Myocardial Perfusion
- Myocardial Ischemia
- Myocardial Strain Imaging
- Myocardial Drug Delivery
- Systolic & Diastolic Functions
- Cardio Toxicity
- 4D IMAGING

ONCOLOGY



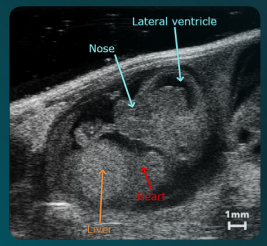
- Angiogenesis
- Hypoxia & Therapy Monitoring
- Biodistribution & Perfusion
- Tumor Implantation & Drug Delivery
- Earliest Tumor Detection
- 2D/3D Volume Quantification
- WHOLE BODY IMAGING

NEUROLOGY



- Cerebral Ischemia
- Cerebral Thrombosis
- Biodistribution
- Implantation & Biopsy
- Hemodynamics
- Cerebral Perfusion
- BRAIN IMAGING

EMBRYOLOGY



- Placental Hypoxia
- Placental Vascularity
- Congenital Heart Disease
- Embryo Manipulation
- Embryonic Development
- Embryo Morphology
- EMBRYO IMAGING

Seeing More Matters | visualsonics.com

Abstracts

Abstract 3: Graduate or Medical Student

Sympathetic splenic denervation ameliorates psychological trauma-induced inflammatory and redox shifts in T-lymphocytes

Elkhatib SK[1], Moshfegh CM[1], Watson GF[1], Patel KP[1], and Case AJ[1]

[1]Department of Cellular & Integrative Physiology, University of Nebraska Medical Center, Omaha, Nebraska

Post-traumatic stress disorder (PTSD) is a devastating psychological disorder that increases the risk for autoimmune disease by >3 fold. While the exact etiology of this risk remains unclear, a known hallmark of PTSD is increased sympathetic tone, which we have previously shown to induce a pro-inflammatory phenotype in T-lymphocytes through a mitochondrial redox-dependent manner. Furthermore, we have demonstrated a preclinical murine model of PTSD, known as repeated social defeat stress (RSDS), recapitulates autonomic and inflammatory aspects of the human condition. The spleen serves as a primary site of T-lymphocyte activation and is exclusively innervated by sympathetic efferent nerves. Therefore, we hypothesized local reductions in splenic sympathetic tone through splenic denervation (Dnx) would reduce RSDS-induced inflammation through alterations in mitochondrial redox. To test this, C57BL6 mice underwent Dnx or sham-operation ± RSDS. Splenic Dnx robustly reduced splenic NE content by 80% ($p<0.0001$) as compared to sham-operated animals. In circulation, RSDS Dnx animals displayed attenuated levels of T-lymphocyte-specific cytokines interleukin-2 (IL-2), interleukin-17A (IL-17A), and interleukin-22 (IL-22) as compared to sham-operated RSDS group ($p=0.0133$, 0.0001, and 0.0359, respectively), whereas other non-specific inflammatory cytokines (*e.g.,* IL-6, TNF-α, CCL2, and CXCL2) remained elevated in RSDS Dnx mice. Furthermore, Dnx reversed RSDS-induced increases in mitochondrial superoxide within T-lymphocytes ($p=0.0035$), while T-lymphocytes after Dnx showed relative decreases in gene expression of IL-2, IL-6, IL-17A, and IL-22 ($p = 0.0039$, 0.0122, 0.0009, and 0.0039, respectively). Overall, our data suggest that psychological trauma via RSDS results in altered inflammation through sympathetic modulation of splenic T-lymphocytes.

Abstracts

Abstract 4: Junior Faculty

Exercise-Based Cardiac Rehabilitation Modulates Prefrontal Cortex Oxygenation during Submaximal Exercise Testing in Cardiovascular Disease Patients

Terence Moriarty [1,2,*] , Kelsey Bourbeau [1,2], Christine Mermier [2], Len Kravitz [2], Ann Gibson [2],Nicholas Beltz [3], Omar Negrete [4] and Micah Zuhl [2,5]

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Evidence suggests that adults with high cardiovascular fitness have lower prefrontal cortex (PFC) oxygenation during incremental exercise compared to their age-matched sedentary counterparts. The purpose of this study was to investigate if prefrontal cortex (PFC) oxygenation during incremental exercise is altered among cardiovascular disease (CVD) patients who completed 6 weeks of exercise-based cardiac rehabilitation (CR). Nineteen (male = 14, female = 5; 65.5 ± 11.5 years) participants from an outpatient CR program were enrolled in the study. Each participant completed a submaximal graded treadmill evaluation at intake and again upon completion of 18 individualized CR sessions. Functional near-infrared spectroscopy (fNIRS) imaging was used to measure left- and right- PFC (LPFC and RPFC) oxygenation parameters during the submaximal exercise evaluations. Patients showed improvements in cardiorespiratory capacity (pre 5.5 ± 2.5 vs. post 6.9 ± 2.8 metabolic equivalents (METs)). A significant decrease in LPFC and RPFC oxygenation was observed during the post-CR exercise test compared to pre-CR (see figure 1 below). CVD patients enrolled in 6 weeks of CR showed significant improvements in functional capacity along with decreased cortical oxygenation during submaximal exercise. Exercise training may cause distribution of cortical resources to motor regions that support sustained exercise. Future research is warranted to investigate adaptations to other brain areas during exercise as well as to examine the specific duration of time by which a CVD patient can benefit from this important adaptation while living a normal lifestyle outside of and following regimented CR.

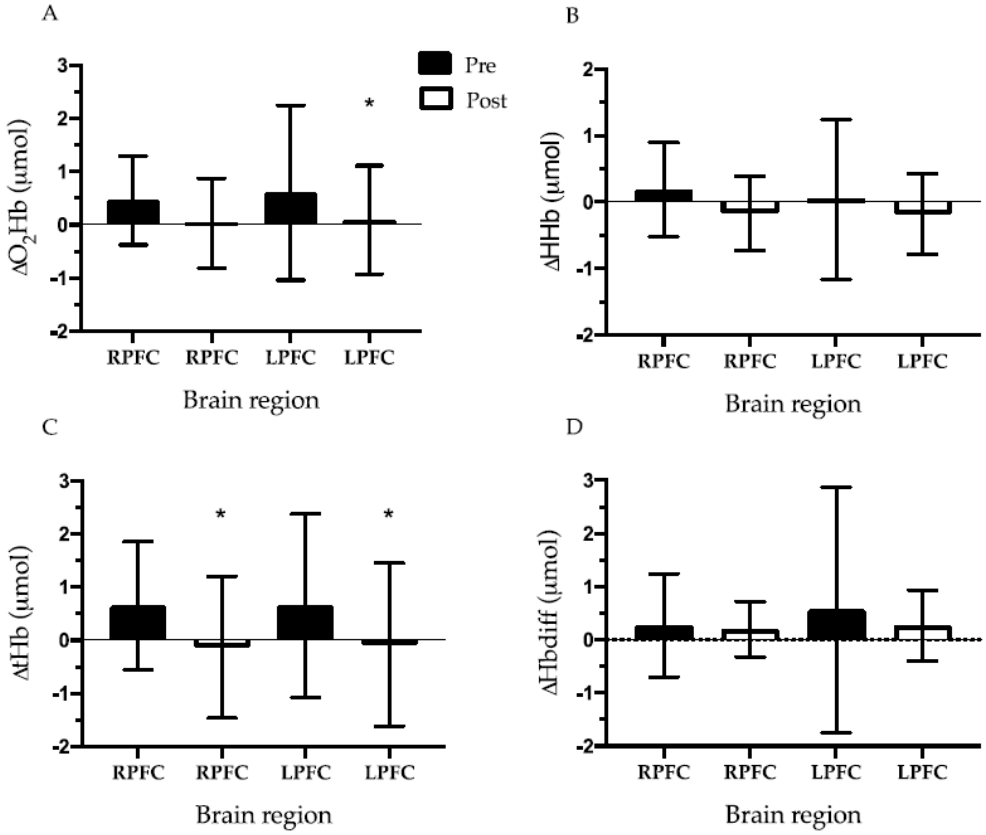

Figure 1. Prefrontal cortex relative changes for functional near infrared spectroscopy measures during the submaximal exercise test pre- and post- cardiac rehabilitation. * significantly lower than pre-cardiac rehabilitation, $p < 0.05$. Δ = change from baseline (0 μmol), O_2Hb = oxyhemoglobin (**A**), HHb = deoxyhemoglobin (**B**), tHb = total hemoglobin (**C**), Hbdiff = oxyhemoglobin difference (**D**), LPFC = left prefrontal cortex, RPFC = right prefrontal cortex. Data are mean ± SD, *N* = 19.

Abstracts

Abstract 5: Other

Sleep Quantity, Quality and Resting Heart Rate in Division III Off-Season College Student-Athletes

David Pavlat, Luke Pavlat, Kyle Johnson, Michael Huisman.

Human Performance Lab, Exercise Science Department, Central College, Pella, Iowa

Introduction: It is believed that sleep is an important recovery tool. Strength and conditioning coaches with the institution remind student-athletes to get eight hours of sleep per night during their voluntary workouts. Therefore, the purpose of this study was to determine sleep quantity, sleep quality and resting heart rate in off-season student-athletes at a division III college.

Methods: Twenty-four student-athletes completed an institutionally approved informed consent. Subjects recorded their sleep quantity in hours and minutes. Sleep quality was recorded against a Likert scale, with 1 being the worst sleep ever and 5 indicating the best sleep ever. Subjects were also asked to measure their resting heart rate via their smart watch or by taking their heart rate before getting out of bed.

Results: The twenty-four student-athletes had the potential of 40 nights to record their sleep values. On average each student-athlete recorded their values 26.24 ± 10.28 days or 65.6% of the possible entries. The mean sleep was 8.06 ± 0.79 hours per day. The mean sleep quality was 3.52 ± 0.47 based on a 1 – 5 Likert scale. The mean resting heart rate was 63.63 ± 7.92 beats per minute.

Discussion: It was surprising that off-season student-athletes averaged just over eight hours of sleep per night. In the future it will be important to try and increase the reporting rate. Future research could include looking at student-athletes in-season versus out-of-season.

Abstracts

Abstract 6: Graduate or Medical Student

The Effects of Static Versus Dynamic Stretching on Power Output in College Aged Students

Whitney Pavlat, David Pavlat

Western Michigan University and Human Performance Lab, Exercise Science Department, Central College, Pella, Iowa

Introduction: Traditionally, static stretching exercises have been a prominent feature of warm-up routines. However, professionals in the strength and conditioning community argue dynamic stretching is an alternative and better way to prepare an athlete for physical performance and to decrease the risk of injury. The purpose of this study was to determine the effects of static stretching versus dynamic stretching on power when performing a standing vertical jump, standing long jump, and the ten-yard dash.

Methods: Eighteen college-aged students participated with a mean age of 21.11 ± 0.74 years, mean weight 157.41 ± 28.24 pounds, mean heights of 67.53 ± 3.12 inches. All subjects signed an institutionally approved informed consent and a PAR-Q. Participants were split into two groups, static verses dynamic. Each subject had a 10-yard sprint, horizontal jump and vertical jump measured and recorded the best of three attempts. Paired t-tests were completed on each of the variables.

Results:

Variables	Static Stretching	Dynamic Stretching	T-Test Value	P-Value
10 Yard Sprints (Seconds)	1.87 ± 0.08	1.87 ± 0.11	0.12	0.907
Standing Vertical Jump (Inches)	23.67 ± 3.79	24.28 ± 3.85	3.20	0.005*
Standing Long Jump (Inches)	89.81 ± 9.52	87.75 ± 8.98	1.33	0.201

* Statistically Significant

Discussion: This research study discovered that static stretching versus dynamic stretching has no significant impact on the performance in the ten-yard dash or long jump. However, there was a significant difference in the vertical jump.

Abstracts

Abstract 7: Undergraduate Student

Sleep Changes Brought on by Covid-19 in Off-Season Division III College Student-Athletes

Luke B. Pavlat, David J. Pavlat, Kyle G. Johnson, and Michael C. Huisman

Human Performance Lab, Exercise Science Department, Central College, Pella, Iowa

Introduction: Student-athletes were sent home because of Covid-19 midway through a sleep study. The purpose of this study was to determine sleep quantity, sleep quality and resting heart rate in out of season student-athletes at a division III college. Because of changes in students leaving campus due to Covid-19 we continued to monitor sleep habits of students who went home.

Methods: Twenty-two student-athletes completed an institutionally approved informed consent. Subjects recorded their sleep quantity in hours and minutes. Sleep quality was recorded against a Likert scale with 1 being the worst sleep ever and 5 indicating the best sleep ever. Subjects were also asked to measure their resting heart rate via their smart watch or by taking their heart rate prior to getting out of bed.

Results: Three paired-t tests were run on the 22 subjects completing their entries.

Table 1: Results of on-campus versus off-campus time.

Pre-Spring Break Mean Sleep Quantity (Hours)	Post-Spring Break Mean Sleep Quantity (Hours)	T-Test Value	P-Value
7.32 ± 0.50	8.24 ± 1.67	-2.56	0.018*
Mean Sleep Quality (Likert Scale 1-5)	Mean Sleep Quality (Likert Scale 1-5)		
3.20 ± 0.53	3.41 ± 0.45	-1.27	0.219
Resting Heart Rate (Beats per Minute)	Resting Heart Rate (Beats per Minute)		
60.11 ± 7.39	61.85 ± 8.07	-2.34	0.029*

* indicates a significant difference

Discussion: There was a significant difference between sleep quantity values and resting heart rate values. Future research should look at changes of sleep patterns throughout the week.

Abstracts

Abstract 8: Undergraduate Student

Measurement of Sleep Quantity, Sleep Quality, Resting Heart Rate and Vertical Jump to Determine Recovery in Track and Field Athletes

Erin Manion[1], David Pavlat[2], Jack Sagan[2], Luke Pavlat[2], Kyle Johnson[3] and Cody Huisman[2]

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[2]Students and Faculty in the Human Performance Lab, Exercise Science Department, Central College, Pella, Iowa. [3]Strength and Conditioning Coach, Athletic Department, Central College, Pella, Iowa.

Introduction: The purpose of this study was to determine anaerobic recovery in relation to sleep quantity, quality and RHR in track and field athletes through the measurement of sleep quality, sleep quantity, RHR, and vertical jump.

Methods: The participants in this study were seven male and seven female track and field athletes. The mean height was 69.57 ± 3.02 inches, the mean weight was 154.51 ± 20.63 pounds, the mean percent body fat was 10.90 ± 4.91%, and the mean age was 19.50 ± 1.23 years.

Subjects were required to fill out and sign an institutionally approved informed consent as well as a PARQ+. Every Monday, after a warm-up, participants performed three vertical jumps. Subjects recorded sleep and RHR values daily.

Results:

Table 1. Means and standard deviations of sleep quantity, sleep quality, resting heart rate and vertical jump.

	Mean	Standard deviation
Sleep Quantity (Hours)	7.76	0.65
Sleep Quality (Likert scale 1-5)	3.50	0.37
Resting Heart Rate (BPM)	56.14	6.64
Vertical Jump (Inches)	22.47	8.04

Table 2. Mean correlations and p-values of comparative samples for all five weeks.

		Correlation (r)	P-value
Sleep Quality	Sleep Quantity	0.874	0.008*
RHR	Sleep Quantity	0.699	0.171
RHR	Sleep Quality	0.570	0.049*
Vertical Jump	Sleep Quantity	-0.203	0.520
Vertical Jump	Sleep Quality	-0.207	0.458
Vertical Jump	RHR	-0.083	0.565

*statistically significant

Discussion: This study found statistically significant correlational relationships ($p < 0.05$) between sleep quantity versus sleep quality and sleep quality versus RHR. We did not find any significant correlations between vertical jump and sleep.

Abstracts

Abstract 9: Graduate or Medical Student

Reduced glucose uptake heterogeneity after 3 mA tDCS in a woman with multiple sclerosis

Alexandra C. Fietsam[1], Craig D. Workman[1], Laura L. Boles Ponto[2], John Kamholz[3], Anne Cooper[1], and Thorsten Rudroff[1, 3]

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An early symptom of multiple sclerosis (MS) is unilateral muscle weakness of the lower limbs, which is associated with gait and balance impairments, increased muscle energy cost, and early fatigue. MS-related motor deficits and disability may be further compounded by the inability to activate muscles homogeneously due to a reduced number of motor units. Transcranial direct current stimulation (tDCS) may be an effective method to enhance cortical excitability and increase neural drive to the more MS-affected leg. In this case study, one woman with MS underwent two sessions of either Sham or 3 mA tDCS before treadmill walking at a self-selected speed (2.0 mph) for 20 min. Two minutes into the treadmill task, [18F]fluorodeoxyglucose (FDG) was injected and whole-body positron emission tomography (PET) imaging was completed after the walking. Glucose uptake (GU) of the individual leg muscles was determined. The relative dispersion of GU [(standard deviation / mean) × 100] in each muscle was calculated as an index of glucose uptake heterogeneity (GUh). Mean ± SD GUh was calculated for each functional muscle group (i.e., knee extensors/flexors). After tDCS, GUh decreased in the left and right knee extensors (-23.7% ± 13.3% and -24.7% ± 18.7%, respectively), but not the left and right knee flexors (3.1% ± 11.2% and -1.6% ± 33.4%, respectively). In some muscles, it is suggested that GUh declines as the number of recruited motor units and activated muscle fibers increases. These findings demonstrate that neural drive and, in turn, motor unit recruitment may be increased after tDCS.

Abstracts

Abstract 10: Postdoctoral Fellow – *Selected for Oral Presentation*

Dorsolateral Prefrontal Cortex tDCS Does Not Immediately Affect Cerebral Blood Flow in People with Multiple Sclerosis

Craig D. Workman[1], Laura L. Boles Ponto[2], Alexandra C. Fietsam[1], John Kamholz[3], and Thorsten Rudroff[1,3]

[1]Department of Health and Human Physiology, University of Iowa, Iowa City, IA 52242, USA
[2]Department of Radiology, University of Iowa Hospitals and Clinics, Iowa City, IA 52242, USA
[3]Department of Neurology, University of Iowa Hospitals and Clinics, Iowa City, IA 52242, USA

Multiple sclerosis (MS) affects ~2.3 million people worldwide and is characterized by treatment-resistant symptoms (neuropathic pain, gait disturbance). Developing effective therapies, like transcranial direct current stimulation (tDCS), to alleviate symptoms is a high priority. tDCS elicits physiological changes in transcranial magnetic stimulation (TMS) motor evoked potential (MEP). Other studies indicate high response variability, and most of the induced current might be shunted before reaching the cortex. This pilot investigation examined individual alterations in cerebral blood flow from 5 min of tDCS over the dorsolateral prefrontal cortex. Three subjects with MS (m/f = 2/1, age = 45.3 ± 19 years) completed two blocks of six [15O]water positron emission tomography scans (baseline, and sham, 1 mA, 2 mA, 3 mA, 4 mA tDCS). Subjects performed a counting task (i.e., 1, 2, 3, 1, 2, 3…,) during the 100 s scan, which commenced immediately after tDCS stopped. Global (gCBF) and relative regional cerebral blood flow (rCBF; areas under the electrodes) were determined and mean rCBF was calculated for each condition. Between block (e.g., sham 1 vs. sham 2) correlations for all subjects indicated moderate to high consistency (Pearson's r = 0.51 – 0.97). There were no notable changes in rCBF at any intensity (≤ ± 4.2% relative to baseline). Thus, 5 min of tDCS might be insufficient to alter cerebral blood flow immediately after stimulation, which contradicts seminal TMS-MEP studies with similar stimulation parameters. Longer stimulation durations (> 5 min) or time to allow the stimulation effects to manifest are suggested for future investigations.

Abstracts

Abstract 11: Graduate or Medical Student

Measurement of Sleep and Resting Heart Rate versus Game Statistics in Division III College Basketball Student-Athletes

Joseph Weber, David Pavlat and Michael Huisman

Human Performance Lab, Exercise Science Department, Central College, Pella, Iowa

Introduction: Previous research has determined that an increase in sleep quantity can have a positive effect on basketball performance. The purpose of this study was to determine the relationship between sleep quantity, sleep quality and resting heart rate versus basketball game statistics during a competitive basketball season.

Methods: Eleven members from a men's and women's basketball team participated in the study. Mean age was 20.00 ± 1.15 years, mean height was 72.60 ± 3.27 inches, and mean weight was 181.30 ± 29.76 pounds. All subjects signed an institutionally approved informed consent and PARQ+. Sleep quantity and quality and RHR were reported daily by the subjects. Points scored, field goal percentage, three-point percentage, free throw percentage, assists, steals, fouls, rebounds, block and turnovers were all recorded. A series of correlations were completed between all variables.

Results: The mean sleep quantity was 7.19 ± 0.54 hours, sleep quality was 3.45 ± 0.67 on a Likert scale of 1- 5 and resting heart rate mean was 57.28 ± 8.25 beats per minute.

Table 1. Correlations between Sleep and Basketball Statistics

	Correlation	Significance
Sleep Quantity vs. Rebounding	0.608	0.047*
Sleep Quantity vs. Points Scored	0.559	0.074
Sleep Quantity vs. Free Throw Percentage	0.573	0.065

* Statistically Significant

Discussion: This study was done for only half a basketball season. We propose doing the study again for a full basketball season. We also noticed that a few of the initial subjects didn't report sleep information as often as we would have liked.

Abstracts

Abstract 12: Other

Attending the flipped classroom is not a flop when learning ECG interpretation skills.

Sarah Clayton and Matthew Henry.

Physiology & Pharmacology Department, Des Moines University; Des Moines University; Des Moines, IA.

Interpreting ECGs is a critical skill taught at various points in the medical curriculum. This skill is taught using a flipped classroom format to allow practice of interpretive skills with faculty guidance during a cardiovascular system course at Des Moines University (DMU). Comparatively, the other units of cardiology and vascular biology are delivered using a lecture-based format. The implementation of classroom capture and casting technologies has changed access to content. Students can now access live, streaming, and/or recorded formats of material. Broadening this accessibility has introduced flexibility for both the learner and instructor, as well as altered the necessity to be in attendance. There are many reports that investigate the changing classroom attendance climate and potential impact on student outcomes. At DMU, a variety of techniques have been employed to encourage student attendance and track the impact attendance has on student performance. We hypothesized that student attendance has a favorable impact on ECG interpretation skills-based training as compared to knowledge-based instruction. The results demonstrate that both incentivized attendees and self-selected attendees outperform their classmates in their ability to interpret ECGs and related content. Also, there is a significant correlation between attendance and performance in this setting. However, the attending student does not appear to have a performance advantage when content is delivered by lecture. This evidence can help students prioritize their time when deciding about whether to attend class. Further, the information can guide curricular change to help programs identify curricular activities that have a clear attendance benefit.

Abstracts

Abstract 13: Graduate or Medical Student

Redox-Regulated Calprotectin Potentiates Psychological Trauma Induced Pro-Inflammatory T-Lymphocyte Differentiation

Cassandra Moshfegh, Safwan Elkhatib, Gabrielle Watson, Adam Case

Department of Cellular & Integrative Physiology, University of Nebraska Medical Center

Post-traumatic stress disorder (PTSD) is a debilitating psychological disorder that increases the risk of comorbid inflammatory diseases by >3 fold, but the mechanisms linking PTSD to inflammation remain elusive. Using a preclinical model of PTSD known as repeated social defeat stress (RSDS), we identified elevated calprotectin (+216%, p=0.0009), a pro-inflammatory protein, in the circulation of mice after RSDS. Calprotectin correlated with T-lymphocyte mitochondrial superoxide levels and inflammatory cytokine expression. Therefore, we hypothesized that psychological trauma leads to pro-inflammatory T-lymphocytes through calprotectin-mediated signaling, which predisposes inflammatory diseases. To investigate the mechanism of calprotectin on T-lymphocytes, we examined the effects of exogenous calprotectin on T-lymphocytes *ex vivo*. Intriguingly, calprotectin did not alter pro-inflammatory cytokine expression or mitochondrial superoxide when directly supplemented to T-lymphocytes. However, when calprotectin was supplemented to dendritic cells prior to co-culture with T-lymphocytes, we observed an approximate 20% increase in mitochondrial superoxide in T-lymphocytes (similar to *in vivo* levels after psychological trauma) compared to no calprotectin (p=0.02). Furthermore, T-lymphocytes showed elevations in the secreted pro-inflammatory cytokines interleukin 17A (14%, p=0.1495), interleukin 15 (24%, p=0.004), and interleukin 23 (8%, p=0.0069). *In vivo*, with continuous calprotectin infusion in control and RSDS mice, we observed circulating calprotectin levels were tightly correlated with mitochondrial superoxide levels in T-lymphocytes (r=0.5372, p<0.0001) and dendritic cells (r=0.4077, p=0.0014). Together, these data suggest that psychological trauma-induced calprotectin promotes a pro-inflammatory T-lymphocyte phenotype via mitochondrial superoxide redox signaling in both dendritic cells and T-lymphocytes, which provides a novel biological target underlying the connection between psychological trauma and inflammation.

Abstracts

Abstract 14: Graduate or Medical Student

Chronic In Vivo Administration of MnTnBuOE-2-PyP^{5+} Does Not Decrease Hypertensive Blood Pressure

Sarah L. Schlichte[1], Elizabeth A. Kosmacek[2], Rebecca E. Oberley-Deegan[2], Matthew C. Zimmerman[1]

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[2]Department of Biochemistry and Molecular Biology, University of Nebraska Medical Center, Omaha, NE

Elevated levels of superoxide ($O_2^{\bullet-}$) contribute to the pathogenesis of hypertension. Scavenging $O_2^{\bullet-}$ via superoxide dismutase (SOD) protein or mimics decreases hypertensive blood pressures. Previous results from our lab have shown that bolus injection of MnTnBuOE-2-PyP^{5+} (BuOE), a manganese porphyrin SOD mimic currently in clinical trials as a normal tissue radioprotector in cancer patients, acutely decreases mean arterial pressure (MAP) in normotensive and angiotensin II (AngII)-induced hypertensive mice. We sought to expand upon these acute findings and test the hypothesis that chronically administered BuOE reduces hypertensive blood pressure long-term. Using radiotelemetry to measure MAP and subcutaneous osmotic minipumps to infuse AngII to establish hypertension, we observed that intraperitoneal (IP) injection of BuOE (1 mg/kg) twice per week for two weeks did not significantly decrease hypertensive blood pressure (MAP in vehicle-treated mice = 127.4 ± 5.2 mmHg vs. BuOE-treated mice = 126.3 ± 6.2 mmHg; n = 6-8; $p > 0.05$). To determine if a different route of administration elicited an antihypertensive response, AngII hypertensive mice were intravenously (IV) injected with BuOE (1 mg/kg, 2x/wk). Similar to IP injection, IV administration of BuOE did not alter hypertensive blood pressure (MAP in vehicle-treated mice = 128.4 ± 1.7 mmHg vs BuOE-treated mice = 129.9 ± 1.6 mmHg; n = 3-4; $p > 0.05$). These data indicate that multiple injections of BuOE (1 mg/kg) does not chronically impact blood pressure, which is beneficial to cancer patients receiving BuOE as a radioprotector. Ongoing studies in our lab are designed to determine if higher doses, different routes of administration, and/or various dosing regimens of BuOE lead to a chronic decrease in hypertensive blood pressure.

Abstracts

Abstract 15: Other

Increasing Academic Rigor in a Physiology Course and its Effect on Student Mastery of Course Objectives

Aaron K. Bunker

Morningside College, Sioux City, IA 51106

Low academic rigor/challenge has been a recurring issue at a small private (~1200 students), Midwestern, liberal arts college for several years. A scoring rubric was used assess student mastery of course objectives with 4-basic levels: Advanced, Proficient, Partially Proficient, and Not Proficient. Following an increase in course academic rigor from year 2 to year 3 the percent of students performing at the Advanced level decreased significantly ($p<0.05$) for Exam2 (-11%) and Exam3 (-19%) course objective assessment questions. Mean exam scores also decreased significantly ($p<0.05$) from year 2 to year 3 for Exam2 (-11%) and Exam3 (-14%). Discussions with students during year 3 revealed that course objective assessment questions for Exam2 and Exam3 were not clear, and additional academic support for the increase in academic rigor was not provided for the students. Prior to year 4, exam questions were revised to better reflect changes in course academic rigor, more forms of academic support were added, and two new formative assessment strategies were created. From year 3 to 4 the percent of students performing at the Advanced level increased significantly ($p<0.05$) for Exam2 (+23%) and Exam3 (+42%) course objective assessment questions. Mean scores also increased significantly for Exam2 (+10%) and Exam3 (+11%) ($p<0.05$). Exam questions can be key indicators in changes of student mastery of course objectives following increases in course academic rigor.

Abstracts

Abstract 16: Other

Human PBMC *In Vitro* Cytokine and Proliferation Responses to Tinctures from Dried *Echinacea laevigata* Plant Material

David S. Senchina[1] and M. Ann Perera[2]

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Echinacea supplements are marketed to prevent or reduce symptoms of upper respiratory infections, presumably by modulating the immune system through bioactive molecules such as alkamides and caffeic acid derivatives. Both manufacturers and lay herbalists often dry plant material prior to extraction. The purpose of this experiment was to assess the biochemical composition and immunomodulatory abilities of tinctures produced from dried *Echinacea laevigata* aboveground parts. High-performance liquid chromatography (HPLC) was used to quantify levels of alkamides and caffeic acid derivatives from *E. laevigata* tinctures. Peripheral blood mononuclear cells (PBMCs) were isolated from adult subjects and challenged *in vitro* with the tinctures, solvent vehicle controls, or positive controls. PBMC cytokine production (IFN-g, IL-1B, IL-2, IL-4, IL-10, and TNF) and proliferation were measured between 24-72 hours, depending on parameter. Background bystander endotoxin levels in the tinctures were below the threshold necessary to affect this model. Alkamide and caffeic acid derivative levels were generally unchanged or higher in tinctures made from dried material versus fresh. None of the extracts made from dried material were able to modulate PBMC cytokine production or proliferation; by comparison, extracts made fresh from the same stock plant material were able to augment TNF production, IL-10 production, and proliferation. These results suggest that drying may abrogate the immunomodulatory abilities of tinctures produced from *E. laevigata* aboveground parts, though this effect appears unrelated to alkamide or caffeic acid derivative changes.

Abstracts

Abstract 17: Graduate or Medical Student

Effect of chronic intermittent hypoxia on inflammation and redox related gene expression in renal cortex

Kalie A. Savage[1], Andrew Philipose[1], Kiefer W. Kious[2], Jayson P. Kemble[1], Luke J. Smith[1], Hugo S Díaz[3], Rodrigo Del Rio[3], Noah J. Marcus[1,2]

[1]College of Osteopathic Medicine, Des Moines University Medicine and Health Sciences, Des Moines, IA
[2]Department of Physiology and Pharmacology, Des Moines University Medicine and Health Sciences, Des Moines, IA
[3]Laboratory of Cardiorespiratory Control, Pontificia Universidad Católica de Chile, Santiago, Chile

Renal hypoxia is recognized as an important factor in the pathogenesis of renal injury and chronic kidney disease (CKD). Renal hypoxia can be precipitated by a wide array of hormonal and hemodynamic factors. Sleep apnea syndrome (SAS) causes repeated bouts of hypoxemia, coupled with hemodynamic abnormalities and neurohormonal activation. Despite clinical correlations between sleep apnea and CKD few studies have addressed molecular pathways that may lead to CKD in patients with SAS. The aim of this study was to identify changes in renal gene expression associated with exposure to chronic intermittent hypoxia (CIH), a model of SAS. We hypothesized CIH would elicit increases in pro-inflammatory, pro-oxidative, and pro-fibrotic gene expression. To address these hypotheses, we exposed rats to 10 days of CIH (or sham) and examined renal cortical expression of lL1β, IL6, TNFα, Nrf-2, GCLC, NQO1, MnSOD, CuZSOD, P40phox, P67phox, SP1, CTGF, and Collagen III via qRT-PCR. Preliminary data suggests CIH results in upregulation of lL1β, IL6, TNFα, Nrf-2, MnSOD, NQO1, GCLC, SP1, CTGF, and Collagen III mRNA in renal cortex. These preliminary studies suggest that short term exposure to CIH is sufficient to promote induction of inflammation and pro-fibrotic genes, and adaptive expression of antioxidant defense programs. Further study is required to more clearly delineate the links between CIH and activation of these gene programs in the kidneys. A better understanding of the molecular pathways activated by CIH is important for understanding CKD pathophysiology in patients with SAS and related pathology such as the cardio-renal syndrome in heart failure.

This study was funded by a grant from the Heart Lung and Blood Institute (HL#138600-01 to NJM).

Abstracts

Abstract 18: Undergraduate Student

Changes in Aerobic Capacity Following Two Weeks of High Intensity Interval Training

Courtney Simon[1], David Pavlat[2], Trevor Mabeus[2] and Brady Johnson[2]

[1]College of Chiropractic Education, Life University, Marietta, Georgia. [2]Human Performance Lab, Exercise Science Department, Central College, Pella, Iowa.

Introduction: Aerobic capacity is a factor that can separate athletes from others in athletic competitions. Recently, there have been more studies looking at improvement in aerobic capacity through high intensity interval training. The purpose of our research was to examine the effect Wingate training has on an individual's aerobic capacity by determining maximal oxygen uptake pre and post Wingate training.

Methods: Eleven college aged students, 8 males and 3 females. Mean age was 20.82 ± 1.33 years, mean height was 70.16 ± 4.35 inches, and mean weight was 166 ± 30.41 pounds. Prior to participation all subjects completed an institutionally approved informed consent and PARQ+. Subjects began the testing by completing a VO_{2peak} test on a Monark Cycle Ergometer using a Parvo Medic True One 2400 Metabolic cart. This test was repeated after five anaerobic training sessions (two weeks). The anaerobic training sessions consisted of two Wingate training rides per day with a minimum of 24 hours in-between. Subjects were verbally encouraged during all sessions.

Results: The VO_{2peak} increased from 3.08 ± 0.64 L/min to 3.31 ± 0.79 L/min. A paired t-test was completed with a t-value of 2.34 and a p-value of 0.042 which is a statistically significant.

Discussion: There have been some recent studies that show a positive relationship between high intensity interval training and increases in maximal oxygen capacity. Two Wingate rides per day is an intense anaerobic training program but most subjects liked the shorter time involved to create better aerobic capacity.

Abstracts

Abstract 19: Graduate or Medical Student

Soluble guanylate cyclase activation increases proteasome activities and facilitates degradation of misfolded proteins in cardiomyocytes

Mingqi Cai, Xuejun Wang

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Background: The ubiquitin-proteasome system mediates the selective degradation of misfolded proteins and most cellular proteins that are normal but no longer needed, thereby playing important roles in diverse cellular processes. Proteasome dysfunction and proteotoxicity are implicated in the genesis of a large subset of cardiovascular diseases. We recently discovered that activation of the cGMP-dependent protein kinase (PKG) facilitates proteasome functioning. Here we sought to test whether activation of the soluble guanylate cyclase (sGC) activate the proteasome and improve proteasomal degradation of misfolded proteins in cardiomyocytes.

Methods and Results: In cultured neonatal rat cardiomyocytes (NRCMs), treatment with an sGC activator (cinaciguat) led to increases in the levels of Ser239-phosphorylated vasodilator-stimulated phosphoprotein (VASP) in a dose-dependent fashion, indicating that the sGC activator treatment increases PKG activity. In-gel proteasome chymotrypsin-like activity assays revealed that cinaciguat treatment increased the activities of both the single-cap and the double-cap 26S proteasomes. Recombinant adenoviruses harboring an expression cassette of an HA-tagged *bona fide* misfolded protein R120G-CryAB (Ad-HA-R120G-CryAB) were employed to overexpress HA-R120G-CryAB in the cultured NRCMs. Western blot analyses for total HA-R120G-CryAB in the NRCMs treated with cinaciguat, proteasome inhibitor bortezomib (BZM), or both showed that proteasomal degradation of HA-R120G-CryAB was enhanced by cinaciguat treatment. Furthermore, protein solubility assessments unveiled that cinaciguat treatment significantly reduced the levels of HA-R120G-CryAB oligomers, indicating that the cinaciguat treatment promotes degradation of the misfolded species of HA-R120G-CryAB.

Conclusions: Activation of sGC with cinaciguat increases PKG activity, activates the 26S proteasome, and thereby facilitates the degradation of misfolded proteins in cardiomyocytes.

Abstracts

Abstract 20: Graduate or Medical Student

CellSurfer Platform for semi-automated cell surface *N*-glycoprotein profiling of human primary cells reveals chamber-specific cardiomyocyte surface maps

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In the heart, cell surface glycoproteins in cardiomyocytes (CM) are essential for sustaining normal cardiac function by facilitating proper contraction of the myocardium. Improper function and/or expression of cell surface proteins can result in life-threating disorders and sudden cardiac death. Despite the critical roles that cell surface glycoproteins play in cardiac biology and disease, a detailed cell type- or chamber-resolved view of the cell surface proteome of normal adult human heart does not exist yet.

We developed a new analytical platform, CellSurfer, which integrates efficient sample handling and streamlined data analysis workflows for rapid, quantitative discovery of cell surface *N*-glycoproteins. CellSurfer includes a semi-automated sample preparation workflow, Microscale Cell Surface Capture (μCSC) that enables discovery of >300 *N*-glycosylated surface proteins from less than <1 mg total cellular proteins (1-10 million cells). μCSC was applied to primary CM isolated from four anatomical regions of human hearts (n=4) to identify plasma membrane and extracellular matrix *N*-glycoproteins.

Integrating CellSurfer with an optimized strategy for isolating intact CM from human heart tissue resulted in the generation of the first chamber-specific map of the cell surface *N*-glycoproteome of adult human CM. Overall, >450 cell surface *N*-glycoproteins were identified, including transmembrane, GPI-anchored, and extracellular matrix proteins. These data will enhance our understanding of the distinct phenotypic fingerprint of CM that reside in each of the four chambers of the human heart and reveal new potential targets for immunophenotyping, drug delivery, and benchmarking CM derived from human pluripotent stem cells.

Abstracts

Abstract 21: Undergraduate Student – *Selected for Oral Presentation*

Effects of heated water-based versus land-based exercise training on vascular function in individuals with peripheral artery disease

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Peripheral artery disease (PAD) is an atherosclerotic disease associated with poor vascular function, walking impairment, and reduced quality-of-life. Land-based exercise therapy (LBET) is frequently recommended to improve walking and reduce symptoms. Recently, evidence has suggested that heated-water exercise therapy (HWET) is an effective intervention for PAD. However, the efficacy of LBET versus HWET in PAD patients had not been elucidated. Therefore, we sought to compare effects of LBET with HWET on cardiovascular function, exercise tolerance, physical function (PF), and body composition (BC) in PAD patients. PAD patients (n=53) were recruited and randomly assigned to a LBET group (n=25) or HWET group (n=28). The LBET group performed treadmill walking, whereas the HWET group performed walking in heated water for 12 wk. Leg (legPWV) and brachial-to-ankle arterial stiffness (baPWV), blood pressure (BP), ankle-brachial index (ABI), 6-min walking distance (6MWD), claudication onset time (COT), PF, and BC were assessed before and after 12 wk. There were significant group-by-time interactions ($P<0.05$) for legPWV, BP, 6MWD, COT, BC, and resting metabolic rate (RMR). Both groups significantly reduced ($P<0.05$) legPWV, BP, and body fat percentage, and HWET measures were significantly lower than LBET measures. Both groups significantly increased 6MWD, COT, and RMR, and HWET group measures were significantly greater than LBET measures. A time effect was noted for baPWV reduction in both groups ($P<0.05$). These results suggest that both LBET and HWET improve cardiovascular function, exercise tolerance and BC, and HWET showed considerably greater improvements compared with LBET in patients with PAD.

Abstracts

Abstract 22: Graduate or Medical Student

Novel isoform of Curcumin (*cis-trans* Curcumin) binds to Adenosine Receptors A_{2A} and A_{2B}

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All four of the adenosine receptor (AR) subtypes mediate pain and have been targeted by pharmacologists to generate new therapeutics for chronic pain. The vanilloid phytochemicals, which include curcumin, capsaicin, and gingerol, have been shown to alleviate pain. However, there is little to no literature on the interaction of vanilloid phytochemicals with ARs. We used photochemical methods to generate a novel isomer of curcumin (*cis-trans* curcumin or CTCUR) and studied the interaction of both curcumin and CTCUR with the two G_s-linked AR subtypes. Human embryonic kidney (HEK) cells transfected with either A_{2A} or A_{2B} were used. Binding affinity was measured by competitive binding assays, docking analysis, and confocal microscopy, toxicity was tested using cell survival assays, and receptor activation was monitored using cAMP activation assays. Competitive binding results indicate that CTCUR binds to both A_{2A} and A_{2B} with K_i values of 5 µM and 7 µM, respectively, and docking results concur. Curcumin did not show binding at either of these receptors. Confocal microscopy results confirm binding for A_{2B} but are unclear for A_{2A}. Cell survival results show that CTCUR is nontoxic up to 100 µM. Receptor activation results require further work to determine whether CTCUR is an agonist or antagonist at these receptors. Overall, our results suggest that the antinociceptive effects of vanilloid phytochemicals may be modified by interactions with ARs. In conclusion, we have identified a novel isoform of curcumin which can bind to ARs and can be further explored to develop a new class of AR therapeutics.

Abstracts

Abstract 23: Graduate or Medical Student – *Selected for Oral Presentation*

Hydrogen Sulfide Protects the Heart against Ferroptosis in Diabetic Cardiomyopathy

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Hyperglycemia-induced death of terminally differentiated cardiomyocytes in diabetic cardiomyopathy (DMCM) leads to heart failure. Ferroptosis is a newly discovered form of cell death triggered by intracellular iron and oxidative stress. While little is known about ferroptosis in DMCM, hyperinsulinemia stimulates intracellular iron uptake, which would be predicted to increase ferroptosis. H_2S is an endogenous gaseous signaling molecule which may inhibit ferroptosis. H_2S donors increase glutathione substrate for glutathione peroxidase 4 (GPX4), which removes lipid peroxidation and is the primary inhibitor of ferroptosis. However, no study has investigated the role of H_2S in ferroptosis during DMCM. We tested the hypothesis that increased ferroptosis contributes to DMCM, which is ameliorated by restoring H_2S levels, by measuring ferroptosis in the hearts of db/db mice with DMCM after H_2S donor treatment. GPX4 expression was decreased (3.21±0.41 GPX4/total protein in db/+ control mice vs. 1.84±0.26 in db/db, $P<0.05$, n=6/group) and 4-HNE lipid peroxide was increased (7.37±0.98 µg 4-HNE/total protein in db/+ control mice vs. 8.73±0.84 in db/db, $P<0.05$, n=3/group) in the left ventricle of db/db mice indicating increased ferroptosis in DMCM. H_2S donor GYY4137 treatment increased GPX4 expression and activity and reduced 4-HNE formation in the db/db heart indicating reduced ferroptosis. We observed a prevention of cardiac interstitial fibrosis, hypertrophy, and restoration of systolic function with GYY4137 treatment in conjunction with the prevention of ferroptosis. This study establishes ferroptosis as a new, non-apoptotic, form of cell death in DMCM, and H_2S as a novel regulator of cardiac ferroptosis.

Abstracts

Abstract 24: Graduate or Medical Student

Dietary nitrate intake improves vascular function and walking capacity in patients with peripheral artery disease

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Peripheral artery disease (PAD) is an atherosclerotic vascular disease which manifests as leg pain and impaired walking capacity. Recently, nitrate supplements have been used to improve leg blood flow and exercise tolerance in PAD. However, a standard nitrate supplement protocol and mechanistic study to examine the effects of nitrate intake on oxygen delivery and utilization in the skeletal muscle of PAD has yet to be determined. Therefore, we sought to determine the impacts of a moderate dose of nitrate normalized for body mass (0.11 mmol nitrate/kg) on vascular function, skeletal muscle oxygen utilization capacity, and exercise tolerance in patients with PAD. 11 PAD patients received either the nitrate supplement or placebo in a randomized crossover design. At both visits, measures of blood pressure (BP), brachial and popliteal artery endothelial function (FMD), arterial stiffness (PWV), augmentation index (AIx), maximal walking capacity, time to claudication (COT), and skeletal muscle oxygen utility were measured pre-and-post nitrate and placebo intake. There were significant group by time interactions (p<0.05) for systolic BP (Δ-4.7mmHg), central systolic BP (Δ-8.2mmHg), brachial FMD (Δ1.3%), and maximal walking distance (Δ92.8m). A time-effect (p<0.05) was noted for popliteal artery FMD and maximal walking time following nitrate intake (Δ1.6% and Δ56.3s, respectively), and a group-effect (p<0.05) was noted for reduced deoxygenated hemoglobin during exercise. There were no changes in PWV, AIx, or COT (p>0.05). These results indicate that a moderate dose of nitrate may be an effective supplement strategy for improving vascular function, oxygen utility, and walking capacity in patients with PAD.

Abstracts

Abstract 25: Other

BDNF secretion from C2C12 cells is enhanced by methionine restriction

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Brain derived neurotrophic factor (BDNF) is produced in skeletal muscle as a myokine that plays a role in muscle metabolism. However, how metabolic changes affect skeletal muscle BDNF expression and release remains to be fully understood. Amino acid restrictions such as methionine restriction (MR) are considered as an alternative fasting approach. Here we reported that in C2C12 myotubes, MR enhanced BDNF release, which was measured using ELISA, cell immunostaining, and Western blot. Inhibition of protein transport pathway blocked the MR enhanced BDNF release, confirming that MR-induced BDNF release involved classic protein secretory pathway. MR increased L-lactate product in media, suggesting that MR promoted glycolysis. Treatment with 2-deoxy glucose (2-DG) attenuated lactate production as well as BDNF release, suggesting that glycolysis is involved in the enhanced BDNF release induced by MR. Moreover, treatment with L-Lactate, the end-product of glycolysis, enhanced BDNF release in control cells in a dose dependent manner, suggesting lactate produced by glycolysis may mediate the enhanced BDNF release by MR. Overall, the results of this study suggest that MR promotes BDNF secretion from C2C12 myotubes at least partially via enhancing glycolysis and lactate production.

Abstracts

Abstract 26: Graduate or Medical Student – *Selected for Oral Presentation*

Novel mechanism of neural control of breathing in Acute Lung Injury (ALI)

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Increased respiratory rate (RR) usually develops within a few days after ALI. However, the neural mechanisms underlying the breathing dysfunction are not fully understood. We investigated the role of chemoreceptor afferents and pulmonary spinal afferents in the control of breathing in ALI. ALI was induced in male SD rats (200-250g) using intra-tracheal injections of bleomycin (Bleo) or saline for controls (day 0) and measured RR, Tidal Volume (TV), and MV (Minute Ventilation) weekly from W1-W4 using whole body plethysmography. Chemoreceptor activation was assessed as the ventilatory responses to hypoxia (10% O2) and hypercapnia (5-7% CO2) from rest (21% O2). Resting MV increased after Bleo at W1 and W2 due to a large increase in RR but not TV. MV and RR levels in response to hypoxia and hypercapnia were not different from controls suggesting the chemoreceptors were not sensitized. Chemoreceptor inhibition by 90% O2 (hyperoxia) produced no suppression of MV or RR, suggesting no tonic chemoreceptor activation in either group. We ablated TRPV1-positive lung spinal afferents in bleo rats by bilaterally injecting RTX (0.25ug/5µl) or 5µl saline in control rats into the stellate ganglion (day 3 after bleo) and measured ventilation at day 7. RTX ablation of pulmonary spinal afferents reduced resting MV and RR in bleo rats to near control levels. These results suggest that pulmonary spinal afferent activation play a major role in the increased RR in ALI; whereas, chemoreceptor function is not affected.

Abstracts

Abstract 27: Graduate or Medical Student

Renal Cortical KLF15 and KLF2 are downregulated in chronic heart failure

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Type II cardiorenal syndrome is characterized by renal dysfunction resulting from chronic heart failure (CHF). CHF is associated with increased sympathetic stimulation of the kidney, hemodynamic abnormalities, and activation of the renin-angiotensin system (RAS) which are thought to collectively contribute to renal hypoxia and tissue injury. KLF15, which is downregulated by both RAS activity and hypoxia, plays an important protective role in the kidney by constraining pro-fibrotic connective tissue growth factor (CTGF). Hemodynamic abnormalities in CHF may lead to downregulation of the shear-sensitive transcription factor KLF2, which can mitigate fibrosis via activation of Nrf2. In addition, hypoxia has been shown to cause downregulation of anti-fibrotic E-cadherin. We hypothesized that KLF15, KLF2, and E-cadherin expression would be reduced and that CTGF, and Collagen I & III expression would be increased in CHF. To test these hypotheses, CHF was induced via coronary artery ligation (CAL) and verified using echocardiography. At 8 weeks post-CHF induction, rats were euthanized, and RNA was extracted from renal cortex and converted to cDNA. cDNA was plated with primers for KLF15, KLF2, CTGF, E-cadherin, Collagen I & III, and β-Actin, and analyzed via qRT-PCR. Two-factor independent samples T-tests or Mann-Whitney U tests were used for statistical analysis, as appropriate. We observed that KLF15, KLF2, E-cadherin, and Collagen III, were downregulated in CHF vs sham. In conclusion, renal hypoperfusion, RAS activation, and attendant tissue hypoxia may lead to repression of KLF15, KLF2, and E-cadherin and related disinhibition of pro-fibrotic signaling in CHF.

This study was funded by a grant from the Heart Lung and Blood Institute (HL#138600-01 to NJM).

Abstracts

Abstract 28: Undergraduate Student – *Selected for Oral Presentation*

Protective Effects of Low-dose Metformin Treatment in a Mouse Model of Diabetic Kidney Disease

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Diabetes mellitus (DM) affects more than 30 million people in the US. About one-third of DM patients develop diabetic kidney disease (DKD). Metformin is a widely prescribed antidiabetic medication for patients with type 2 diabetes; however, its direct effects on the renal function are poorly understood. Hence, our study aimed to investigate the effects of a non-glucose lowering, low-dose metformin treatment against the progression of DKD using a genetic mouse model of type 2 diabetes. To accelerate nephropathy, each mouse had their left kidney removed. The study had four treatment groups: 1) vehicle-treated control, 2) metformin-treated control, 3) diabetic, vehicle-treated, and 4) diabetic, metformin-treated. Mice were treated with either vehicle or metformin (100 mg/kg/day) for four weeks. Urine and kidney tissue samples were collected at the end of the study to measure the markers of renal dysfunction, such as elevations in urine albumin-creatinine ratio (UACR) and kidney injury molecule 1 (KIM-1), and the markers of renal fibrosis, such as transforming growth factor-beta (TGF-β) and alpha-smooth muscle actin (α-SMA). Our results indicate that metformin-treatment in diabetic mice decreased UACR (117.53 ± 61.56 vs. 205.3 ± 112.5) and KIM-1 immunostaining (1.5 ± 0.5 vs. 2.3 ± 0.7) as compared to vehicle-treated diabetic mice. Similarly, the metformin-treated diabetic mice kidneys showed decreased immunostaining for TGF-β (0.7 ± 0.2 vs. 1.3 ± 0.3) and α-SMA protein expression compared to vehicle-treated diabetic mice kidneys. Further studies are required to confirm the nephroprotective effects of low-dose Metformin treatment on the diabetic kidney.

Abstracts

Abstract 29: Graduate or Medical Student

Defining molecular mechanism promoting neointimal hyperplasia by CSN8 hypomorphism.

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Despite the strong evidence linking the COP9 signalosome (CSN) to cell cycle regulation, direct study of CSN in vascular smooth muscle cell (VSMC) proliferation is lacking. To fill this critical gap, we performed the present study to test the hypothesis that CSN8 hypomorphism increases free CSN5 or CSN5-containing mini-complex, facilitates the nuclear exclusion of p27, accelerates VSMC proliferation, and thereby exacerbates neointimal hyperplasia. *In vivo*, we subjected adult CSN8 hypomorphic and the littermate control mice to left common carotid artery (LCCA) ligation and collected the LCCA segment proximal to the ligation for analyses. Compared to non-hypomorphic controls, the CSN8 hypomorphic mice displayed more severe neointimal thickening at both 1- and 4-week after ligation, a markedly greater increase in PCNA and significantly greater prevalence of Ki67-positive VSMCs at 1 week after ligation. *In vitro*, PDGF-BB stimulated CSN8 hypomorphic VSMCs also showed a significant increase in PCNA compared to the control VSMCs. Next, we found that ligation-induced increases in p27 and p53 proteins were significantly less in hypomorphic mice than in the control. Furthermore, nuclear fractionation revealed that the nuclear to cytoplasmic ratio for p27 and CSN5 proteins were markedly smaller in hypomorphic mice. In addition, native gel electrophoresis also showed an increase in the cytoplasmic CSN5 mini-complex in hypomorphic mice suggesting that in response to vascular injury, increasing VSMC proliferation by CSN8 hypomorphism may be caused by increased CSN5-mediated nuclear exclusion of p27. Hence, our data strongly support our hypothesis and suggest an important role for CSN in regulating neointimal hyperplasia.

Abstracts

Abstract 30: Graduate or Medical Student

Ser14-Psmd11/Rpn6 phosphorylation is required for activation of the 26S proteasome by PKA but is dispensable for cardiac responses to increased proteotoxic stress

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In cultured cells, cAMP-dependent protein kinase (PKA) was shown to activate the 26S proteasome through directly phosphorylating Serine 14 of PSMD11/Rpn6, a non-ATPase subunit of the 19S proteasome. To test the hypothesis that Psmd11-Ser14 phosphorylation is required for PKA-mediated activation of the proteasome in vivo and protects against cardiac proteotoxicity, we generated via CRSPR/Cas9 gene editing a mouse model, in which the codon for Ser14 in the *Psmd11* gene was mutated to encode Alanine (*Psmd11*^{S14A}) for blocking Ser14-Psmd11 phosphorylation. Treatments that activate the cAMP-PKA pathway increased Ser14-phosphorylated Psmd11 (p-Ser14-Psmd11) and enhanced proteasome activity in wild-type, but not Psmd11^{S14A}, mouse embryonic fibroblasts (MEFs) and mouse hearts, indicating that p-Ser14-Psmd11 is required for the activation of 26S proteasome by PKA. To test the role of p-Ser14-Psmd11 in cardiac response to increased proteotoxic stress (IPTS) in mice, we cross-bred the S14A mice with CryAB^{R120G} transgenic mice (a model of cardiac IPTS) and monitored cardiac phenotypes among the resulting littermates. Surprisingly, serial echocardiography showed neither heterozygous nor homozygous Psmd11^{S14A} knock-in mitigated the progression of cardiac hypertrophy and malfunction induced by CryAB^{R120G}. Kapan-Meier survival analysis revealed no significant difference in lifespan between Psmd11^{S14A}::CryAB^{R120G} and CryAB^{R120G} mice. Consistently, by 3 month of age, heterozygous Psmd11^{S14A} knock-in did not affect myocardial proteasome activities or the accumulation of ubiquitin conjugates and CryAB proteins in the CryAB^{R120G} mice. These data suggest that p-Ser14-Psmd11 is dispensable for cardiac response to IPTS although it is required for the activation of the 26S proteasome by PKA.

Abstracts

Abstract 31: Graduate or Medical Student

Pancreatic ductal adenocarcinoma highly expresses activin A: implications in adipose tissue and cancer cachexia

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Background: Cancer cachexia occurs in approximately 50% of all cancer patients and 80% of patients with advanced cancers. Cancer cachexia is seen in over 85% of pancreatic cancer patients who often have the most severe degrees of cachexia and experience adipose tissue loss prior to skeletal muscle loss early in the disease process. Several factors have been proposed to induce cachectic symptoms in human patients, including inhibin subunit βA, also known as activin A.

Hypothesis: We hypothesized that there is a correlation between the marked increase in activin A production in PDAC patients and the remodeling of adipose tissue and consequent cancer-associated cachectic state.

Experimental Design: We measured activin A levels in the serum of PDAC patients and analyzed the expression of activin A in human PDAC cell lines and tumor biopsies as well as tumors from an orthotopic PDAC mouse model. We further investigated the effect of activin A on remodeling of adipose tissue secondary to tumor progression.

Results: We found that there is a clear correlation between elevated levels of activin A and the progression of CAC (cancer-associated cachexia). We observed that adipose tissue in our mouse model underwent increased adipose tissue loss mediated by autophagy. Furthermore, our studies revealed that the expression of extracellular matrix proteins (ECM) such as collagen I and fibronectin is dramatically upregulated with adipose tissue loss.

Discussion: Our results reveal a novel role of activin A in relation to the loss of adipose tissue in the progression of cachectic state.

Funding Resource: KIM NRI COLLAB SEED 3132051012 and Dr. Kim's Startup Package

Abstracts

Abstract 32: Graduate or Medical Student

The Acute Effects of Exercise and Temperature on mtDNA Remodeling

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Researchers have widely used mitochondrial copy number, the ratio of genomic DNA (gDNA) to mitochondrial DNA (mtDNA), to quantify the amount of mitochondria within tissue. Variations in this ratio (mtDNA:gDNA) have been linked to deficient mitochondria leading to common diseases, *e.g.*, cancer, Alzheimer's and the aging process. The mtDNA plasmid has been divided into the Major (mtMAJ) and Minor (mtMIN) regions. The mtMAJ contains most of the genes that transcribe the electron transport chain proteins, and thus, more susceptible to deletions/mutations. Exercise also stresses the mitochondria; however, its influence over these mtDNA regions, is unknown. Gene expression data has suggested environmental temperature, when paired with exercise, can increase mitochondrial development/turnover. Therefore, the purpose of this study is to analyze the acute effects of exercise in three temperature conditions on regional mtDNA relative to a genomic reference gene (B2M). Thirty-six male subjects performed 1h of cycling in 1 of 3 temperature conditions (hot=33°C, cold=7°C, or neutral=20°C). Muscle biopsies were taken from the *vastus lateralis* at three time-points (Pre, Post, and 4h Post). Acute exercise did not have an influence over mtMIN copy number over time (p>0.416) or temperature (p=0.177). However, exercise did decrease mtMAJ copy number post-exercise (p=0.008) but it returned to pre-exercise values at 4h Post (p=0.195). When time-points were combined (main effect), exercising in the cold maintained mtMAJ copy number above the neutral (p=0.04) and hot (p=0.002) conditions. These data provide evidence to support the role of exercise and temperature in the remodeling of the mtDNA.

Abstracts

Abstract 33: Graduate or Medical Student

Effect of Local Cold Application during Exercise on Gene Expression Related to Mitochondrial Development

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BACKGROUND: Exercise training increases mitochondrial content in active skeletal muscle. Previous work suggests that mitochondrial-related genes respond favorably to exercise in cold environments. However, the impact of localized tissue cooling is unknown.

PURPOSE: is to determine the impact of local muscle cooling during endurance exercise on human skeletal muscle mitochondrial-related gene expression.

METHODS: Twelve subjects (age 28±6 y) cycled at 65% Wpeak. One leg was cooled (C) for 30 minutes before and during exercise with a thermal wrap while the other leg was wrapped but not cooled, room temperature (RT). Muscle biopsies were taken from each *VL* before and 4 hours post-exercise for the analysis of gene expression.

RESULTS: Muscle temperature was lower in C (29.2±0.7°C) than RT (34.1±0.3°C) after pre-cooling for 30minutes before exercise ($p<0.001$) and remained lower after exercise in C (36.9±0.5) than RT (38.4±0.2, $p<0.001$). *PGC-1α* and *NRF1* mRNA expression were lower in C ($p=0.012$ and $p=0.045$, respectively) than RT at 4-h post. There were no temperature related differences in other genes ($p>0.05$).

CONCLUSION: These data suggest that local cooling has an inhibitory effect on exercise-induced *PGC-1α* and *NRF1* expression in human skeletal muscle. Those considering using local cooling during exercise should consider other systemic cooling options.

Abstracts

Abstract 34: Graduate or Medical Student

Exercise in the Heat Blunts Improvements in Aerobic Capacity

Monica Kwon, Dustin Silvka, Robert Shute, Katherine Marshall, Megan Opichka, Halee Schnitzler, Walter Hailes, Brent Ruby

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The exercise-induced rise in PGC-1a is blunted when acute exercise takes place in the heat. However, it is unknown if this alteration has functional implications after heat acclimation and exercise training. Purpose: To determine the impact of three weeks of aerobic exercise training in the heat compared to training in room temperature on thermoregulation, PGC-1a mRNA response, and aerobic capacity. Methods: Twenty-one untrained college aged males (age, 24 ± 4 yrs; height, 178 ± 6 cm) were randomly assigned to three weeks of aerobic exercise training in either 33°C (n=12) or 20°C (n=11) environmental temperatures. Results: The 20°C training group increased VO2peak from 3.21 ± 0.77 to 3.66 ± 0.78 L·min-1 ($p<0.001$) while the 33°C training group did not improve (pre, 3.16 ± 0.48 L·min-1; post, 3.28 ± 0.63 L·min-1; $p=0.283$). PGC-1a increased in response to acute aerobic exercise more in 20°C (6.6±0.7 fold) than 33°C (4.6±0.7 fold, $p=0.031$) before training, but was no different after training in 20°C (2.4±0.3 fold) or 33°C (2.4±0.5 fold, $p=0.999$) at the same absolute workload. No quantitative alterations in mitochondrial DNA were detected with training or between temperatures ($p>0.05$). Conclusions: This research indicates that exercise in the heat may limit the effectiveness of aerobic exercise at increasing aerobic capacity. Furthermore, this study demonstrates that heat induced blunting of the normal exercise induced PGC-1a response is eliminated after 3-weeks of heat acclimation.

Abstracts

Abstract 35: Keynote Speaker

Getting to the heart of the matter: The "hole" story of environmental physiology & medicine?

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The foramen ovale is part of the normal fetal cardiopulmonary circulation that fails to close after birth in ~35% of the population and represents a potential source of right-to-left shunt. Despite the prevalence of patent foramen ovale (PFO) in the general population, cardiopulmonary, exercise, thermoregulatory, and altitude physiologists have likely underestimated the potential effect of this intracardiac shunt on normal physiological processes in otherwise healthy humans. Because this shunted blood bypasses the respiratory system, it would not participate in either gas exchange and may have impacts on other physiological processes that remain undetermined. Compared to those otherwise healthy humans without a PFO, those with a PFO may have 1) a greater alveolar-to-arterial oxygen difference ($AaDO_2$) at rest and during exercise, 2) blunted ventilatory acclimatization to high altitude, 3) a blunted hypercapnic ventilatory response, 4) blunted thermal hyperpnea and 5) surprisingly, a higher core body temperature (~0.4°C) at rest and during exercise. There is also an association of PFO with high-altitude pulmonary edema and acute mountain sickness. These effects on physiological processes are likely dependent on both the presence and size of the PFO, with small PFOs not likely to have significant/measurable effects. The PFO can be an important determinant of normal physiological processes and should be considered a potential confounder to the interpretation of former and future data, particularly in small data sets where a significant number of PFO+ subjects could be present and significantly impact the measured outcomes.

Abstracts

Abstract 36: Graduate or Medical Student

Transgenic overexpression of miR-133a mitigates metabolic remodeling by upregulating terminal fatty acid metabolism in the diabetic heart

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Diabetic mellitus (DM) cardiomyopathy is a metabolic disorder in which energy dependence on fatty acid (FA) metabolism causes FA influx overload. While we reported that miR-133a overexpression prevented deleterious lipid accumulation in the diabetic Akita heart, it is unclear whether miR-133a regulates diabetes-induced metabolic remodeling in the DM heart. Thus, we performed deep sequencing on the heart from diabetic Akita (Ak), sibling wild-type (WT), cardiac-specific miR-133aTg (Tg), and Ak/Tg mice. Ingenuity pat1hway analysis showed that FA oxidation (FAO) was the highest activated pathway in the DM heart (*P*-value=4.59E-11). We hypothesized that miR-133a overexpression in the DM heart improves cardiac metabolism by increasing FA clearance via enhancing FAO. Notably, mitochondrial FA transport protein carnitine palmitoyltransferase-1 (CPT1) was upregulated in the diabetic heart, and was restored by miR-133a overexpression (WT: 0.02±0.01, Ak: 0.06±0.02, Ak/Tg: 0.17±0.02, Tg: 0.06±0.01). Furthermore, citrate synthase activity, the initiation enzyme of the TCA cycle, was highly upregulated by miR-133a overexpression in the diabetic heart (WT: 0.79±0.04, Ak: 0.74 ±0.03, Ak/Tg: 0.99±0.06, Tg: 0.06±0.02), suggesting increased utilization of FA. Remarkably, miR-133a overexpression in the diabetic heart attenuated increased expression of 3-Hydroxy-3-Methylglutaryl-CoA Synthase 2 (HMGCS2), the rate-limiting enzyme of ketogenesis, the FAO spillover pathway (WT: 0.13±0.02, Ak: 0.74±0.13, Ak/Tg: 0.39±0.07, Tg: 0.93±0.01). These results support that increased miR-133a in the diabetic heart contributes to improved FAO and terminal FA metabolism via the TCA cycle, thus downregulating FA deposition and ketogenesis in the diabetic heart.

Abstracts

Abstract 37: Postdoctoral Fellow

Cytomegalovirus infection inhibits cell death mechanisms in cardiomyocytes

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Cytomegalovirus (CMV) infection increases the risk of cardiovascular diseases. However, the underlying molecular mechanisms are unclear. Although CMV infection induces immune cells death, the role of CMV infection on cardiomyocytes death is unclear. Since cardiomyocytes death ultimately leads to heart failure and mortality, we hypothesized that CMV inhibits cardiomyocytes death for its own survival and proliferation. To determine the role of CMV infection on cardiomyocytes death, we infected murine neonatal cardiomyocytes with CMV (MOI 5) for 24 h and evaluated cell death mechanisms. Our results showed increased cell survival (ATP, CT= 100 ± 1.7, CMV-treated = 123 ± 6.8) and reduced cell death (LDH, CT= 100 ± 2, CMV-treated = 51 ± 1) in CMV-treated cardiomyocytes. We also evaluated different forms of cell death by determining apoptosis and necroptosis (a non-apoptotic form of cell death). Our results showed reduced apoptosis (cl/t caspase-3, CT= 1.10 ± 0.18, CMV-treated = 0.04 ± 0.01) and necroptosis (pMLKL/MLKL, CT= 3.0 ± 0.5, CMV-treated = 1.3 ± 0.2*;* pRIPK3/RIPK3, CT= 2.0 ± 0.1, CMV-treated = 1.2 ± 0.1) in CMV-treated cardiomyocytes. Because oxidative stress induces cell death mechanisms, we measured both cellular and mitochondrial ROS in CMV-treated cardiomyocytes CMV infection reduces both cellular (CT= 11 ± 0.4, CMV-treated = 9 ± 0.1) and mitochondrial (CT= 15 ± 0.2, CMV-treated = 12 ± 0.2) ROS in cardiomyocytes. These findings demonstrate that CMV infection inhibits cell death via suppressing apoptosis and necroptosis, plausibly by reducing oxidative stress, in cardiomyocytes.

Abstracts

Abstract 38: Graduate or Medical Student

Combined anthocyanins and bromelain supplement improves endothelial function and skeletal muscle oxygenation status in adults: a double-blind placebo-controlled randomized crossover clinical trial

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Anthocyanins and bromelain have gained significant attention due to their antioxidative and anti-inflammatory properties. Both have been shown to improve endothelial function, blood pressure (BP), and oxygen utility capacity in humans, however the combination of these two and the impacts on endothelial function, BP, total antioxidant capacity (TAC), and oxygen utility capacity have not been previously investigated. The purpose of this study was to investigate the impacts of a combined anthocyanins and bromelain supplement (BE) on endothelial function, BP, TAC, oxygen utility capacity, and fatigability in healthy adults. Healthy adults (n=18, age 24±4) received BE or placebo in a randomized crossover design. Brachial artery flow-mediated dilation (FMD), BP, TAC, resting heart rate, oxygen utility capacity, and fatigability were measured pre-and post-BE and placebo intake. The BE group showed significantly increased FMD, reduced systolic BP, and improved oxygen utility capacity compared placebo group ($p<0.05$). Tissue saturation and oxygenated hemoglobin significantly increased following BE intake while deoxygenated hemoglobin significantly decreased ($p<0.05$) during exercise. Additionally, TAC was significantly increased following BE intake ($p<0.05$). There were no significant differences for resting heart rate, diastolic BP, or fatigability index. These results suggest that BE intake is an effective nutritional therapy for improving endothelial function, BP TAC, and oxygen utility capacity, which may be beneficial to support vascular health in humans.

Abstracts

Abstract 39: Undergraduate Student

RNA Bulk Sequencing Analysis and Differential Gene Expression of Multiple Myeloma Susceptibility Strains: KaLwRij and CIH

Mackenzie Berschel, Maggie Peng, Hongwei Xu, Michael Tomasson, and Melissa Bates

University of Iowa

Multiple myeloma is a cancer of the plasma cells and is classified as terminal cancer. Two mouse strains that have been identified as susceptible to multiple. KaLwRij is a tumor-prone, spontaneous mutant of the control mouse C57BL/6J and has a high rate of benign idiopathic paraproteinemia (BIP), which is analogous to human MGUS. Similarly, the chronic intermittent hypoxia (CIH) mouse represents the induced malignant plasma cell line through increased oxidative stress and models sleep apnea. We used RNA sequencing data to determine significant genes that may contribute to multiple myeloma susceptibility. Initial RNA sequencing data was analyzed to reveal the differential gene expression of the control mouse (BL6) in contrast to the two susceptible strains, KaLwRij and CIH. We identified significant genes that were under or overexpressed in comparison to BL6. We identified 400 genes of interest for the KaLwRij mouse and 69 genes of interest for the CIH mouse. These genes were chosen based on constraints defined on the respective volcano plots comparing statistical significance versus change in gene expression, or fold change. Genes were significant if they possessed a $\log_2$(fold change) of greater than 1 or less than -1 coupled with p-adjusted values less than 0.05. Genes corresponding to KaLwRij and CIH were assessed for overlap, identifying 31 duplicates. Overlapping genes were further investigated using QIAGEN Ingenuity Pathway Analysis (QIAGEN IPA). The goal of QIAGEN IPA is to visualize and interpret large amounts of biological data within the context of other genes, pathways, and cell functions.

Abstracts

Abstract 40: Graduate or Medical Student

16s metagenomic analysis of THC induced weight loss, a novel therapeutic approach?

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Gut microbiota has been found to play a role in maintaining organism health in numerous biological functions; increasing evidence also implicates gut microbiota involvement in bidirectional signaling with the host nervous system.

Tetrahydrocannabinol (THC) is a chemical compound found in cannabis and known to be the pharmacologically active metabolite that causes psychotropic effects. Little is known about the other effects of THC; currently there is no known connection between THC consumption and weight control.

In male and female C57 mice fed a chronic high fat diet to simulate obesity, mice administered dietary THC (10mg/kg) daily experienced a 20% reduction in weight within 10 days compared to vehicle treated mice. 16S rRNA amplicon analysis of fecal bacteria using the QIIME2 bioinformatics platform identified significant differences in microbiota beta diversity between THC and vehicle treated mice.

Further analysis identified a respective 14 and 18 unique features in male and female THC mice that were absent from vehicle mice. Of which, 2 features were common and phylogenetically mapped back to the *Bacteriodes* genus and Clostridiales order. Additionally, different features from the *Allobaculum* genus were found in THC mice but absent from vehicle mice; other studies have connected *Allobaculum* to weight control.

The weight loss effects and varied beta diversity compared to vehicle mice provide evidence of a connection between the weight response and microbiota changes. Based on these findings, additional trials are to be performed with emphasis on determining if the microbiota changes precede weight loss and thus further support a causative relationship.

Abstracts

Abstract 41: Other

Role of Lipocalin-2 (Lcn2) in the limbic pain processing

Ellesavette Kokkinos, Allison Ash, Dakota Nerland, Gabriel Berenbeim, Benjamin Wilke, Lori Winter, Maximillian Striepe, Lauren Points and Vanja Duric

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Brain mechanisms linking chronic pain conditions and major depressive disorder are still largely unknown. Our recent whole genome microarray profiling has identified lipocalin-2 (Lcn2) as one of the highest upregulated genes in the hippocampus of rats exposed to 21 days of peripheral inflammatory pain. Lcn2 is an iron-related protein with proposed roles in innate immune response and cell differentiation/maturation; however, recent studies further suggest that Lcn2 may also play an important role in emotional behaviors and cognitive function through regulation of neuronal excitability and dendritic spine formation/maturation. However, to our knowledge, Lcn2 has not been previously implicated in the limbic pain processing. Thus, in the current study, we investigated the expression of Lcn2 gene in the affective pain neurocircuitry within specific limbic brain areas. In male rats exposed to the 21-day pain paradigm, robust increases (~ 2-fold) in Lcn2 mRNA levels were observed within the contralateral hippocampus, prefrontal cortex (PFC) and anterior cingulate cortex (ACC). Similar upregulation of the hippocampal Lcn2 gene was also observed in the female animals exposed to the same pain paradigm. Ongoing studies in our lab are further examining the activity of Lcn2 gene in animals exposed to: 1) pain with or without presence of the depressive-like behavioral phenotype, and 2) different types of chronic stress. Overall, the results of this study suggest that chronic pain activates Lcn2 within several different limbic brain regions, which may contribute to the neural mechanisms underlying the development of mood disorders associated with the chronic pain state.

Keywords: pain, depression, gene, hippocampus, prefrontal cortex, limbic, Lcn2

Supported by a PhRMA Foundation Starter Grant (V.D.) and Iowa Osteopathic Education and Research Funds (V.D.)

Abstracts

Abstract 42: Junior Faculty

Increased NMDA Receptor Function during Protracted Withdrawal from Chronic Intermittent Ethanol Exposure.

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Functional dysregulation of the glutamate system during withdrawal from chronic drug exposure is a primary driver of drug craving and relapse. Animal models of psychostimulant use have demonstrated dynamic alterations in both AMPA and NMDA receptor function and expression that contribute to drug seeking behavior. These changes begin as early as 5 days following cessation of drug use are persistently expressed into long term withdrawal (>60d). Evidence of AMPA and NMDA receptor dependent changes during short term withdrawal (24h) suggest that similar mechanisms may drive drug craving and relapse behaviors following chronic exposure to ethanol. To this end, we investigated NMDA receptor mediated synaptic function during protracted withdrawal from chronic intermittent ethanol (CIE) exposure using whole cell patch clamp electrophysiology. We focused on the basolateral amygdala (BLA), as glutamatergic signaling in this region is robustly modulated by short term (24h) withdrawal from CIE (10d, 12hr/day) and regulates anxiety like behavior expressed during withdrawal. Adolescent male rats were exposed to repeated cycles of CIE (12hr/day, 4d on/3d off, 3 cycles) demonstrated increased functional contributions of NMDA receptors in comparison to animals exposed to room air (CON) after >35days of withdrawal. These results mirror increased NMDAR function found during protracted withdrawal from cocaine self-administration suggesting possible common mechanisms underlying aberrant synaptic function during withdrawal from multiple drugs of abuse. Ongoing studies are focused on elucidating the specific contributions of NMDA receptor subunits (GluN2B/GluN3) to the overall functional increases found.

Abstracts

Abstract 43: Graduate or Medical Student

Dysfunction of Renal Glucose Handling Restored by Central Leptin Receptor Blockade in Model of Estrogen Deficiency.

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Hormonal changes accompanying menopause have several effects on women, such as weight gain in the form of adipose tissue. This associates with increased production of the adipocyte-derived hormone, leptin. Leptin plays a primary role in regulation of glucose homeostasis, and indirectly regulates body weight. In an estrogen-deficient adult female rodent model (ovariectomized; OVX), we observed significant weight gain, increase in glomerular filtration rate (GFR), and expression of an early biomarker of kidney injury. The mechanism proposed for increase in GFR and renal damage is lipotoxicity due to intrarenal lipid accumulation associated with increased perirenal adipose tissue.

In this study, we aim to determine the influence of leptin in renal glucose handling in the OVX rodent model. Sodium-glucose cotransporter-2 (SGLT2) is the main mediator of renal glucose handling and is co-expressed in renal proximal tubules (PTs) with Na/H exchanger-3 (NHE3), a key player of salt regulation. Using immunohistochemistry, we measured significant reduction in renal SGLT2 and NHE3 protein expression in OVX animals when compared to controls. The effect on SGLT2 expression was completely reversed by treatment with a leptin receptor antagonist (LAN), delivered for four weeks into the lateral ventricle. NHE3 expression was not affected by LAN treatment.

These findings suggest that leptin may play a role in regulating the activity of SGLT2 in the absence of estrogen. This may shed light in the understanding of leptin's regulation of glucose homeostasis and lead to potential benefits against kidney dysfunction caused by intrarenal lipid accumulation that develops during estrogen deficiency.

Abstracts

Abstract 44: Graduate or Medical Student

Genetic Variants on the Calcineurin Homologous Protein Genes Associated with an Increase in Blood Pressure.

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Hypertension directly affects about one in five adults in United States and approximately 1,300 Americans die from hypertension-related causes every day. Hypertension is known to be highly heritable through genetics; however, the effect of genetic variants in blood pressure regulation is not well established. In a 200,000-individual genome study, we identified five single nucleotide polymorphisms (SNPs) on the calcineurin homologous protein (CHP) genes that were significantly correlated with increased blood pressure. Using computational analysis, we mapped the SNPs location within putative transcription factor binding sites in non-coding regions of CHP genes. CHP is a binding partner of Na^+/H^+ exchanger-3 (NHE3), a key player in renal salt regulation and blood pressure control. Furthermore, the level of CHP protein expression is known to regulate NHE3 activity. We hypothesized that these SNPs affect NHE3 activity through CHP gene regulation, with a downstream effect on blood pressure. We cloned the human CHP promoters and measured activity of each SNP on its respective CHP promoter expressed in human kidney cells using the luciferase reporter system. Major to minor allele replacements of two of five SNPs revealed significant effects on CHP promoter activity. Expression of the other three SNPs did not show significant effect on promoter activity. Ongoing research involves identifying changes in binding of transcription factors to SNP regions of CHP genes dependent on the switch from major to minor alleles. Functional analysis of CHP genetic variants might aid the discovery of novel susceptibility loci responsible for genetic predisposition to the development of hypertension.

Abstracts

Abstract 45: Graduate or Medical Student

The Calcineurin Homologous Protein 2 Induces Acidification of Extracellular pH in Human Osteoblast Cells.

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Extracellular acidosis inhibits osteoblast function by reducing bone mineralization, thereby weakening bone matrix, and may play a role in devolvement of osteosarcoma. Acidification of extracellular pH in cancer is primarily due to dysregulation of pH dynamics mediated by constitutive activation of Na^+/H^+ exchanger-1 (NHE1), the main transporter responsible for pH regulation. Indeed, inhibition of NHE1 activity is emerging as potential target for cancer treatment. Calcineurin homologous protein (CHP) family (isoforms 1 to 3) binds to NHE1 and regulates its activity. CHP1 is expressed in non-cancerous cells, whereas CHP2 is expressed predominantly in cancerous cells. We hypothesize that NHE1 constitutive activation in cancer cells is due to its binding to CHP2 rather than to CHP1. We determined that osteoblast cells, hFOB: **1.** expressed NHE1; NHE activity in hFOB cells was completely blocked by a highly selective NHE1 inhibitor (zoniporide, 10^{-9} M), **2.** expressed primarily CHP1 and only traces amount of CHP2. In differentiated hFOB cells, a decrease in CHP1 and increase in CHP2 expressions were induced by serum removal (serum deprivation for 48 hours) to mimic tumor's metabolic microenvironment. Increase in CHP2 protein expression induced by serum deprivation in differentiated hFOB cells was associated with significant increase in NHE1 activity. These findings align with our previous studies in osteosarcoma and chondrosarcoma cells that expressed only CHP2, where silencing of CHP2 restored NHE1 regulation by serum deprivation. Our results aid the understanding of CHP2 action as NHE1 signaling regulator and its potential as a novel therapeutic target for primary bone cancer treatment.

Abstracts

Abstract 46: Graduate or Medical Student

Hepatocyte-Specific Thromboxane Prostanoid Receptor Deletion Alleviates Alcohol-Associated Liver Disease

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Alcohol-associated liver disease (AALD) is a major health concern with a limited treatment option. Thromboxane prostanoid receptor (TP-R), a G-protein-coupled receptor, is expressed in liver and an alcohol diet increases TP-R mRNA levels in liver cells. However, the role of hepatocyte TP-R in AALD still remains unknown. Here, we used hepatocyte-specific TP-R knockout mice (KO) and wild type littermate control (WT) mice and fed them a Lieber-DeCarli control or ethanol (ET) diet (5%) for 4 wk. Mice were divided into four groups: 1) WT:Cont, 2) WT:ET, 3) KO:Cont, and 4) KO:ET. RNA sequencing of liver samples showed that drug and alcohol metabolism markers (*Cyp2b10, Cyp26b1, Cyp2c55*), pro-inflammatory makers (*Nfkb1, Ccl9, Gpnmb, Lcn2*), and pro-fibrogenic makers (*Col3a1, Col4a2, smad2, smad4*) were decreased in KO:ET mice compared to WT:ET group. Further realtime PCR analyses showed that the mRNA level of *Cyp2b10*, a member of microsomal ethanol oxidation system, increased 17-fold in WT:ET-fed mice ($P<0.0001$) compared to WT:Cont mice. On the other hand, TP-R deficiency suppressed both the mRNA and protein levels of Cyp2b10 upon ethanol feeding ($P<0.001$). The expression of inflammatory markers including *Ccl2* and *IL-6* were increased significantly only in WT:ET mice but not in KO:ET mice compared to controls. Interestingly, the mRNA level of *Lcn2*, which is required for neutrophil infiltration, was significantly increased in WT:ET-fed mice whereas Lcn2 expression was down-regulated in KO:ET group ($P<0.01$). These findings indicate that hepatocyte TP-R plays a role in contributing to AALD and that it may be a novel target for AALD treatment.

Abstracts

Abstract 47: Graduate or Medical Student

Activin A regulates white/brown adipose tissue switch in cancer cachexia mice

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Background: Nearly 50% cancer patients suffer from cachexia, a wasting syndrome with atrophy of white adipose tissue (WAT) and skeletal muscle. Cachexia leads to negative energy balance, limits cancer therapies, and reduces survival rate. It has been reported that WAT switches to brown adipose tissue (BAT) characterized by the high expression of UCP1 (uncoupling protein 1), a browning marker. Thus, inhibition of WAT browning represents a promising approach to ameliorate cachexia in cancer patients.

Hypothesis: We hypothesize that activin A regulates the switch between WAT and BAT during cancer cachexia progression.

Experimental Design: PIK3CA* mouse which showed cachexia symptoms in the progression of cancer was used for DEXA and calorimetry analysis. Both WAT and BAT were harvested from pre-cachectic and cachectic mice. Immunohistochemistry and qPCR were performed. Serum activin A and interleukin-6 (IL-6) were measured. FST288, an activin-binding protein, was *i.p.* injected.

Results: As cachectic symptoms progressed, serum activin A level elevated. Adipocytes in WAT released lipid droplets and decreased diameter, showing the remodeling of adipocytes. BAT changed to WAT-characteristic adipose tissue. Calorimetry analysis did not display an increase in energy expenditure in cachectic mice. Mouse treated with FST288 kept the constant body weight and adipose tissues in the progression of cachexia.

Conclusion: During the progression of cachexia, mice exhibited the alterations with loss of adipose tissues, change of adipocyte diameter and gene expression. Serum activin A levels elevated without a dramatic increase in IL-6. FST288 study support the key role of activin A during cancer cachexia progression.

Funding Resource: KIM NRI COLLAB SEED 3132051012 and Dr. Kim's Startup Package

Abstracts

Abstract 48: Graduate or Medical Student

Dispensability of cABL in oocyte death pathway by Cyclophosphamide

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Background: Current cancer therapies have been improved but still have detrimental damages on ovarian germ cells. It has been issued for prepubertal and premenopausal women because of endocrine dysfunction and infertility with the treatment. Cyclophosphamide (CPA), a widely used chemotherapeutic agent has been known for the toxicity by causing DNA crosslinks in proliferating cells. However, the mechanism of premature ovarian insufficiency (POI) by CPA remains controversial. Recently, it was proposed that TAp63 is phosphorylated by CPA, and c-ABL tyrosine kinase inhibitor prevents it, suggesting that cABL> TAp63 is the key pathway of CPA-induced oocyte death.

Hypothesis: We hypothesize that c-ABL and TAp63 are necessary for oocyte death by the treatment of CPA.

Experimental Design: Oocyte-specific *p63* and *abl1* knockout mouse models were generated and ovaries were cultured with 4-hydroxycyclophosphamide (4-HC). PD7 oocyte-specific *p63* and *abl* knockout mice were *i.p.* injected with CPA. Ovarian tissues were serial sectioned and analyzed.

Results: The quantification of surviving follicles from the ovaries of oocyte-specific *abl1*$^{f/f}$ mice showed that 90% of primordial follicles were lost in both *ex-vivo* and *in-vivo* CPA treatment, keeping most of the growing follicles inside of the ovary. In addition, there was no phosphorylation of TAp63 in the CPA-treated mouse ovary, suggesting that the death of primordial follicles does not involve in the cABL> TAp63 pathway.

Conclusions: CPA induces oocyte death in primordial follicles, suggesting that oocytes from primordial follicles are sensitive to CPA. Besides, c-ABL is dispensable for oocyte death by the treatment of CPA in the mouse ovary.

Funding Resources: Dr. Kim's Startup Package and 1R01HD096042 (Development of Mechanism-Based Ovarian Reserve Protecting Adjuvant Therapies Against Gonadotoxic Therapeutic Agents).

Abstracts

Abstract 49: Junior Faculty

Movement Screens for the Division III Football Student-Athlete

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Introduction: According to the National Collegiate Athletic Association (NCAA), from 2004/05-2008/09, football players' injury rate is 8.1 injuries per 1,000 exposures (games and practices combined). It is believed that if a player has better movement patterns, they will experience less micro- and macro-traumatic injuries. The purpose of this study was to determine if a pre-participation movement screen is a useful tool at predicting injury and length of time missed.

Methods: Forty-three first-year Division III football student-athletes completed a movement screen protocol with the strength & conditioning staff during the start of the fall 2019 season. Three tests were used in the movement screen: overhead squat, single-leg hurdle step, and single-leg vertical jump. The mean height was 68.54 ± 14.24 inches, and the mean weight was 197.88 ± 40.80 pounds. Players progressed through a regular football season with injuries assessed and monitored by the athletic training staff.

Results: The mean movement score was 7.628 ± 1.291 out of 9. A total of 36 injuries occurred, with some participants sustaining multiple injuries. This study found no statistically significant correlation ($p<0.05$) between a football athlete's movement score versus injury rate ($r= -0.057$, p-value= 0.717), movement score versus the total number of injuries ($r= 0.201$, p-value= 0.196), and movement score versus days missed due to injury ($r= -0.010$, p-value= 0.948).

Discussion: This study did not support the use of movement screens to predict injury in first-year football athletes. Future studies should see if one movement screen is better than another at predicting injury rates.

Abstracts

Abstract 51: Graduate or Medical Student

Gene expression profiling of the limbic brain areas during chronic pain

Allison Ash[1], Ellesavette Kokkinos[1], Dakota Nerland[1], Gabriel Berenbeim[1], Benjamin Wilke[1], Maximillian Striepe[1], Lori Winter[1], Lauren Points[1], Matthew Girgenti[2], Ronald Duman[2] and Vanja Duric[1]

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Up to 50% of all clinical chronic pain patients suffer from major depressive disorder (MDD); however, the exact neural events linking these neurological illnesses are still largely unknown. In the current study, we used a genome-wide microarray analysis to examine the genetic profile of the hippocampus from male rats exposed to 21 days of peripheral inflammatory pain. Functional group analysis has identified a number of significantly dysregulated genes with known roles in either neuroinflammation or neurodegenerative processes. Bioinformatic gene network/canonical pathways analyses have identified a significant network associated with the Akt (protein kinase B) as the main hub gene. Altered activity of Akt-related signaling pathways (e.g., PI3K/Akt/mTOR) has been previously linked to both the development of depressive state and antidepressant treatment. Furthermore, expression of several dysregulated genes of interest (i.e., Gzma, Gzmk, Mis18a, S100a9, CCL5, and Lrg1) was also assessed in other limbic areas involved in mood regulation, as well as in the brains of female rats exposed to the same 21-day pain paradigm. Ongoing studies are further investigating the expression of these target genes in pain animals with or without presence of the depressive-like behavioral phenotype (i.e., high vs. low responders). The results of this study further elucidate the presence of transcriptional alterations in the hippocampus during the chronic pain state. Additionally, the dysregulation of genes involved in neuroinflammatory and neurodegenerative processes in the limbic brain areas continues to strengthen the idea that these processes may be involved in the development of mood disorders during the chronic pain state.

Keywords: pain, depression, gene, hippocampus, prefrontal cortex, limbic, Akt

Supported by a PhRMA Foundation Starter Grant (V.D.) and Iowa Osteopathic Education and Research Funds (V.D.)

Abstracts

Abstract 52: Undergraduate Student – *Selected for Oral Presentation*

Effects of Playing Breath-Controlled Instruments on Heart Rate and Mean Arterial Pressure

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We tested the hypothesis that musicians playing breath-controlled instruments would exhibit an increase in heart rate (HR) and mean arterial pressure (MAP) while playing. We also hypothesized that these variables would be higher while playing in a standing versus seated position. Eleven experienced woodwind and brass musicians completed two visits in which they played in either a seated or standing position. The order the subjects completed the visits was randomized. Before playing, supine HR and blood pressure (BP) were recorded. Then, subjects played their own instruments for 30 minutes. HR and BP were recorded every 5 minutes. T-tests were performed to determine the effect of playing position on HR and MAP before and at each time point during playing. One-way ANOVA comparing pre-playing HR or MAP to HR or MAP at each time point were performed for each position. Results presented are means ± standard deviation. There was no difference in HR or MAP between visits for the pre-playing time point. Playing increased MAP and HR at all time points compared to pre-playing in both positions ($p < 0.05$). MAP was higher for standing compared to seated playing at 15 minutes ($p = 0.03$) and 30 minutes ($p = 0.04$) only. HR was higher while standing compared to seated playing at 30 minutes only ($p = 0.03$). Playing breath-controlled instruments increases HR and MAP, regardless of playing position. There may also be a greater MAP and HR while playing in the standing position compared to sitting.

Abstracts

Abstract 53: Graduate or Medical Student

Acute exercise mitigates pro-inflammatory responses in the hippocampus by downregulating the NF-kB pathway in rats

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Exercise has been found to have a positive impact on brain functions such as mood, cognition, stress and anxiety management. However, the neurophysiologic processes behind these findings are unclear. To model exercise effects, rats were provided access to voluntary wheel running chambers and grouped as “high-runners” or “low-runners” based on distance ran during a single 5-hour session following 3 days of training, with a control group of sedentary rats without access to such chambers.

We utilized high throughput screening to profile kinase activity in the hippocampus. The comparison of “high-runners” vs sedentary controls revealed a significant decrease in activity of multiple kinases associated with the NF-kB canonical activation pathway, including IKK, RIPK, COT, and PKD. This change in kinase activity conceivable leads to suppression of NF-kB, a major transcriptional activator of genes responsible for various immune responses. Therefore, we hypothesize that acute exercise causes an anti-inflammatory response in the hippocampus through downregulation of NF-kB.

While inactive, NF-kB is sequestered in the cytosol. Key processes in NF-kB activation include nuclear translocation of the NF-kB subunit p65(RelA) and subsequent phosphorylation of p65 to enhance transcriptional response. We began validation via western blotting and examined expression and phosphorylation of p65 in cytosolic and nuclear fractions.

Preliminary results from hypothalamic tissue show lower levels of total p65 in nuclear fractions of runners versus sedentary rats. We also found smaller ratios of phosphorylated-p65:total p65 in nuclear fractions of runners than sedentary rats. Both results indicate diminished NF-kB activation. Similar results are expected with hippocampal tissue.

Abstracts

Abstract 54: Undergraduate Student – *Selected for Oral Presentation*

Impact of Synthetic Cannabinoids on Cardiovascular Health.

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Cannabinoids encompass natural cannabis and synthetic cannabinoids. While the synthetic cannabinoids interact with the same endogenous system as cannabis, their effects are quite different and poorly understood. In addition to psychological effects triggering their use, these substances are linked to cardiovascular morbidity. We systematically searched PubMed, EBSCOhost, Web of Science, and OVID going back 20 years for data on the cardiovascular impact of synthetic cannabinoids. We also tested the hypothesis that intravenous administration of a synthetic cannabinoid would increase blood pressure in conscious rats.

We found that synthetic cannabinoid use peaked with 7,000 calls to poison control centers in 2011 and has stabilized between 1,000-2,000 calls per year in the US. In humans, cardiovascular effects account for approximately 40% of adverse responses to synthetic cannabinoids. The most frequently reported being tachycardia (50%) and hypertension (20%). To test our hypothesis, Sprague Dawley rats were fitted with chronic indwelling arterial and venous catheters to record blood pressure and heart rate. Conscious rats were given intravenous injections of vehicle (20% cyclodextrin) then incremental doses of the synthetic cannabinoid, WIN 55,212-2 (25, 50, 100 ug/kg + 0.2 ml saline flush). We observed that injection of WIN resulted in rapid onset dose dependent increases in mean blood pressure and heart rate that peaked at approximately 18+/-6 mm Hg and 90+/-15 bpm.

We conclude that synthetic cannabinoids have significant deleterious effects on the cardiovascular system that deserve further study. Supported by University of South Dakota U. Discover and SPURA Summer Research Programs and Basic Biomedical Sciences.

Abstracts

Abstract 55: Junior Faculty

Exercise training protects myocardium against ischemia injury: A role of skeletal muscle Nrf2

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While it has been well-acknowledged that exercise training (ExT) protects myocardium against ischemia injury, the underlying mechanism(s) remain to be elucidated. Here we addressed a hypothesis that skeletal muscle Nrf2 contributes to this benefit effect. Experiment was carried out on muscle-specific Nrf2 deficient mice (MS-Nrf2KO) and GFP reporter mice (MS-mG). Mice received 4 wks of ExT or being sedentary (Sed), followed by a coronary artery ligation surgery. Four weeks later, cardiac hemodynamics and infarct size were analyzed. We found that, compared with WT-Sed, WT-ExT mice displayed a significantly lower left ventricular end-diastolic pressure (LVEDP; 14.8 ± 3.1 *vs* 28.5 ± 4.4 mmHg; $P < 0.01$) and higher left ventricular systolic pressure and dP/dt. These mice also had a smaller infarct size (42.4 ± 7.1 *vs* 81.8 ± 10.6%; $P < 0.01$). However, the ExT-evoked cardioprotective effects were attenuated when skeletal muscle Nrf2 was deleted (LVEDP, 20.8 ± 2.9 in MS-Nrf2KO-ExT *vs* 14.8 ± 3.1 mmHg in WT-ExT; $P < 0.05$; Infarct Size; 61.6 ± 10.6 in MS-Nrf2KO-ExT *vs* 42.4 ± 7.1% in WT-ExT; $P < 0.05$). We further found that, plasma extracellular vesicles (EVs) of WT-ExT mice contained more NQO1 and SOD2 than WT-Sed and MS-Nrf2KO-ExT mice, suggesting that skeletal muscle Nrf2 contributes to the ExT-induced increase in circulating antioxidant EVs. In addition, we demonstrated that ExT promoted skeletal muscle and non-muscle tissues to release EVs with a remarkable effect on muscle. These data suggest that skeletal muscle Nrf2 plays a critical role in ExT-induced cardioprotection *via* circulating EVs-mediated antioxidant defense.

Abstracts

Abstract 56: Graduate or Medical Student

Fibroblasts of the bovine corpus luteum activate downstream inflammatory signaling pathways and JNK/SAPK signaling.

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The corpus luteum (CL) secretes progesterone to establish and maintain pregnancy. If pregnancy does not occur at the end of the estrous cycle, then the CL regresses into a corpus albicans. Previous studies show that mRNA for pro-inflammatory cytokines, such as IL1β and TNFα, are upregulated in cows that were treated with a luteolytic dose of PGF2α. In other tissues, fibroblasts respond to cytokines as well as secrete their own. However, the function of luteal fibroblasts during regression remains unclear. Therefore, knowledge of the responses of luteal fibroblasts to pro-inflammatory cytokines may provide insight about how cytokines contribute to luteal regression. In this study, fibroblasts were isolated from bovine CL by repeated enzymatic digestion with type II collagenase and purified by affinity purification. Fibroblasts were plated and grown until 80% confluent and then treated with IL1β (10 ng/mL) or TNFα (10 ng/mL). Western blot analysis was used to determine IκBα degradation and NFκB (p65) activation. IL1β and TNFα rapidly stimulated NFκB (p65) phosphorylation (S536) and IκBα degradation. Both TNFα and IL1β also enhanced phosphorylation of ERK p42/p44 (T202/Y204), p38 MAPK (T180/Y182), JNK/SAPK (T183/Y185) and AKT (S473). The results from this study demonstrate that in response to treatment with pro-inflammatory cytokines, luteal fibroblasts activate typical pro-survival pathways (AKT and NFκB/p65) and cell stress pathways (p38 and JNK/SAPK). Pro-inflammatory cytokines can attenuate the function and decrease viability of steroidogenic luteal cells; therefore, during regression luteal fibroblasts will remain to remodel the tissue while other cell types will not.

Abstracts

Abstract 57: Graduate or Medical Student

Phenotypic Differences among Mice with induced Cardiomyocyte-restricted Ablation of *Cops5,* Cops8, or both

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Background- The COP9 signalosome (CSN) holocomplex formed by 8 unique subunits (COPS1~COPS8) regulates Cullin-RING ligases (CRLs) via Cullin deneddylation. The deneddylase activity resides in COPS5. CRLs are the largest family of ubiquitin ligases, crucial for ubiquitination. CSN mini-complexes consisting of some of the CSN subunits may have functions independent of deneddylation. Cardiomyocyte-restricted knockout (CKO) of the *Cops8* gene causes cardiomyocyte necroptosis, dilated cardiomyopathy, and shortened lifespan in mice. This study tests whether the protection against necroptosis by Cops8 is deneddylation-dependent or Cops8-specific.

Methods and Results- CKO of *Cops8*, *Cops5,* or both initiated in adult mice were achieved using a tamoxifen-inducible Cre-LoxP system. Echocardiography performed 21 days after tamoxifen withdrawal showed no significant difference between MCM and Cops5-floxed/Cops8-floxed control groups. Compared with either control group, all CKO groups displayed dilated cardiomyopathy, but the severity in the Cops5-CKO and the Cops8+Cops5 double CKO (dCKO) groups were comparably greater than that in the Cops8-CKO group. Kaplan-Meier survival analyses revealed shortened lifespans for all CKO groups, compared with the MCM group. The post-tamoxifen lifespans of Cops5-CKO and dCKO mice were comparable (42 days) but significantly shorter than that of Cops8-CKO (81 days). We observed a greater number of cardiomyocytes positive for Evan's blue dye uptake and greater increases of myocardial CD45 proteins in Cops5-CKO and dCKO mice than in Cops8-CKO mice.

Conclusions: (1) Cops5-CKO and dCKO are similarly detrimental but are more so than Cops8-CKO; (2) the primary defect caused by Cops8-CKO results from impaired CSN holocomplex formation and thereby loss of Cullin deneddylation.

Abstracts

Abstract 58 – Postdoctoral Fellow – *Selected for Oral Presentation*

Glycan signatures as mechanistic markers of beta cell injury in diabetes

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Diabetes is denoted by a relative absence or deficiency in the production and release of insulin by pancreatic β-cells. Type-1 diabetes (T1D) results from an autoimmune-mediated death of β-cells that leads to reduced β-cell mass and diminished function. Type-2 diabetes (T2D) progresses from inadequate mediation of blood glucose from insufficient insulin action. Currently, our understanding of the mechanisms responsible for β-cell loss, dedifferentiation, or inability to mediate increased demand for insulin is incomplete. Questions remain unanswered regarding why β-cells fail to release insulin in some obese patients, while other obese patients retain metabolically healthy β-cells. There is an urgent need to investigate mechanisms of β-cell loss and dysfunction, identify predictive biomarkers capable of detection during the asymptomatic phase of disease for earlier intervention, and identify novel targets for preventing autoimmune destruction of β-cells.

Given the important role of glycosylation in regulating glucose transport and β-cell proliferation, defining glycosylation in human serum and islets from T2D, obese, and normal-weight donors may reveal potential biomarkers and contribute to understanding mechanisms involved in disease progression. Application of a mass spectrometry-based approach for glycan isomer quantification identified >200 *N*-glycan structures from human islets. These data revealed four *N*-glycan structures that were more abundant in T2D donor islets. Glycoproteomic analyses and single cell transcriptional profiling are underway to define the proteoforms and glycosylation enzymes that are dysregulated in disease. Our recently developed bioinformatic tool, GlyCoaster, facilitates the integration of glycoproteomics, and transcriptomics data to reveal novel insights linking dysregulation within the glycosylation pathway to disease.

Abstracts

Abstract 59: Graduate or Medical Student – *Selected for Oral Presentation*

Reproducibility of Laser Doppler Flowmetry and Laser Speckle Contrast Imaging During Whole-Body Cooling

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Laser Doppler Flowmetry (LDF) has been extensively used to measure the cutaneous vasoconstriction response to whole-body cold exposure. Laser speckle contrast imaging (LSCI), which provides greater spatial resolution (i.e., a full-field microvascular measurement), may be a more reproducible method of assessment. However, reproducibility of reflex vasoconstriction using either technique is currently lacking. We hypothesized LSCI will have greater reproducibility than LDF when measuring the skin blood flow response during whole-body cooling. Nine healthy young adults participated in two cooling bouts, each separated by 48 hours to 1 week. Participants donned a whole-body suit and were cooled from a baseline skin temperature (T_{sk}) of 34°C to 30.5°C over a 30-minute period. T_{sk} of 30.5°C was maintained for an additional 10-min prior to rewarming. LDF flux and LSCI flux were measured on the dominant and non-dominant ventral forearm, respectively. Cutaneous vascular conductance (CVC) was calculated as CVC = flux/MAP at each 0.5°C reduction in T_{sk} and expressed as percent change from baseline (%ΔCVC). Reproducibility was assessed using coefficient of variation (CV) for inter-day and intra-day between measurements and visits. The vasoconstriction response reached a plateau of 26±0.9% for LSCI and 32±1.0% for LDF ($p<0.001$). Inter-day analysis displayed similar reproducibility for LSCI (CV=7.0%) to LDF (CV=7.8%) at plateau. Intra-day analysis showed similar reproducibility for visit 1 (CV=10.6%) compared to visit 2 (CV=10.8%). These data indicates good to moderate intra- and inter-day reproducibility, thereby suggesting that LSCI is a reliable alternative for measuring the reflex cutaneous vasoconstriction response.