The Interdisciplinary Biomedical Research Symposium (IBRS) is an annual event hosted by the A.T. Still Research Institute of the A.T. Still University (ATSU) and Sigma Xi. The event gives students, residents, faculty, and regional researchers the opportunity to present their current biomedical research and provides a foundation for promoting collaborative biomedical research with the Institute. The IBRS consists of oral presentations, poster presentations, and a keynote address.

**Table of contents**

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agenda</td>
<td>2</td>
</tr>
<tr>
<td>Short talks</td>
<td>3</td>
</tr>
<tr>
<td>Keynote talk</td>
<td>5</td>
</tr>
<tr>
<td>Poster Presentations</td>
<td>6</td>
</tr>
<tr>
<td>Abstracts</td>
<td>12</td>
</tr>
<tr>
<td>Winners</td>
<td>64</td>
</tr>
<tr>
<td>Acknowledgments</td>
<td>65</td>
</tr>
</tbody>
</table>

Sponsored by: A.T. Still Research Institute, A.T. Still University, Sigma Xi.
**Agenda**

CITC Lobby & Blumenthal Osteopathic Skills Lab
7:00-8:00 a.m. Registration, poster set-up, and complimentary continental breakfast

McCrieght Classroom
8:00-8:10 a.m. Welcome and opening comments: Margaret Wilson, DO, dean Kirksville College of Osteopathic Medicine, A.T. Still University

8:10-10:55 a.m. Short talks: Various speakers

10:55-11:00 a.m. Keynote talk speaker introductions: Craig Phelps, DO, president, A.T. Still University and Brian Degenhardt, DO, director of the A.T. Still Research Institute and assistant vice president of osteopathic research at ATSU, and director of the practice-based research network, DO-Touch.NET

11:00 a.m.-Noon Keynote talk: “Training Clinician Scientists” J. Justin McCormick, PhD; University Distinguished Professor; Dept of Microbiology & Molecular Genetics; Dept of Biochemistry & Molecular Biology; COM, Associate Dean for Research & Graduate Studies

Blumenthal Osteopathic Skills Lab
Noon-12:45 p.m. Lunch break

12:45-2:45 p.m. Poster presentations (odd #s, session 1; even #s, session 2)

2:45-3:00 p.m. Closing remarks and awards
042-G: Infectious diseases
Opposing Roles of Pyruvate Dehydrogenase and Branched-Chain α-Keto Acid Dehydrogenase in Branched-Chain Membrane Fatty Acids in Staphylococcus aureus
Robert P. Ring, BS; Sirisha Sirobhushanam, MS; Saumya Singh; Craig Gatto, PhD; Brian J. Wilkinson, PhD; and Vineet K. Singh PhD

077-G: Exercise science
Cardiac Structure-Function and Aerobic Capacity in a Cross-Section of College Athletes
Ty M. Fullmer, BS; Brent W. Lambson, BS; Nicholas A. Wasinger, BS, MS; Tatyana V. Kondrashova, MD, PhD; and William F. Brechue, PhD, FACSM

057-G: Neuroscience
Blunted respiratory responses in the STZ-induced rat model of Alzheimer’s disease
Dalton L. Ebel, OMSIII; Christopher G. Torkilsen, OMSIII; and Tim D. Ostrowski, PhD

081-G: Health care
Comparison of Ultrasonography Utilization in Rural Versus Urban Emergency Departments Across the State of Missouri
Michael S. Mengarelli, BS, OMSI; Anthony J. Nepusz, BS; and Tatyana Kondrashova, MD, PhD

009-G: Musculoskeletal
The Role of Obesity and Meniscal Instability in the Progression of Osteoarthritis
Taylor L. Ernest, BA; and Peter Kondrashov, PhD

051-U: Neuroscience
The Cognitive Symptomology of Post-Concussion Syndrome: A Pilot Study
Brandall C. Bond, BA; and Janet L. Gooch, PhD, CCC-SLP
062-G: Oral health
Ketones Alleviate Neuroinflammation through Modulation of Metabolic Sensors
Austin J. Shackelford, BA; Hyungil Oh, PhD; Shun-Chieh Ma, BS; and Do-Young Kim, PhD, DVM

043-G: Infectious diseases
Antimicrobial Properties of Tyrosol can be Linked to the Inhibition of Microbial ATP Synthase
Amon Amini, BS; and Zulfiqar Ahmad, PhD

003-U: Musculoskeletal
Modeling Lumbar Vertebral Motion
Mikayla Petesch; Thomas Kekeisen; Steve Webb, BS; Shalini Bhatia, MS; and Brian Degenhardt, DO

058-U: Neuroscience
Investigating Modulators of the Protein kinase R-like ER kinase (PERK) pathway of the ER Stress Response.
Louis O. Darkwa; and Yohei Norimatsu, PhD

036-G: Cancer biology
Heparan Sulfate 3-O-Sulfation Increases Progenitor Cell Expansion
Charles A. Taylor, BS, MS; Vaishali N. Patel; S. A. Smith; and Matthew P. Hoffman, BDS, PhD

037-U: Cancer biology
Investigation of Affinity at Binding Site Between Human Epidermal Growth Factor Receptor 2 (HER2) and Herceptin
Maria Kondrashova, and Bill R. Miller III, PhD
Dr. McCormick serves as the associate dean for research and graduate studies for Michigan State University’s College of Osteopathic Medicine and is the director of the DO-PhD program. He facilitated the establishment of a research institute in the college to study the fundamental mechanisms involved in osteopathic manipulative therapy. Since 1976, he has trained 24 graduate students, 19 postdoctoral research associates, and numerous undergraduate research students. Since the inception of the DO-PhD Physician Scientist Training Program in 1979, he has also assisted 37 candidates complete their DO and PhD degrees, with another 45 still enrolled. Dr. McCormick is also a university distinguished professor in the Department of Microbiology and Molecular Genetics and in the Department of Biochemistry and Molecular Biology and director of the Carcinogenesis Laboratory at Michigan State University.

His research focuses on the nature of the genetic changes involved in the malignant transformation of human fibroblasts, so that strategies can be developed to interrupt this malignant transformation. Using various molecular techniques, Dr. McCormick’s research group has identified 15 genes in human fibroblasts that can play a causal role in malignant transformation.

Dr. McCormick served as a member on numerous committees and study sections for National Institutes of Health (NIH), and a member of the AOA Research Bureau from 1993-2013. He is the author of more than 164 papers in refereed journals, 76 chapters, and more than 444 abstracts. He has been awarded funding research from federal agencies, including the Department of Energy, the National Cancer Institute, the National Institute of Environmental Health Sciences, and the National Institute on Aging. During the past 40 years, more than $18 million in direct federal funding to support cancer research in the Carcinogenesis Laboratory was awarded to Dr. McCormick and Carcinogenesis Laboratory Co-Director, Veronica M. Maher, PhD, MS. This placed them above the 95th percentile for the distribution of (extramural) NIH grants over the last 30 years. Dr. McCormick is also the recipient of the following awards: Michigan State University, Distinguished Faculty Award (1990); The Catholic University of America, Alumni Achievement Award for the Field of Science; and Kenneth P. Dubois Award, for the Midwest Regional Chapter Society of Toxicology (1997).
Musculoskeletal

001-U Quantitative Analysis of the SA201 Concerning Tissue Distinction
Dillon Giles; Jacob Bouchier; Vanessa Pazdernik, MS; and Brian Degenhardt, DO

002-G Accuracy of Landmark Asymmetry Assessment between Male and Female Osteopathic Medical Students
Tajana Kundacina, OMSIII; Shalini Bhatia, MS; Amy Meyer, OMSIII; and Brian Degenhardt, DO

003-U Modeling Lumbar Vertebral Motion
Mikayla Petesch; Thomas Kekeisen; Steve Webb, BS; Shalini Bhatia, MS; and Brian Degenhardt, DO

004-G Assessing Diagnostic Accuracy of Lumbar Vertebra Rotational Preference in Osteopathic Medical Students using Force and Displacement Measurements
Evan Symons, OMSIII; Vanessa Pazdernik, MS; Dalton L. Ebel, OMSIII; Steve Webb, BS; Theodros Zemanuel, OMSIII; Tajana Kundacina, OMSIII; Christa Mckahan, OMSIII; and Brian Degenhardt, DO

005-FS Effect of Postural Sway and Breathing on Postural Measurements Using Surface Topography
Brian Degenhardt, DO; Zane Starks, MS; Shalini Bhatia, MS; and Geof Franklin, MBA

006-G Effects of Lumbar Transverse Process Localization Approaches on Accuracy of Osteopathic Medical Students
Dalton L. Ebel, OMSIII; Shalini Bhatia, MS; Sarah Jane Lewis, OMSIII; Evan Symons, OMSIII; Steve Webb, BS; Christa C. Mckahan, OMSIII, Theodros M. Zemanuel, OMSIII, and Brian Degenhardt, DO
Interstitial Oxygen Kinetics in the Rat Extensor Digitorum Longus and Soleus muscles after IOP Supplementation
Scott A. Cammack, BS; Sarah E. Dobard, BS; and William L. Sexton, PhD

Measurement of Myocardial Microvascular PO$_2$: Impact of Sumatriptan
Sarah E. Dobard, BS; Scott A. Cammack, BS; Spencer M. Batten, MS; Joshua H. Buell, MS; and William L. Sexton, PhD

The Role of Obesity and Meniscal Instability in the Progression of Osteoarthritis
Taylor L. Ernest, BA; and Peter Kondrashov, PhD

Cardiovascular disease

Age-related Lipid Profiles Changes in MCPIP1 Deficient Mice
Chalen Yang, BS; and Yingzi Chang, MD, PhD

Role of MCPIP1 in High Insulin-Related Endothelial Cell Dysfunction
Renee A. Chen, BS; and Yingzi Chang, PhD, MD

Cancer biology

In-Vitro Determination of the Biological Bases for Increased Male Mortality in Melanoma Based on Mouse and Human Melanoma Cell Models
Travis Hohenbery, OMSI; Alexander Miller, OMSII; and Pandurangan Ramaraj, PhD

Preliminary Evaluation of Pancreatic Cancer in SCID Mice Models Treated with Rabbit Umbilical Cord Stem Cells Loaded with Interferon-β
Clayton J. Marolt, BS; and Raja S. Rachakatla, PhD

Fine Epitope Mapping of Monoclonal Antibodies to the RadA DNA Repair Protein
Stephanie N. Nachtrab, BS; Deborah A. Hudman, MS; Jacob L. Hiatt, DO; Neil J. Sargentini, PhD; and Melissa K. Stuart, PhD

Escherichia coli Fis Protein Impact on Radiation Survival, Mutagenesis and DNA Recombination
Muhammed B. Hussain, MS, Deborah A. Hudman, MS; and Neil J. Sargentini, PhD
TGFβ Engages MEK/ERK to Differentially Regulate Benign and Malignant Pancreas Cell Function
Andrew M. Diaz, BA; Daniel R. Principe, MS; Carolina Torres, PhD; Riley J. Mangan, BS; Brian DeCant, BS; Andrew Lowy, MD; Hidayatullah G. Munshi, MD; Barbara Jung, MD; and Paul J. Grippo, PhD

Heparan Sulfate 3-O-Sulfation Increases Progenitor Cell Expansion
Charles A. Taylor, BS, MS; Vaishali N. Patel; S. A. Smith; and Matthew P. Hoffman, BDS, PhD

Investigation of Affinity at Binding Site Between Human Epidermal Growth Factor Receptor 2 (HER2) and Herceptin
Maria Kondrashova, and Bill R. Miller III, PhD

Refining the Path to Personalized Medicine with Psychometric Analysis of Oral Cancer Biomarkers
J. Michael Menke, DC, PhD

Cav-1 Upregulation Slows Migration Velocity in BLM Melanoma
S. Skyler Kinsey, BS; Robert W. Baer, PhD

Infectious diseases

Predictive Modeling of the Number of Active, Off-Host Adult Lone Star Ticks from Long-Term Monitoring Data
Matthew J. Mangan; Nathan B. Wikle, BS; Stephanie A. Foré, PhD; and Hyun-Joo Kim, PhD

Opposing Roles of Pyruvate Dehydrogenase and Branched-Chain α-Keto Acid Dehydrogenase in Branched-Chain Membrane Fatty Acids in Staphylococcus aureus
Robert P. Ring, BS; Sirisha Sirobhushanam, MS; Saumya Singh; Craig Gatto, PhD; Brian J. Wilkinson, PhD; and Vineet K. Singh PhD

Antimicrobial Properties of Tyrosol can be Linked to the Inhibition of Microbial ATP Synthase
Amon Amini, BS; and Zulfiqar Ahmad, PhD

Inhibition of Escherichia coli ATP Synthase and Cell Growth by Safranal and its Analogs
Mason Liu, BS; and Zulfiqar Ahmad, PhD
045-G  Effect of Synergistic Action of Oxidants and Cell Wall Inhibitors on *Staphylococcus aureus* with and without Methionine Sulfoxide Reductases  
Arhum A. Shahab, BS; and Vineet Singh, PhD

046-G  Characterizing the Effects of Carotenoid and Branched Chain Fatty Acid Deficiencies in *Staphylococcus aureus*  
Hannah J. Braungardt, BS; Rachel Chung, BS; and Vineet K. Singh, PhD

**Neuroscience**

051-U  The Cognitive Symptomology of Post-Concussion Syndrome: A Pilot Study  
Brandall C. Bond, BA; and Janet L. Gooch, PhD, CCC-SLP

052-FS  Target-Dependent Retrograde Signaling Mediates Synaptic Plasticity at the Drosophila Neuromuscular Junction  
Brett A. Berke, PhD, and Haig Keshishian, PhD

053-G  Effects of Amentoflavone on the Aggregation and Disaggregation of Amyloid β  
Erika Y. Choi, OMSII; and Byunghee Henry Han, PhD

054-G  Does Ghrelin Effectively Reduce Depressive-like Symptoms in Juvenile Rats?  
Thomas M. Jackson, BA; Erica M. Stanley, BS; Tim D. Ostrowski, PhD; and David S. Middlemas, PhD

055-G  Anti-Muscarinic Drug Effects on Murine Cognition  
Ashley N. Blanchard, BS; Cecil H. Morgan; and Robert J. Theobald, Jr., PhD

056-FS  Using Specific Blockers to Identify TTX-S NaV Channels Subtypes in Rat Muscle Afferent Neurons  
Renuka Ramachandra, PhD; and Keith S. Elmslie, PhD

057-G  Blunted Respiratory Responses in the STZ-Induced Rat model of Alzheimer’s Disease  
Dalton L. Ebel, OMSIII; Christopher G. Torkilsen, OMSIII; and Tim D. Ostrowski, PhD

058-U  Investigating Modulators of the Protein kinase R-like ER kinase (PERK) pathway of the ER Stress Response  
Louis O. Darkwa; and Yohei Norimatsu, PhD
Oral health

061-FS  Output Characterization of Clinically Applied Diode Laser Systems for Management of Chronic Periodontal Disease
Inder Raj S. Makin, MD, PhD; Chandhana Pedapati, MS; Varisha Parikh, BS; Robert Levine, DDS; and Marc Shlossman, DDS, MS

062-G  Ketones Alleviate Neuroinflammation through Modulation of Metabolic Sensors
Austin J. Shackelford, BA; Hyungil Oh, PhD; Shun-Chieh Ma, BS; and Do-Young Kim, PhD, DVM

063-G  Oral Microbiome Analysis using Ion Torrent Next-Gen Sequencing Technology
Molly S. Walkenhorst, BS; Zachary T. Siress, BS; Leticia Reyes, PhD; and Priscilla L. Phillips, PhD

Exercise science

071-U  Relationship of Fat-Free Mass and Fat Mass to Body Weight in College Football Players
Lauren Houk, BS; Olivia Simpson, BS; Abigail Meyer, BS; Mitch Nichols, BS; Taranjit Sohal, BS; Jerry L. Mayhew, PhD; and William F. Brechue, PhD

072-G  Time-Dependency of Fatigue is Independent of Blood Pressure and Heart Rate Variability Response
Kade E. Kinney, BS; and William F. Brechue, PhD

073-U  Comparison of Techniques for Tracking Body Composition Changes Across a Basketball Season
Ashley Ploudre, BS; Jana L. Arabas, MS; Jerry L. Mayhew, PhD, and William F. Brechue, PhD

074-G  Gait Transition Not Related to Kinematic or Metabolic Input in Humans
Dallyn Udall, BS; Brian Vause, BS; and William F. Brechue, PhD

075-FS  Biological Variation and Bilateral Asymmetry of Human Gait
Maggie M. Swift, BS; and William F. Brechue, PhD

Caleb Bischoff; Nathan T. Gorman; Jerry L. Mayhew, PhD; and William F. Brechue, PhD, FACSM
077-G  Cardiac Structure-Function and Aerobic Capacity in a Cross-Section of College Athletes
Ty M. Fullmer, BS; Brent W. Lambson, BS; Nicholas A. Wasinger, BS, MS; Tatyana V. Kondrashova, MD, PhD; and William F. Brechue, PhD, FACSM

078-U  Improvement in Upper-Body Strength is Independent of Initial Fat-Free Mass and Strength Level in College Men and Women
Katelyn Welker, BS; Jana L. Arbas, MS; Jerry L. Mayhew, PhD; and William F. Brechue, PhD, FACSM

079-U  Accuracy of Bench Press Load and Repetitions-to-Failure for Tracking Changes in 1RM Bench Press in College Women
Alicia Hunsaker, BS; Katelyn Welker, BS; Jana L. Arbas, MS; Jerry L. Mayhew, PhD; and William F. Brechue, PhD

Health care

081-G  Comparison of Ultrasonography Utilization in Rural Versus Urban Emergency Departments across the State of Missouri
Anthony J. Nepusz, BS; Michael Mengarelli, BS, OMS1 and Tatyana Kondrashova, MD, PhD

082-G  Quasi-experimental Methods for Real World Data: Regression Discontinuity Design
Lauren Hilmes, BS; Stan Grogg, DO; and Barbara Grogg, NP

083-FS  Respiratory Effects of the Eruption of Momotombo Volcano in Chacraseca, Nicaragua
J. Michael Menke, DC, PhD

Basic science

091-G  Biophysics of the varanid Tympanic Membrane
Dawei Han, BS; and Bruce A. Young, PhD

092-U  Effects of a Cyclophilin 1 Mutation on Drosophila Locomotion
Andrew P. Wohlschlaeger; and Brett A. Berke, PhD
Quantitative Analysis of the SA201 Concerning Tissue Distinction

Dillon Giles¹,², Jacob Bouchier¹,³, Vanessa Pazdernik, MS⁴, Brian Degenhardt, DO¹,⁵

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**Background:** The SA201 is a durometer that generates a standard piezoelectric force once a pre-load is applied. This force is transferred between the device and the tissue to generate a waveform of the viscoelastic hysteresis. Four values correspond to the waveform: fixation, frequency, mobility, and motoricity.

**Methods:** Two aspects of the SA201 were studied: reliability and its ability to distinguish between tissue types. The SA201 was used on 7 standardized test blocks with varying levels of hardness. Two operators each performed 4 trials consisting of 10 pushes for each durometer block at the same temperature within the same hour. Reliability was observed within trials, between trials, and between operators for each block. The SA201 was then used on 9 different tissue landmarks for 20 human participants (ages between 18-70). Two operators performed 10 pushes each on each location and all of the landmarks were compared to each other.

**Results:** Data from the block trials exhibited the strongest correlations between pushes for one operator within one trial (ICC=0.80 for fixation; 0.86 for frequency). The data from the participants suggests significant differences in fixation between muscle, tendon, and bone landmarks (all P<0.0001). The same trend can be observed in frequency values (all P<0.0001). Landmark similarities of fixation and frequency values within tendon and muscle tissue types were significant (all P<0.03). The similarities in mobility and motoricity across landmarks were significant (P<0.001).

**Conclusions:** The SA201 is most precise with one operator in one trial. For participant trials the intraoperator reliability was higher for each landmark than the interoperator reliability. The values that were generated to distinguish between tissue types were fixation and frequency. The data showed that the SA201 was able to distinguish between muscle and bone and tendon and bone, but it was not able to distinguish between the softer tissue.

**Faculty Information:** Brian Degenhardt, DO; bdegenhardt@atsu.edu; 660.626.2304

**Keywords:** SA201; tissue hysteresis; tissue distinction
[002-G] Accuracy of Landmark Asymmetry Assessment between Male and Female Osteopathic Medical Students

Tajana Kundacina OMSIII; Shalini Bhatia MS; Amy Meyer OMSIII; Brian Degenhardt, DO

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Hypothesis: Research suggests visuospatial differences between the sexes, with males having more precise hand-eye coordination and women greater peripheral vision. We hypothesize that this difference may result in women being more accurate when evaluating wider spaced pelvic landmarks.

Methods: First-and second-year osteopathic medical students (OMS I; II) evaluated 5 calibrated pelvic landmark models for positional asymmetry. The anterior superior iliac spine, ischial tuberosity, pubic tubercles, posterior superior iliac spine, and iliac crests were assessed at different asymmetries (2-12 mm).

Data Analysis: A random effect glimmix model was fitted to the data to determine whether accuracy in assessing landmark asymmetry differs between sexes, while accounting for landmark, absolute asymmetry at the landmark, and OMS year.

Results: Data from 417 males and 283 females (8541 female & 12287 male observations) were analyzed. Overall, men showed a 3.73% greater accuracy for the total data points and consistently showed greater accuracy at each of the landmarks. Differences were found incorrectly assessing landmark asymmetry between sexes (P<.001), landmark (P<.001), and absolute asymmetry at the landmark (P=<.001). No difference was found between class years(P=.15).

Conclusion: Results suggested males had higher diagnostic accuracy for all landmarks. This may indicate that the landmarks were not separated far enough to warrant testing of peripheral vision capabilities. However, it does agree with other studies that show males outperforming females in visuospatial processing. Yet it appears that this difference is not significant enough to warrant change in training or use of the tests based on gender.

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Keywords: Pelvic landmark assessment accuracy, diagnostic accuracy male vs. female,
Background: Models simulating the human body allow medical students to practice in controlled conditions to help calibrate and standardize skills. Currently, no teaching model exists to provide feedback on student’s assessment of glides of joints such as vertebral motion.

Methods: Lumbar vertebral motion testing was quantified on 5 humans using force and displacement parameters. A single examiner (BD) applied forces of 10, 20, 30, and 40N to the transverse processes of L2 to L4 and the resultant displacement was recorded. A lumbar model was developed, consisting of two separate rubber tubes connected to a regulator that allows each side to be inflated and metered independently in an attempt to simulate characteristics of deforming tissue. The tubes are covered by a neoprene sheet to simulate skin and subcutaneous tissue. The procedure performed on humans was repeated on each side of the model at different psi levels (4, 8, 12, & 16 psi). A T-test was used to compare the slopes of force and displacement data from all human participants.

Results: Two women and three men participated in the study. Mean age and BMI were 26.6(SD=13.1) and 23(SD=2.7) respectively. Slopes for each participant were not different from the mean 0.47(p=0.8). Tissue deformation was more prominently visible in humans (Slope=0.47) than in the model (Slope=0.21). Psi had no discernible effect on the model’s slope.

Conclusions: The way human tissue responds to graded forces is similar among participants, with some variation likely due to body composition and muscle tone. Currently, the model is not an ideal representation of lumbar vertebral motion due to its small slope and lower variability. Altering the diameter and elasticity of the model’s tubes may improve its representation of human characteristics. Data could be collected on other regions of the body to see if the current model is representative of those regions. Displacement is independent of psi and more testing should be done to determine perceptible psi differences between model sides.

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Keywords: vertebral motion; palpation; model development
MUSKULOSKELETAL

[004-G] Assessing Diagnostic Accuracy of Lumbar Vertebra Rotational Preference in Osteopathic Medical Students using Force and Displacement Measurements

Evan Symons, OMSIII¹, Vanessa Pazdernik, MS², Dalton L. Ebel, OMSIII¹, Steve Webb, BS², Theodros Zemanuel, OMSIII¹, Tajana Kundacina, OMSIII¹, Christa McKahan, OMSIII¹, Brian Degenhardt, DO³

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Kirksville, MO

Introduction: Although palpatory assessment of lumbar vertebral motion is taught at all osteopathic medical schools, no known reports exist of objective measurements that assess the accuracy of an examiner’s diagnosis. We propose that when a rotational preference at a lumbar vertebra exists based on instrumentation values for force and displacement, the examiner’s diagnosis will agree with the objective parameters 70% of the time.

Methods: Over three years, 38 second-year osteopathic medical students each performed passive lumbar diagnosis on 4 of 12 total volunteers. Students assessed lumbar vertebral motion around a vertical axis to obtain a rotational somatic dysfunction diagnosis. Examiners applied anterior pressure with their thumbs on transverse processes of L1 to L5 on prone volunteers, verbalizing the rotational diagnosis of the segment. Force and displacement of the examiner’s thumbs were measured by a force and motion capture system.

Results: The average displacement from the initial position to the last 2 pushes and the average force in the last 2 pushes were calculated for right and left thumbs for each test. The restricted side was objectively determined as the side with less displacement when equal or greater force was applied on that side. Frequencies and cross tabulations were calculated for examiner’s diagnosed restriction and restriction based on objective data. Logistic regression with random examiner effects estimated the probability a student’s diagnosed restriction was supported by objective force and displacement data. Thirty-eight examiners assessed 3 to 20 vertebral levels for a total of 439 collective tests. In 281 (64%) tests, one side exhibited both greater displacement and force with no objective determination of restriction possible. For objective evidence supporting right side restriction (n=96), 47 (49%) were diagnosed as right restriction. For left side restriction (n=62), 39 (63%) were diagnosed as left restriction. The probability a student’s diagnosed restriction was supported by objective data was 0.20 (95% confidence interval, 0.15–0.24).

Conclusions: Results indicate a need for improving diagnostic skills to achieve an accurate rotational somatic dysfunction diagnosis of vertebra. Future studies should evaluate methods to improve palpatory techniques for diagnosis of lumbar vertebral motion preference.

Faculty Information: Brian Degenhardt, DO; bdegenhardt@atsu.edu; 660.626.2304

Keywords: lumbar vertebral motion; palpation assessment; lumbar rotational preference
[005-FS] Effect of Postural Sway and Breathing on Postural Measurements using Surface Topography

Brian Degenhardt, DO¹, Zane Starks, MS¹, Shalini Bhatia, MS², Geof Franklin, MBA¹

¹A.T. Still Research Institute, A.T. Still University, Kirksville, MO
²Research Support, A.T. Still University, Kirksville, MO

Background: A surface topography (ST) instrument (DIERS formetric, DIERS Medical Systems, Chicago, IL) uses rasterstereography to produce, measure, and correlate a 3-dimensional model of the posterior trunk, with underlying spinal curve deformities. The manufacturer reports that data from one average image from a six-second scan evaluating 40 spine shape parameters is an appropriate method of removing measurement error due to postural sway. The purpose of this study was to evaluate the stability of 40 spine shape parameters on an immobile object and evaluate how the addition of postural sway and breathing influences the meaning of these results.

Methods: Using the ST instrument, 30 human volunteers were scanned (0.5 hz) while standing quietly 30 times over a period of five days. As a control, a mannequin was scanned 42 times over seven days. Values for 40 spine shape parameters were exported. Mean and variance components were calculated by building individual nested random effects glimmix models. Within scan variance components were tested for significant variability.

Results: A total of 900 scans were completed on 15 male (age 31.9 ± 11.5 years, BMI 27.5 ± 4.1) and 15 female (age 28.6 ± 7.3 years, BMI 27.1 ± 4.8) volunteers. On the mannequin, within scan variance was nearly zero for all but two of the forty spine shape parameters (Max=1.6, Min=0.0). In humans, significant within scan variance was observed for all 40 spine shape parameters (Max=36.04, Min=0.06, P<.001).

Conclusions: The current study suggests that postural sway and breathing cause variability in the spine shape parameters reported by the ST instrument. The minimal variability observed in the mannequin was evidence of the ST instrument’s high within scan stability. With the introduction of postural sway and breathing in humans, significant within scan variance was observed. Because within scan variability is not reported with the result, the clinical usefulness alone is limited. An estimate of variance provides additional information to determine a normal range of spine shape parameters, so it can become apparent when a clinically relevant change has occurred.

Faculty Information: Brian Degenhardt, DO; bdegenhardt@atsu.edu; 660.626.2304

Keywords: formetric; rasterstereography; postural sway; posture; surface topography
Introduction: To increase the likelihood of successful osteopathic manipulative treatment, physicians need to accurately diagnose positional and motion characteristics of the spine. Somatic dysfunction diagnosis is highly dependent on accurate localization of the transverse processes. We propose that examiners who use a stepwise localization technique will exhibit improved accuracy of lumbar landmark palpation.

Methods: Location of lumbar vertebral transverse processes (TPs) and spinous processes (SPs) were determined using ultrasound to establish a gold standard. Reflective markers were placed on the skin overlying both processes and their relative location was quantified using a motion capture system. Blinded from the ultrasound findings, 16 osteopathic medical students performed two methods of localizing spinal landmarks. The first approach was a stepwise localization technique where the SP was localized first followed by the associated TPs at each vertebral level. For the second approach, students had reflective markers on their thumbs, and localization was performed using their natural diagnostic approach.

Results: Statistical Analysis: Euclidean distance in the XY plane between the gold standard for L1-L5 and examiners' objective localizations of L1-L5 was calculated for both methods. Descriptive statistics were calculated for these distances, and a random effect glimmix model was fit to the data to compare the localization distance for stepwise and naturally performed techniques while accounting for landmark and side (left vs right). A significant difference was found in the Euclidean distance between the two diagnostic approaches (P=.02) and between lumbar levels (P<.001). The stepwise localization technique localized landmarks better than the natural technique. Mean Euclidean distance between the stepwise localization technique and naturally performed localization was 21.3 vs 28.1 for L1, 19.5 vs 23.1 for L2, 18.1 vs 23.1 for L3, 18.1 vs 19.6 for L4, and 16.2 vs 21.4 for L5.

Conclusions: The significant difference between stepwise localization and naturally performed localization suggested that the stepwise localization approach of identifying an easier landmark (SP) first and then using that reference point to identify the deeper landmark (TP) increased accuracy of TP localization. Therefore, medical educators should focus localization training on an accurate stepwise method to obtain the most reliable diagnosis.

Keywords: localization, transverse process, spinous process, ultrasound, distance.

Faculty Information: Brian Degenhardt, DO; bdegenhardt@atsu.edu, 660.626.2304
Interstitial Oxygen Kinetics in the Rat Extensor Digitorum Longus and Soleus muscles after IOP Supplementation

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**Background:** Skeletal muscle produces reactive oxygen species (ROS) during muscle contractions. ROS decrease calcium sensitivity and depress force in contracting muscle. The polysaccharide extract of the mushroom *Inonotus obliquus* (IOP) has been proposed to have antioxidant properties and to delay the onset of fatigue. Contractile function in skeletal muscle is dependent on the balance between oxygen delivery (QO$_2$) and oxygen consumption (VO$_2$) and is reflected by the interstitial partial pressure of oxygen (PO$_2$i) within the muscle. The purpose of this study was to examine the effects of IOP supplementation in rats on; 1) the time to exhaustion during treadmill running, and 2) PO$_2$i kinetics in rat hindlimb skeletal muscles.

**Methods:** All rats (n=10) were acclimated to the treadmill and then randomly divided into two groups; control (C, n=5) and IOP supplementation (IOP, n=5). IOP was dissolved in the drinking water at 300 mg/kg/day. On day 14 all rats were placed on the treadmill at a 20% incline and the speed was increased 5 ft/min each minute until the rats could no longer continue. This was recorded as the time to exhaustion. On day 16 a second treadmill test was performed wherein speed was held constant at 70 ft/min (20% incline) and the rats ran until they could no longer maintain this speed. Starting on day 18 of supplementation the rats were anesthetized with pentobarbital sodium (50 mg/kg ip) and the soleus and extensor digitorum longus (EDL) muscles of the rats were surgically isolated. The muscles were electrically stimulated to study PO$_2$i kinetics using phosphorescence quenching at both a low intensity (1 Hz, 2 ms) and then at a higher intensity (2 Hz, 20 ms).

**Results:** The time to exhaustion during the first treadmill test was not different between groups (15:28 ± 1:11 vs. 15:26 ± 1:10 m). Treadmill running times during the second test were also not different (7:44 ± 0.06 vs. 7:45 ± 0.04 m). During isolated muscle contractions, the initial PO$_2$i and kinetics at the onset of contractions were not different between C and IOP in either the soleus or EDL muscles.

**Conclusions:** These preliminary data for IOP supplementation in rats are not consistent with the notion that IOP increases time to exhaustion (i.e., endurance) or results in changes in QO$_2$ relative to VO$_2$ during contractions. This study will be repeated with a larger sample size and will include muscle tension analysis to examine the potential effects of IOP supplementation in more detail.

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**Keywords:** oxygen kinetics; chaga mushroom; *Inonotus obliquus* polysaccharide
Measurement of Myocardial Microvascular \( \text{PO}_2 \): Impact of Sumatriptan

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**Background:** Triptan drugs (e.g., sumatriptan) are 5-HT\(_{1B/1D}\) receptor agonists that are prescribed for treatment of migraine. It has been suggested that triptans may increase the risk of adverse cardiac events. The purpose of this study was to assess the impact of sumatriptan on the microvascular partial pressure of oxygen (\( \text{PO}_{2\text{mv}} \)) in a novel beating heart preparation. \( \text{PO}_{2\text{mv}} \) reflects the real-time balance between oxygen delivery (\( \text{QO}_2 \)) and oxygen consumption (\( \text{VO}_2 \)) at the tissue level. We predicted that sumatriptan would impair coronary vasodilation as reflected by a greater fall in \( \text{PO}_{2\text{mv}} \) compared to control.

**Methods:** Female Sprague-Dawley rats (n=22, 262 ± 4 g) were anesthetized with pentobarbital sodium (50 mg/kg ip). A tracheal cannula was inserted and the carotid artery and jugular vein were cannulated. A left lateral thoracotomy exposed the heart and ventilation was initiated (4-6 ml at 60 bpm; arterial \( \text{PO}_2 \) was 74 ± 2 mmHg, \( \text{PCO}_2 \) was 43 ± 2, and pH 7.32 ± 0.01. \( \text{PO}_{2\text{mv}} \) was measured using the phosphorescence quenching method. The fiber optic probe of the phosphorometer was positioned over the left ventricular free wall to measure left ventricular \( \text{PO}_{2\text{mv}} \) during steady-state conditions and after the following interventions; 1) bolus infusion of sumatriptan (1 mg, n=7), 2) infusion of dobutamine - a positive inotropic drug (9 and 18 µg/min, n=5), 3) infusion of sumatriptan (37.5 and 75 µg/min, n=5), and 4) simultaneous infusion of both dobutamine and sumatriptan (n=5).

**Results:** Left ventricular \( \text{PO}_{2\text{mv}} \) averaged 75 ± 2 mmHg and mean arterial pressure (MAP) averaged 93 ± 5 mmHg. With bolus infusion of sumatriptan \( \text{PO}_{2\text{mv}} \) fell 5 ± 1 mmHg and MAP fell 25 ± 4 mmHg whereas infusion of an equivalent volume of saline vehicle had no effect. Dobutamine infusion caused \( \text{PO}_{2\text{mv}} \) to fall 25 + 3 mmHg and MAP to fall 39 ± 8 mmHg. Sumatriptan infusion did not impact \( \text{PO}_{2\text{mv}} \) (0 ± 1 mmHg) or MAP (2 ± 2 mmHg). Simultaneous infusion of dobutamine and sumatriptan caused \( \text{PO}_{2\text{mv}} \) to fall 19 ± 1 mmHg and MAP to fall 14 ± 5 mmHg. As a positive control, isoproterenol was infused (10 µg) at the end of each experiment to ensure responsiveness of the system.

**Conclusion:** The bolus infusion of sumatriptan caused left ventricular \( \text{PO}_{2\text{mv}} \) to fall suggesting a decrease in \( \text{QO}_2 \) due to vasoconstriction. In contrast, infusion of a low dose of sumatriptan did not impact \( \text{PO}_{2\text{mv}} \). These findings do not support the notion that sumatriptan may elicit a profound vasoconstriction that would compromise cardiac function.

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**Keywords:** oxygen delivery, oxygen consumption, oxygen partial pressure, myocardium
[009-G] The Role of Obesity and Meniscal Instability in the Progression of Osteoarthritis

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Background: Osteoarthritis (OA) is the most common joint disorder and is characterized by the progressive degeneration of articular cartilage, bone remodeling, and chondrocyte apoptosis. The menisci are vital for the normal function and long-term health of the knee joint. The focus of this study is to determine whether obesity and meniscal destabilization will cause changes in the histology of the knee menisci and cause articular cartilage damage indicative of knee OA.

Methods: Female Lewis rats (n=42) were randomly assigned to 4 groups: Group 1 received a sham surgery and had a regular diet; Group 2 received a medial meniscus destabilization (DMM) surgery and was on a regular diet; Group 3 received a sham surgery and was on a high-fat diet; and Group 4 received a DMM surgery and was on a high-fat diet. Surgical intervention occurred 4 weeks after the diet was started by transecting the medial meniscotibial ligament. During sham surgery (control) the knee capsule was opened but no ligament was cut. Rats were sacrificed and their surgical limb was harvested 4 weeks post-surgery. The progression of osteoarthritis was evaluated histologically in the four knee surfaces (lateral and medial femoral condyles and lateral and medial tibial plateaus) using the Osteoarthritis Research Society International (OARSI) scoring system by two blinded scorers. Linear mixed models were used to test effects of diet within sham and DMM groups for the four surfaces and overall score.

Results: Data from 42 rats, 9-12 per group showed a significant difference in OARSI scores between the two sham groups. The high fat diet group had higher OARSI scores than the normal diet group by 0.74 points (SE .28) in total score (both P<.02). The medial femoral condyle and lateral tibial plateau exhibited a significant diet effect and the lateral femoral condyle exhibited a marginally significant effect. DMM surgery showed significantly greater score ratings in both the lateral and medial compartments of the knee in both groups (P=.004). Although not statistically significant, the medial tibial plateau and medial femoral condyle of the high-fat diet DMM surgery group had an overall score that was 2 points higher than the regular diet DMM surgery group.

Conclusions: These results suggest that diet may play an important role in the spontaneous onset of osteoarthritis. The results of this study emphasize the importance of preventative care in patients who are at risk of developing osteoarthritis.

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Keywords: osteoarthritis; meniscal destabilization; obesity
Objective Investigation of Vertebral Palpation Diagnoses

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Background: Evaluating movement characteristics of vertebrae is a basic component of diagnostic palpation in osteopathic manipulative medicine. Little is known about the objective characteristics of this testing. In this study, quantitative data of vertebral motion was compared with the diagnoses of a single examiner to determine what objective characteristics of lumbar vertebrae motion relate most strongly to the examiner’s diagnoses.

Methods: On five prone volunteers (mean [SD] age 30 [10], mean [SD] BMI 23 [2]), an osteopathic physician (BD) localized the tissues overlying the transverse processes of the L2-L4 lumbar vertebrae and performed standard testing for motion within the horizontal plane. A diagnosis of right restricted, left restricted, or neutral was made for each level. A 3-dimensional printed, model thumb apparatus was created and used to apply forces of varying strengths as performed by the examiner. Forces of 10 N, 20 N, 30 N, and 40 N were applied in an alternating fashion to the right and left transverse processes. Participants were asked to relax while holding their breath during data collection. The desired force was applied for 10 seconds and measured at 100 Hz using Novel Pliance pressure pads placed between the thumb and skin. The height of a Vikon Nexus marker affixed to the model thumb apparatus was measured before and at the 10th second of force application. Data were compared for final height of the marker and displacement. If one side had a greater final height than the other, it was considered restricted in height. If one side had a lower displacement, it was considered restricted in displacement. Data and diagnoses were only compared when asymmetries were detected by the examiner.

Results: Eleven of 15 vertebral levels were diagnosed as restricted. Of these vertebral levels, 86.4% were supported by final height data, while 65.9% of non-neutral diagnoses were supported by displacement data. Data for vertebrae with neutral diagnoses did not, on average, show a smaller difference between right and left final height or displacement.

Conclusions: Examiner diagnoses seemed to support at least one measurable physical characteristic. This finding suggests lack of interexaminer reliability in previous studies may have been the result of changes in the vertebrae from prior palpation or from examiners detecting different physical characteristics when making their diagnoses.

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Keywords: vertebral motion; lumbar vertebrae; vertebral palpation
CARDIOVASCULAR DISEASE

[021-G] Age-related Lipid Profiles Changes in MCPIP1 Deficient Mice

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Background: Chronic inflammation is associated with metabolic disorders, such as impaired lipid homeostasis, which can lead to atherosclerotic plaque formation and ultimately myocardial infarction or stroke. Monocyte chemotactic protein-induced protein-1 (MCPIP1) is a negative regulator in inflammatory processes. Previous studies have shown that mice without the MCPIP1 gene display phenotypic changes such as splenomegaly, lymphadenopathy, growth retardation, decrease adipose deposit, and increased pro-inflammatory cytokines. Our current project is to investigate the age-related lipid profile changes in MCPIP1 deficient mice.

Method: Plasma and liver tissues are collected from wild-type (WT) and MCPIP1 knockout (KO) C57/BL6 mice at ages 2, 4, and 6 weeks. HDL and LDL-VLDL are separated by LDL-VLDL precipitation buffer that is supplied by Sigma-Aldrich Quantitative Kit. Plasma and liver triglycerides are prepared by using Cayman Chemical Triglyceride Assay Kit. All samples are quantified by Biotek-Epoch spectrophotometer, measuring the ocular density at 570 nm.

Results: The data collected from eight samples of each age group showed MCPIP1 deficient mice having a decrease HDL level of 12.5% at 2 weeks, 25.8% at 4 weeks, and 24.5% at 6 weeks when compared to control group. The knockout mice showed an increasing trend of LDL-VLDL level of 75.8% at 2 weeks, 76.8% at 4 weeks, and 62.5% at 6 weeks. At four weeks, KO mice had increased plasma triglyceride of 75.5% and increased liver triglyceride of 36.4%.

Conclusions: From the data collected thus far, there is a trend of decreased HDL and increased LDL-VLDL levels in MCPIP1 deficient mice as they age from 2, 4, and 6 weeks. Plasma and liver triglycerides in knockouts also increased with age. These trends suggest that MCPIP1 is important in regulating lipid homeostasis and can potentially be involved in preventing hyperlipidemia and other lipid imbalances that could potentially lead to vascular complications.

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Keywords: MCPIP1, MCPIP-1, age-related lipid changes, lipid homeostasis
Background: Vascular complications are one of the major adverse outcomes for diabetic individuals. Elevated inflammatory cytokines are thought to contribute to impaired vascular function. MCP-1-induced protein 1 (MCPIP1) is a negative regulator in inflammatory response. Previous research has shown that the proinflammatory cytokine MCP-1 induces endothelial cell migration and proliferation that is mediated by the induction of MCPIP1. The goal of this project is to better understand the role of MCPIP1 in hyperinsulinemia-associated endothelial dysfunction.

Methods: We will conduct western blot analysis to determine the effects of hyperinsulinemia on MCP-1 and TNF-α-induced MCPIP1 expression in human umbilical vein endothelial cells (HUVEC). A scratch migration assay and BrdU cell proliferation assay will also be conducted to determine whether or not a hyperinsulinemic state can suppress MCP-1/TNF-α induced cell migration and proliferation.

Results: Our preliminary data show that pre-treatment of vascular smooth muscle cells suppresses MCPIP1 expression, suggesting that downregulation of MCPIP1 in diabetic patients may contribute to the development of endothelial dysfunction and subsequent vascular complications. Western blots analysis of dose-response curves and time-course studies on human umbilical vein endothelial cells (HUVEC) have confirmed that MCPIP1 is inducible with the pro-inflammatory cytokines, MCP-1 and TNF-α.

Conclusions: We hypothesize that high levels of insulin will suppress MCP-1/TNF-α-induced MCPIP1 expression and inhibit MCP-1/TNF-α-induced MCPIP1 cell migration and proliferation.

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Keywords: MCPIP1, endothelial dysfunction, hyperinsulinemia, inflammation
Introduction: Melanoma is a fatal form of skin cancer. Epidemiological SEER data showed a higher mortality rate in males than in females. Clinical studies showed that menstruating females were better protected in melanoma than post-menopausal women and men of any age, suggesting the involvement of sex steroid hormones in the protection. But clinical studies did not show any direct effect of sex steroids on melanoma. Our previous studies with progesterone, a female sex hormone showed a direct effect of significant inhibition of mouse and human melanoma cell growth. Aim: This observation raised the question, whether androgens were responsible for increased male mortality in melanoma?

Methods: Dose curve studies of androgens (androstenedione and testosterone) showed a dose-dependent inhibition of mouse melanoma cells, suggesting androgens also inhibited melanoma cells and might not be responsible for increased male mortality in melanoma. Since, inhibition of mouse melanoma cell growth by progesterone was already shown, co-incubation of androgens with progesterone was carried out. Addition of progesterone as low as 10 µM to androgens showed an additive effect on mouse melanoma cell growth inhibition. This result suggested that lack or deficiency of progesterone in males could be responsible for increased male mortality. Literature survey showed that progesterone level was very low in males and its level was drastically low in post-menopausal women, the two groups which lacked protection in melanoma according to the clinical studies. In-vitro experiments along with literature survey and clinical studies suggested that progesterone could be involved in the protection.

Results: So the study was extended to human melanoma (BLM) cells. Androgens showed inhibition of human melanoma cell growth also, but at higher concentrations (100 and 200 µM). Addition of 10 µM concentration of progesterone to androgens showed an additive effect on human melanoma cell growth inhibition, indicating a protective function of progesterone. In order to further investigate the protective functions of progesterone, in-vitro adhesion and migration assays were carried out after co-incubation of melanoma cells with androgens and progesterone. Protective effects were shown by the significant decrease in adhesion and migration (essential for metastasis) functions of co-incubated cells compared to various control cells. Biochemical basis of this protective function of progesterone was checked by carrying out an ELISA array, which showed a specific suppression of IL-8 cytokine secretion.

Conclusions: Lack of protective biological functions (such as decreased melanoma cell growth, adhesion and migration) due to deficiency of progesterone in males could be the biological bases for increased mortality in males in melanoma.

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Keywords: androgens, progesterone, protective biological functions, mortality rate in males
Preliminary Evaluation of Pancreatic Cancer in SCID Mice Models Treated with Rabbit Umbilical Cord Stem Cells Loaded with Interferon-β

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Background: Pancreatic cancer is one of the deadliest and most aggressive forms of cancer, with a five-year survival rate after diagnosis of 6.7%. There are numerous treatments available, but none are able to effectively target the cancer cells directly without harming nearby healthy cells, causing unwanted side effects to the patient.

Methods: The objective of this study is to determine how effective rabbit umbilical cord stem cells (rUCSC) are at targeting Pan02 pancreatic cancer cells and delivering interferon-β (IFN-β) to kill the cancer cells in vitro and in vivo. We investigated the trophic ability of rUCSC towards Pan02 cells.

Results: This study showed that as Pan02 cell concentration increased, the amount of stem cell migration increased as well. We then investigated the anti-cancer ability of rUCSC-IFN-β on Pan02 cells as compared to regular rUCSC. Pan02 cells both alive and dead were counted. This study showed that wells with rUCSC-IFN-β had higher amounts of dead Pan02 cells compared to the control wells with rUCSCs.

Conclusions: We are currently investigating the trophic effects of rUCSC-IFN-β on SCID mice tumor models by examining tumor size, and the localization of injected stem cells by examining various tissues.

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Keywords: pancreatic cancer; stem cells; drug delivery; interferon-beta
Background: Repair of DNA damage is vital to the health and survival of all organisms. In *Escherichia coli*, the RadA protein participates in recombinational repair, a process that uses an undamaged DNA strand as a template to repair damaged DNA. In a prior report, we described the production of monoclonal antibodies (Mabs) specific for the RadA protein. Here, we identify the epitopes on the RadA protein that are recognized by two of the antibodies, Mabs 2A2 and 6F5. Such knowledge may prove useful in future investigations of RadA protein function.

Methods: Structural changes in the RadA protein were introduced by: 1) protein truncation achieved by introducing ochre mutations into the *radA* gene, 2) alanine scanning mutagenesis, and 3) partial digestion of the RadA protein with staphylococcal V8 protease. The effects of the structural changes on recognition of the RadA protein by Mabs 2A2 and 6F5 were evaluated by SDS-PAGE and western blotting. Additionally, overlapping synthetic peptides comprising RadA sequences at positions 245-276 were evaluated by competitive ELISA to determine whether each peptide could block antibody recognition of full-length RadA protein immobilized on an ELISA plate. Peptides with the ability to significantly lower antibody binding to the immobilized antigen, compared to the PBS competitor control, were deemed blocking peptides.

Results: Truncation experiments showed that Mab 2A2 binds to RadA protein truncated at position 279, but not at position 258. Mab 6F5 recognized full-length RadA protein (460 amino acids long), but failed to recognize any of the truncated proteins produced by ochre mutants, including a protein truncated at position 457. Among alanine substitutions made between positions 258 and 279, only substitution N265A destroyed RadA recognition by Mab 2A2. Two substitutions at the extreme C-terminus of the RadA protein, I444A and D452A, completely destroyed RadA recognition by Mab 6F5, while the additional substitutions L450A, S455A, D458A, and L460A had significant but less severe effects. Partial V8 protease digestion of RadA generated a 20-kD fragment that was recognized by Mab 6F5 but not by Mab 2A2. Edman degradation of the fragment yielded the N-terminal sequence LGVFAMTE, corresponding to amino acids 267-274 of the RadA protein. In the competitive ELISA, a synthetic peptide with the sequence AVNELGVFAMT spanning residues 263-273 of the RadA protein blocked the binding of Mab 2A2 to immobilized RadA by 97.2%.

Conclusions: We infer from our results that Mab 2A2 is specific for an epitope located between positions 263 and 273 of the RadA protein, and that residue N265 is integral to the Mab 2A2 binding site. MAb 6F5 binds to the extreme C-terminus of the RadA protein, just downstream of a region that shows homology to the Lon protease.

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Keywords: RadA; DNA repair; *Escherichia coli*; monoclonal antibodies; epitope mapping
[034-FS] *Escherichia coli* Fis Protein Impact on Radiation Survival, Mutagenesis and DNA Recombination

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**Background:** The factor for inversion stimulation (*fis*) gene produces a nucleoid-associated protein (Fis) involved in growth regulation in *Escherichia coli*. Previous work suggested *fis*-associated radiation sensitivity so we investigated this finding in more depth and probed the role of Fis in DNA repair after UV- or X-irradiation, DNA recombination, and in spontaneous and UV-radiation mutagenesis.

**Methods:** The delta*fis779::kan* mutation was introduced into *E. coli* K-12 AB1157 and related DNA repair-deficient strains (*uvrA, recA, recB, recC, recF, polA5*). Cells were grown in LB or LBG broth at 37°C with aeration to log or stationary phase. Cell survival studies relied on plating assays after cells were treated with UV- (254 nm) or X- (160 kV) radiation. DNA recombination studies relied on an Hfr-dependent conjugation assay. Mutagenesis studies relied on an *argE3* (base-substitution) reversion assay. Statistical analysis was performed by interpreting radiation doses yielding 1% cell survival from triplicate, multi-dose, survival curves and t test was used to determine if differences were significant at $P \leq 0.05$.

**Results:** Wild-type cells, at 1% cell survival, were sensitized by the *fis* mutation by 8 to 25-fold, if grown to log- or stationary-phase, respectively. To probe the *fis*-effect on specific DNA repair pathways, we compared the cell survival of stationary-phase cells after UV-irradiation. The *fis* mutation sensitized *uvrA* cells 7-fold ($P<0.001$). The *recF* strain was sensitized only 2-fold ($P=0.019$). However, *fis* did not sensitize the other *rec* strains tested, in fact *fis* protected the *recB* ($P=0.007$) and *recC* ($P=0.015$) strains about 2-fold. The *recA* strain was not protected ($P=0.069$). After X-irradiation, *fis*-sensitization was much greater, i.e., 125-fold and the *fis* mutation sensitized *polA5* cells 7.5-fold ($P=0.018$). In associated studies, the *fis* mutant was 48% deficient in His+ DNA recombination ability ($P=0.010$) and 32% deficient in Leu+ recombination ability ($P=0.045$), normal for spontaneous mutagenesis, and more susceptible to UV-radiation mutagenesis (at 45J/m$^2$; $P=0.005$).

**Conclusions:** Fis plays a greater role in the survival of X-irradiated vs. UV-irradiated cells, and its role in DNA repair most likely impacts recombinational repair (especially for DNA double-strand breaks) rather than nucleotide excision repair.

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**Keywords:** *E. coli*, Fis nucleoid-associated protein, radiation survival
[035-G] TGFβ Engages MEK/ERK to Differentially Regulate Benign and Malignant Pancreas Cell Function

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Background: While TGFβ signals are anti-proliferative in benign and well-differentiated pancreatic cells, TGFβ appears to promote the progression of advanced cancers.

Methods: To better understand dysregulation of the TGFβ pathway, we generated mouse models of neoplastic disease with TGFβ receptor deficiencies. These models were deficient in pERK, irrespective of KRAS mutation. Furthermore, TGFβ lead to rapid and sustained TGFBR1-dependent ERK phosphorylation in cultured pancreas ductal cells. Pharmacological inhibition of ERK phosphorylation mitigated TGFβ-induced upregulation of growth suppressive targets pSMAD2 and p21, prevented the downregulation of the pro-growth signal CDK2, and ablated TGFβ-induced EMT.

Results: These observations suggest that ERK is a key factor in growth suppressive TGFβ signals, yet may also contribute to pathological TGFβ signaling. However, in neoplastic cells, pERK was not necessary for either TGFβ-induced pSMAD2 phosphorylation or CDK2/Cyclin E repression. Yet, pERK was still required for the upregulation of p21 and EMT in these cells, suggesting a partial divergence between TGFβ and MEK/ERK in early carcinogenesis.

Conclusions: In advanced cancer cells, pERK had no effect on TGFβ-induced upregulation of pSMAD2 and p21, suggesting the two pathways have completely diverged with respect to the cell cycle. Furthermore, inhibition of pERK lead to reduced levels of CDK2 irrespective of exogenous TGFβ and prevented TGFβ-induced EMT, consistent with the majority of observations identifying pERK as a tumor promoter. Combined these data suggest that during carcinogenesis, pERK initially facilitates and later antagonizes TGFβ-mediated cell cycle arrest, yet remains critical for the pathological, EMT-inducing arm of TGFβ signaling.

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Keywords: KRAS; TGFβ; ERK/MAPK; pancreatic cancer
[036-G] Heparan Sulfate 3-O-Sulfation Increases Progenitor Cell Expansion

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Background: Stem/progenitor cell therapy has been proposed to repair the permanent radiation damage to salivary glands that occurs during therapy for head and neck cancer. A biopsy would be used to expand the resident stem/progenitor cells in vitro for autologous transplantation. Expanding salivary stem/progenitors in culture for transplantation is an important step. Fibroblast growth factor (FGFR) signaling is critical for salivary stem/progenitor cell expansion during embryonic organogenesis and heparan sulfate proteoglycan co-receptors are required for FGFR signaling. We aim to identify sulfated heparan sulfate (HS) epitopes that specifically increase FGFR signaling and salivary progenitor expansion. Previously we showed that treatment of primary fetal salivary epithelium with over-3-O-sulfated HS increased epithelial proliferation and expansion of KIT+ progenitors by increasing endogenous 3-O-sulfated HS.

Methods: The kidney HS used in these studies to generate the 3-O-sulfated HS has an undefined GAG chain and very low levels of endogenous 3-O-sulfation. Here we have used more defined HS structures to study FGF10/FGFR2b-dependent KIT+ progenitor growth and morphogenesis. Firstly, HS from Chinese hamster ovary (CHO) cells, which do not express the 3-O-sulfotransferase enzymes, was used. Native CHO-HS (15 kDa) from conditioned media (CHO-HS) was treated in vitro with recombinant 3-O-sulfotransferases. Secondly, we used chemo-enzymatically engineered HS with defined length (10- and 12-mers) and sulfation patterns.

Results: The Hs3st1- and Hs3st3-treated HS increased endbud morphogenesis of primary fetal salivary epithelium. In addition they increased the expression of genes associated with progenitor cells (Kit), proliferation (Ccnd1), HS synthesis (Hs3st3a1, Hs3st3b1, and Hs3st6), and Fgfr2b-signaling (Etv5).

Conclusions: Defining the minimum saccharide sequences of HS that determine the selectivity and specificity of their function will facilitate the synthesis of small HS mimetics to specifically increase progenitor expansion in vitro.

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Keywords: heparan sulfate, salivary gland, progenitor expansion
[037-U] Investigation of Affinity at Binding Site Between Human Epidermal Growth Factor Receptor 2 (HER2) and Herceptin

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**Background:** Human epidermal growth factor receptor 2 (HER2)-positive breast cancer results from an uncontrolled synthesis of the HER2 protein due to the amplification of the HER2 gene. Over 20\% of breast cancer cases are caused by the overproduction of the HER2 protein, which triggers uncontrolled proliferation of breast cancer cells. The rapid growth and maturation of malignant cells causes HER2-positive breast cancer to metastasize much quicker than any other form of breast cancer yielding a poor prognosis for patients. Modern medicine has developed several antibodies that bind to and inhibit the HER2 receptor, blocking the propagation of malignant cells. Herceptin is a receptor-blocking monoclonal antibody that prevents downstream signaling and also marks the cancer cell for destruction by the immune system. Many patients often develop a resistance to Herceptin, which results from a disturbance between the HER2 receptor and the antibody. This allows the tumor cells to continue replicating. Previous studies have noted that there are three binding sites where Herceptin attaches itself to HER2. The current study investigates the binding energies between the HER2 receptor and Herceptin to determine if the amino acid sequence can be altered to create a stronger interaction between the HER2 receptor and the antibody. This research could potentially increase the efficacy of Herceptin and improve survival rates of patients with HER2-positive breast cancer.

**Methods:** The investigated protein-antibody complex was obtained from the Protein Data Bank (PDB code: 1N8Z). Using the HER2 protein, the Herceptin molecule, and the HER2/Herceptin complex, three computational simulations were performed. These simulations were completed using the AMBER 14 Molecular Dynamics software package. After the simulations were performed, the binding sites of HER2 and Herceptin were analyzed at the atomic level. The Molecular-Mechanics Generalized Born Surface Area (MM-GBSA) method was utilized to determine binding affinity between HER2 and Herceptin.

**Results:** The binding affinity of Herceptin to the HER2 receptor is currently being studied in the present research. Specifically, the amino acids located at the receptor sites on the HER2 protein and Herceptin are being closely evaluated to determine if any can be replaced to create a stronger affinity between HER2 proteins and Herceptin. The calculated binding affinity demonstrated the HER2-Herceptin complex is energetically stable, as expected, and the per-residue decomposed free energies highlight the favorable and unfavorable residues in the three binding sites. Preliminary results suggest that of the three binding sites/loops, the residues in the third loop (residues 1027-1037) have significantly smaller (unfavorable) energies than the first two binding loops (first loop: residues 991-995 and second loop: residues 1004-1007). The computational simulations will be extended to further evaluate the behavior of Herceptin when bound to the HER2 receptor.

**Conclusions:** The binding free energies generated for every residue in the HER2/Herceptin complex allowed us to closely examine each residue’s contribution to binding. The residues in the third loop have less favorable energies, although some single residues in and around the loop have much more favorable energies. Specifically, the least favorable residue in the whole complex is lys1027, which is the starting residue of the third binding loop. Some other residues in that loop that could be mutated in the future are asp1030 and glu1031. Future research will work towards replacing old residues within the third loop and possibly creating another binding loop to further stabilize the HER2/Herceptin complex.

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**Keywords:** HER2, herceptin, binding affinity, free binding energy
[038-FS] Refining the Path to Personalized Medicine with Psychometric Analysis of Oral Cancer Biomarkers

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**Background:** Though we live in and with big data, our methods for translating high volumes of data into useable information and ultimately good decisions lack efficiency and finesse. Current methodology is “shotgun,” where a preponderance of data is “judged” by unspecified heuristics to tip the evidence in favor of some patient care or health policy decision. Psychometrics has been practiced for decades in psychological trait and ability testing. Essentially, psychometrics evaluates information supplied by different queries in their detection of a latent construct that is not directly observable. Under a psychometric approach, biomarkers are informing us about the presence or absence of the latent trait of cancer. Thus, may redundant and less informative biomarkers be omitted to save resources, and to improve the accuracy of biomarker screening and diagnosis.

**Methods:** Positive likelihood ratios, LR’s, were computed from sensitivities and specificities of salivary biomarkers tested singly or in a group (panel) for determining the difference between healthy and cancerous oral tissue. Biomarkers ranked by LR’s from highest to lowest and lowest to highest were compared to conventional shotgun approaches assessed by areas under the curve and ultimately expressed in the number of biomarkers needed to achieve a maximum positive predictive value (PPV).

**Results:** The number of biomarkers required to diagnose / screen could be reduced by about 80% when read in the context of highest to lowest likelihood ratios. The number of biomarkers required to diagnose / screen can be derived by first estimating the prevalence of disease in the population of interest.

**Conclusions:** Biomarker information is best interpreted as LR’s when read in context of highest to lowest, i.e., when read as a sequence of Bayesian posterior probabilities. The number of biomarkers required to diagnose / screen oral squamous cell carcinoma in saliva may be reduce by 80% by reading them ranked from highest to lowest LR. All clinical data including orthopedic tests may be efficiently aggregated as LR’s.

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**Keywords:** oral cancer, salivary biomarkers, screening, diagnosing, efficiency.
[039-G] Cav-1 Upregulation Slows Migration Velocity in BLM Melanoma

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**Background:** Caveolin-1 (Cav-1) is a membrane-associated and cytosolic protein that influences a number of cellular signalling cascades. Changes in Cav-1 expression levels are thought to be responsible for changes in metastatic behaviour of a number of cancers, including melanoma. However, the effect of changes in Cav-1 expression level seem dependent on cell-type and direction of expression change. In highly migratory, metastatic melanoma, Cav-1 expression levels tend to be low. The purpose of this study was to determine the extent to which upregulation of Cav-1 could attenuate basal and CXCL-8-stimulated migration velocity in the human metastatic, BLM melanoma cells.

**Methods:** Wild-type BLM cells were stably transfected (Lipofectamine 2000, Invitrogen) with a Myc-DDK-tagged human Cav-1 gene cloned into a pCMV6-Entry vector (Origene, TrueOrf). Permanent selection was achieved with G418 (1 mg/ml) antibiotic. Cell extracts from wild-type and transfected BLM cells were run on 10%-PAGE gels and transferred to PVDF membranes. Appropriate 1° antibodies were used to confirm Cav-1 upregulation and to test for the presence of the EMT marker N-cadherin. Band detection used infrared 2° antibody detection (LiCor). A wound-healing assay measured migration velocity in wild-type and Cav-1 transfected cells. Following overnight serum starvation, assays were carried out in 24-well plates containing RPMI 1640, 10% FBS media with unbound CXCL8 at doses ranging from 0-100 ng/ml and seeded at 250,000 cells / well. Wound images were collected at 15 m intervals and quantified at 4 h intervals using ImageJ.

**Results:** Successful transfection was confirmed by immunoblot analysis. Immunoblot analysis shows increased expression of the EMT marker N-cadherin in Cav-1 transfected BLMs. Immunohistochemical staining shows similar subcellular distribution Cav-1 in the transfected and wildtype cells. Migration velocity by wound-closure assay decreased with Cav-1 overexpression. In both wildtype and Cav-1 transfected BLM melanoma, we were unable to demonstrate altered cell migration rates when unbound CXCL8 was administered over a 24 h period in RPMI media containing 10% FBS.

**Conclusions:** Cav-1 expression has a significant impact on slowing migration, but it increased expression of EMT markers in BLM human melanoma cells. Under conditions of our current experiments, CXCL8 had no systematically detectable impact on BLM migration rate.

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**Keywords:** melanoma; caveolin-1; CXCL8; interleukin-8, migration, BLM, n-cadherin
[041-G] Predictive modeling of the number of active, off-host adult lone star ticks from long-term monitoring data

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Background: \textit{Amblyomma americanum} (lone-star tick) is a three-host tick of rising importance in pathogen transmission throughout the midwest and southeast United States as evidenced by increases in \textit{Amblyomma}-associated human ehrlichiosis and the emergence of Heartland virus (HRTV). \textit{A. americanum} is an aggressive, non-discriminatory feeder, which increases risk of interaction with humans. As this species spends most of its life off-host, determining how environmental variables are associated with patterns of tick activity is useful in disease management and prevention. The objective of this study was to create a predictive statistical model based on environmental variables that describes the number of active off-host \textit{A. americanum} adults in northeastern Missouri from 2008 to 2013.

Methods: Data for this study come from long-term monitoring in Adair County, MO in which ticks were collected every other week from February to December, using drag and dry-ice-baiting in permanent sampling grids in an old field habitat and second growth-forest habitat. Variables incorporated into modeling were precipitation, day length, the number of nymphs prior to sampling, degree days, saturation deficit, wind speed, extreme high and low temperatures, and habitat. 511 negative binomial models were generated from all possible combinations of the nine variables and compared using 8 model selection criteria.

Results: The best selected model indicates that the number of active off-host adult \textit{A. americanum} is negatively associated with cumulative degree days and extreme low temperatures, and positively associated with saturation deficit, wind speed, day length, and number of nymphs prior to sampling.

Conclusions: Seasonality of \textit{A. americanum} adult activity is likely influenced by annual trends in cumulative degree days and day length. The number of active nymphs prior to sampling may predict magnitude of peaks in adult activity, as this likely represents the same cohort ticks at an earlier stage of development. Metabolic function and behavior are influenced by temperature and humidity, so extremely low temperatures, saturation deficit, and wind speed may further explain variation in daily and seasonal activity. Creating similar models for \textit{A. americanum} nymphs and larvae will further elucidate how life stages differ in their response to environmental changes, which is useful in predicting risk of tick-borne disease transmission on both a temporal and spatial scale.

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Keywords: \textit{A. americanum}; tick-borne disease; population dynamics; multi-model inference
[042-G] Opposing Roles of Pyruvate Dehydrogenase and Branched-Chain α-Keto Acid Dehydrogenase in Branched-Chain Membrane Fatty Acids in Staphylococcus aureus

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**Background:** In order for *Staphylococcus aureus* to overcome diverse environmental conditions such as fluctuating temperatures, it is critical to maintain fluidity of the cytoplasmic membrane, which to a large extent is governed by the presence of branched-chain fatty acids (BCFA). While branched-chain α-keto acid dehydrogenase (BKD) is the key enzyme in BCFA synthesis, a *S. aureus* BKD-deficient mutant still produces substantial levels of BCFA. Pyruvate dehydrogenase (PDH) has structural similarity to BKD and has been speculated to contribute to BCFA in *S. aureus*. This study investigated the role of PDH and BKD in BCFA metabolism and its significance in *S. aureus* using BKD, PDH, and BKD-PDH deficient derivatives of methicillin-resistant *S. aureus* strain (MRSA) strain USA300 (WT).

**Methods:** Membrane BCFA were analyzed using gas chromatography and membrane fluidity was measured using fluorescence polarization. Growth at 37°C and 20°C was measured using spectrophotometry. Carotenoids were extracted using methanol and the A\(_{462}\) measured in petroleum ether. Susceptibility to antibiotics was determined by measuring the minimum inhibitory concentration (MIC).

**Results:** BCFA made up 50% of membrane lipids in wild-type but only 31% in the BKD-deficient *S. aureus*. Surprisingly, the BCFA level was ~80% in the PDH-deficient strain and 38% in the BKD-PDH double mutant. While the BKD-deficient mutant showed decreased membrane fluidity, the PDH-deficient mutant showed an increase in membrane fluidity correlated with the BCFA levels in the cytoplasmic membrane. The BKD- and PDH-deficient strains grew slower and the BKD-PDH double mutant grew slowest at 37°C compared to WT. At 20°C however, the BKD and BKD-PDH double mutants grew only a little followed by autolysis of these cells. In addition, compared to WT, the BKD-deficient strains produced significantly higher levels of staphyloxanthin, while PDH-deficient and the BKD-PDH double mutant produced very little staphyloxanthin. In antibiotic resistance studies, the BKD-deficient strain showed reduced resistance to daptomycin.

**Conclusions:** The BCFA composition of the cell membrane in *S. aureus* is critical to cell growth and appears correlated with membrane fluidity and inversely correlated with staphyloxanthin production. PDH and the BKD enzyme complexes seem to have opposite effects on membrane fatty acid composition due to substrate preferences and their specific roles in BCFA and energy metabolism.

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**Keywords:** pyruvate dehydrogenase, branched-chain fatty acid metabolism, antibiotic resistance, membrane fluidity, carotenoids
Antimicrobial Properties of Tyrosol can be Linked to the Inhibition of Microbial ATP Synthase

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**Background:** A wide range of natural and synthetic compounds including dietary polyphenols are known to bind and inhibit ATP synthase. Dietary polyphenols can be found in a variety of fruits and vegetables such as olives, grapes, tea, coffee, etc. Polyphenols from olives and extra virgin olive oil are known to exhibit antimicrobial, anticancer, and antioxidant properties. Our lab has been involved in understanding if the antimicrobial properties of polyphenols are linked to the selective inhibition of microbial ATP synthase. In this study, we examined the inhibitory profiles of *Escherichia coli* membrane-bound ATP synthase and cell growth in the presence and absence of tyrosol and its analogs; hydroxytyrosol, oleuropein, and dihydroxyphenylglycol.

**Methods:** Wild type *E. coli* pBWU13.4 was grown on minimal media to late log phase. Cells were harvested and then French Pressed to isolate and purify membrane-bound $F_1F_0$ ATP synthase. Our null control was *E. coli* pUC118 with deleted ATPase gene. Tyrosol and its analogs induced inhibitory profiles of wild-type and mutant membrane-bound ATP synthase were performed at 37 °C. Wild-type, mutant, and null cell growth assays on limiting glucose were evaluated at OD595 using an AccuSkan Plate reader over a 24 hour period.

**Results:** Tyrosol and its analogs induced a variable degree of ATP synthase inhibition. While tyrosol induced 100% inhibition of wild-type ATP synthase, hydroxytyrosol, oleuropein, and dihydroxyphenylglycol induced between 40-60% inhibition. Also, tyrosol and its analogs caused variable abrogation of wild-type, mutant, and null cell growth.

**Conclusions:** Tyrosol and its analogs induced inhibitory profiles of ATP synthase and cell growth assays elucidates that the antimicrobial properties of tyrosol and its analogs are at least in part linked to the inhibition of ATP synthase, suggesting its potential use as a molecular drug target.

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**Keywords:** *E. coli* ATP synthase, ATP synthesis, polyphenol, hydroxytyrosol, oleuropein
[044-G] Inhibition of *Escherichia coli* ATP Synthase and Cell Growth by Safranal and its Analogs

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**Background:** A wide range of natural and synthetic compounds including polyphenols are known to bind and inhibit ATP synthase. Safranal a dominant component of saffron is known to have antitumor, cytotoxic, and antimicrobial properties. Our lab has studied safranal and its structural analogs, thymol, cuminol, carvacrol, damascenone, 2,6,6-trimethyl-2-cyclohexene-1,4-dione, 4-isopropyl benzyl bromide, and 4-tert butyl phenol induced inhibition of *Escherichia coli* ATP synthase and their effect on cell growth.

**Methods:** Wild type and mutant *E. coli* strains were grown to late log phase. Cells were harvested by centrifugation and lysed by French Press to isolate the membrane bound F₁F₀ ATP synthase. Null *E. coli* strain with deleted ATPase gene was used as a negative control. Safranal and its analogs induced inhibitory studies were performed on membrane bound F₁F₀ ATP synthase. Growth of wild-type, mutant, and null strain in limiting glucose and succinate was also examined in presence and absence of safranal and its analogs.

**Results:** Safranal and its analogs inhibited wild-type enzyme to variable degrees. While safranal caused 100% inhibition of wild-type F₁F₀ ATP synthase only ~50% inhibition occurred for the mutant ATP synthase. Furthermore, safranal, thymol, cuminol, carvacrol, and damascenone fully abrogated the growth of wild-type *E. coli* cells and had little or no effect on the growth of null and mutant *E. coli* strains.

**Conclusions:** The antimicrobial properties of safranal and its analogs can be linked to their binding and inhibition of ATP synthase. Thus our results support the idea that ATP synthase can be used as a molecular drug target to combat microbial infections.

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**Keywords:** *E. coli* ATP synthase, ATP synthesis, safranal, cuminol, thymol
[045-G] Effect of Synergistic Action of Oxidants and Cell Wall Inhibitors on Staphylococcus aureus with and without Methionine Sulfoxide Reductases

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**Background:** *Staphylococcus aureus* is a major human pathogen resistant to several commonly used antibiotics. Cell wall-active antibiotics induce up-regulation and increased production of methionine sulfoxide reductase (MsrA and MsrB). Msr proteins protect organisms from oxidative stress. However, Msr free staphylococci showed resistance to cell wall antibiotics that was comparable to wild-type bacteria. It was postulated that the simultaneous exposure of Msr-free *S. aureus* to cell wall inhibitors and oxidants would produce a more robust killing compared to the killing of wild-type *S. aureus* under identical conditions. This hypothesis is driven by the assumption that a cell wall inhibitor would destabilize the cell wall allowing the reactive oxygen species to have a more direct and efficient impact on the cellular macromolecules under Msr-free conditions.

**Methods:** This study utilized *S. aureus* strain SH1000 (wild-type) and its MsrA-free derivative (SH1000:msrA123). These strains were treated with oxidants (hydrogen peroxide, sodium nitroprusside, cumene hydroperoxide, and N-ethylmaleimide) and a cell wall inhibitor (oxacillin) either individually or in combination. *S. aureus* strains SH1000 and SH1000ΔmsrA123 were grown to OD$_{600}$ = 0.3 to be treated with a cell wall inhibitor and an oxidant, or both. Growth was measured spectrophotometrically every 30 minutes over a six-hour period.

**Results:** There seems to be synergy between the cell wall inhibitor and oxidant as demonstrated by higher *S. aureus* killing compared to killing by treatment alone. Additionally, there was no significant difference observed in the inhibition of bacterial growth between the wild-type (SH1000) and the MsrA-free (SH1000ΔmsrA123) strains.

**Conclusion:** It is likely that for a more pronounced synergy for cell killing could be observed, if the cells were treated with cell wall inhibitor a bit sooner than treating them with oxidants. A live bacterial count may be needed to further validate this synergy between wild-type and MsrA-free *S. aureus*, because it is likely that the growth kinetics observed spectrophotometrically are not the true representation of bacterial killing.

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**Keywords:** *S. aureus*; cell wall inhibitor; oxidant
[046-G] Characterizing the Effects of Carotenoid and Branched Chain Fatty Acid Deficiencies in Staphylococcus aureus

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Background: Staphylococcus aureus is a major human pathogen in hospitals and communities alike. Its ability to thrive in many different environments enables it to cause infection when given the opportunity. Resistance to a variety of antibiotics makes its presence threatening to many individuals. In order to survive in specific locations with cooler temperatures, S. aureus can alter its membrane lipid profile and increases the amount of branched-chain fatty acids (BCFA). Branched-chain a-keto dehydrogenase (BKD) is the committed enzyme responsible for the production of BCFA. A decrease in BCFAs due to inactivation of BKD leads to a decreased BCFA levels in the bacterial membrane and an increased level of carotenoids in S. aureus. These pigments probably help maintain bacterial membrane fluidity.

Methods: A kanamycin resistance cassette was inserted into the \textit{lpdA} gene of S. aureus. Mutation in the \textit{lpdA} gene was confirmed by using PCR. The \textit{crtM} mutant was created by insertion of a transposon into the coding region. Disruption of the \textit{crtM} coding region was confirmed by the presence of the transposon in a PCR assay. Wild-type and S. aureus mutants were grown at 37ºC and growth was measured spectrophotometrically every 30 minutes. The \textit{crtM} and \textit{lpdA} mutants were complimented with the respective gene loci on a shuttle plasmid. The complemented strains were used for growth comparison with the mutant and the parent S. aureus strains. Mice were used to determine virulence by comparing the clearance of wild type to mutants. Six mice were used for each mutation. They were injected with a mixture of wild type and mutant S. aureus (40:60). Three mice were sacrificed after 8 hours and three after 24 hours. The liver and spleen were harvested and homogenized in 3 and 2 ml (respectively) of TSB+10% glycerol. The mixture was diluted and plated on TSA and TSA containing antibiotics.

Results: When compared to the wild type the \textit{crtM} mutant showed no growth defect in vitro but showed poor survival in vivo. The \textit{lpdA} mutant grew much more slowly \textit{in vitro} and poor survival \textit{in vivo}. The \textit{lpdA:crtM} double mutant showed severe growth defect \textit{in vitro} and very poor survival \textit{in vivo}.

Conclusions: Overall it appears that the BKD- and CrtM-deficient staphylococci were attenuated in terms of their survival in mouse. The lack of growth in the complimented strains may be due to not being grown in media containing antibiotics.

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Keywords: S. aureus; carotenoid; branched-chain fatty acids
[051-U] The Cognitive Symptomology of Post-Concussion Syndrome: A Pilot Study

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Background: The purpose of the study is to examine a group of individuals who have reportedly experienced a concussion to determine if they perform differently than a group of individuals who have not experienced concussion, using two neuropsychological screening measures, one standardized assessment, and a questionnaire commonly used to examine clients with symptoms that might result from mild traumatic brain injury (mTBI)/concussion.

Methods: A control group of twelve typically functioning subjects ranging from ages 16 to 23, and an experimental group of eight students and athletes of ages 16 to 23 who have had previous experiences with one or more concussions were administered the Rivermead Post-Concussion Symptoms Questionnaire [RPQ], the Saint Louis University Mental Status Exam [SLUMS], the Trail-Making Test: A & B [TMT-A &B] and the 3rd edition of the Test of Nonverbal Intelligence [TONI-3].

Results: After examining all twenty subjects, the researcher then compiled the subjects’ reported severity on the RPQ, the numerical and ordinal scores received on the SLUMS, the maximum, minimum, and average time in seconds to completion was computed on the TMT-A (Control: Range =32, Mean = 18; Experimental: Range =16, Mean =18), & TMT-B (Control: Range =44, Mean =49; Experimental: Range =75, Mean =61), as well as the standardized score received on the TONI-3 (Control: Range =28, Mean =105, Standard deviation = 14; Experimental: Range =42, Mean =101, Standard deviation =11). All items on the SLUMS were categorized according to their targeted area of cognitive functioning, and the number of incorrect responses associated with that item, with respect to each group. The correlation between experience with mTBI and the standardized scores on the SLUMS, TONI-3, and Trail-Making Test Parts A & B, were all examined using a box plot model to compare the mean scores of the experimental (concussed) and the control (un-concussed) group. A cross tabulation analysis was run on mTBI and its relationship to the SLUMS.

Conclusions: The results of this study are especially concerning for those who regularly screen individuals for post-concussion syndrome or any lasting deficiencies following mTBI. Practically, when screening for post-concussion deficits, the cognitive areas to assess would be those identified in this study as being poorer in the concussed sample than in their un-concussed counterparts (problem-solving, executive functioning, information processing speed, memory). Because the sample of this study was comprise entirely of adolescent to young adult students, most of who were athletes, academic and athletic institutions should consider the screening tools and protocol to ensure their measures account for, and align with the findings in this study.

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Keywords: mild traumatic brain injury, post-concussion syndrome, diagnostic assessment
Target-Dependent Retrograde Signaling Mediates Synaptic Plasticity at the Drosophila Neuromuscular Junction

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Background: Neurons often innervate multiple postsynaptic cells with distinct synaptic strengths and expressions of activity-dependent plasticity. This local, target-dependent plasticity is thought to mediate learning and memory, though the underlying mechanisms are unknown. Our experiments use Drosophila melanogaster to test the hypothesis that retrograde signaling from postsynaptic cells participates in target-dependent synaptic plasticity.

Methods: To address how activity strengthens one synapse while leaving the other synapses unaffected, we have been studying a Drosophila melanogaster ‘common exciter’ (CE) motoneuron that synapses onto multiple muscle fibers, one of which can be manipulated with transgene expression.

Results: Synaptic plasticity was stimulated with hyperexcitable K+ channel mutations while postsynaptic glutamate receptors (GluRs, GluRC and GluRIIA) were reduced with an RNAi or dominant-negative transgene. In this situation, control NMJs expanded their synaptic size as expected while the manipulated synapse did not, even though it showed comparably robust spontaneous activity. This suggests that each muscle can independently influence the growth and plasticity of its presynaptic motoneuron in a retrograde fashion. We recently showed that neuromuscular junction (NMJ) growth and plasticity requires the Bone Morphogenetic Protein (BMP) molecule Glass bottom boat (Gbb). In the absence of retrograde Gbb signaling, NMJs are small, inefficient, and are cannot be modulated by activity. Gbb expression was therefore rescued in a single CE target muscle of a gbb mutant, which caused synaptic growth to be rescued only for that NMJ. Conversely, the expression of an RNAi-transgene against Gbb blocked activity-dependent plasticity when compared to other CE-innervated fibers. This is intriguing, as Gbb acts through a downstream SMAD1 transcription factor, Mad. Immunolabeling against the activated form of Mad (pMad) showed reduced levels within synaptic boutons opposite the RNAi treated muscle, yet there was no apparent change within nuclei of central motoneurons.

Conclusions: Local retrograde synaptic signaling by BMPs and presynaptic activation of Mad may ‘tag’ presynaptic axonal branches for growth and plasticity. If similar actions occur in the CNS during memory formation, the Drosophila NMJ could be a useful model for identifying the molecular mechanisms underlying memory formation at single synapses.

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Keywords: Drosophila melanogaster, synaptic plasticity, synaptic tagging, retrograde signaling
Effects of Amentoflavone on the Aggregation and Disaggregation of Amyloid β

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**Background:** Alzheimer’s disease is characterized by the accumulation of fibrillar forms of Amyloid β (Aβ) peptides, mainly Aβ42, in the extracellular and perivascular spaces in the forebrain, resulting in dementia. It has been reported that naturally-occurring polyphenolic compounds such as flavonoids slow AD progression, at least, via affecting the formation and/or stability of Aβ fibrils. However, the inhibitory effects of a class of polyphenols, biflavonoids, on Aβ42 aggregation as well as their ability to disaggregate Aβ42 fibrils have not been fully investigated.

**Methods:** To test for the inhibitory effects of mono- and bi-flavonoids on Aβ42 aggregation, a solution containing synthetic Aβ42 with Thioflavin T was incubated with various concentrations of each test compound at 37°C for 24 hours, plated on a clear-bottom 96 well plate, then measured for fluorescence levels using a Biotek plate reader. To test for the effects of the test compounds on Aβ42 fibril disaggregation, preformed Aβ42 aggregates were incubated with various concentrations of each test compound, then measured for fluorescence levels using the same technique as above, with the duration shortened to 7 hours. The final concentrations of each compound were 0.08, 0.4, 2, and 10 µM. Three independent trials were run for both experiments. The IC\(_{50}\) values were calculated and presented as mean ± S.E.M.

**Results:** Among the 10 flavonoids we tested, we found amentoflavone had the most potent inhibitory effect (IC\(_{50}\): 260 nM) on the formation of Aβ42 fibrils, whereas the other structurally related biflavonoids and monoflavonoid apigenin were less effective. In addition, our disaggregation assay demonstrated that flavonoids induced disaggregation of Aβ fibrils in a concentration-dependent fashion. In line with the results from the aggregation assay, amentoflavone had the greatest ability to disaggregate Aβ42 fibrils.

**Conclusions:** Our *in vitro* data show the chemical structure of amentoflavone correlates with a greater inhibition of aggregation and disaggregation of Aβ42 fibrils when compared to other monoflavonoids or biflavonoids. Therefore, amentoflavone may have the potential to slow the progression of Alzheimer’s disease *in vivo*.

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**Keywords:** amentoflavone, biflavonoids, Alzheimer’s disease
[054-G] Does Ghrelin Effectively Reduce Depressive-like Symptoms in Juvenile Rats?

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Background: Depression is a chronic psychiatric disorder that affects children and adolescents across the globe, but there are few treatment options suitable for juvenile patients. The broad, long-term goal of this project is to better understand the etiology and potential treatment of depression in juveniles (individuals under the age of 18 years). The brain-gut peptide hormone ghrelin has been shown to reduce depressive-like behavior and increase brain neuronal growth in adult rodent models. However, there have been no studies to support this same role for ghrelin in juvenile rodents.

Methods: The purpose of this study is to determine if intracerebroventricular injections of ghrelin in juvenile rats will reduce depressive-like behavior and produce an increase in hippocampal mitogenesis and neurogenesis. This question will be addressed using two specific aims. (1) We will determine the most effective dosage of ghrelin (200-pM, 500-pM, or 1-nM) that causes a decrease in depressive-like behavior in the modified forced swim test (FST). (2) We will compare a mitogenic group and a neurogenic group to a placebo group to determine the effects of ghrelin on behavior, stem cell mitogenesis, and neurogenesis in the dentate gyrus of the hippocampus. The proposed experiments will use the exogenous cell tracer BrdU to quantify hippocampal mitogenesis and the endogenous neuronal marker NeuN (along with BrdU) to quantify hippocampal neurogenesis. Mitogenesis and neurogenesis will be quantified by immunohistochemistry and subsequent visualization using a confocal microscope. Changes in mitogenesis will be characterized by the presence of newborn cells within the hippocampal dentate gyrus using fluorescent antibodies to detect BrdU. Neuronal changes will be characterized by the presence of newborn neurons in the hippocampal dentate gyrus using fluorescent antibodies for both BrdU and NeuN.

Results: Ghrelin-treated rats, particularly those treated with 500-pM, tend to eat more food than the placebo group. Comparison of a pre-treatment FST to a post-treatment FST demonstrate a decrease in immobility time following injection, but the ghrelin-treated groups have not been shown to spend less time immobile than the placebo group. Confocal microscopy shows that the rate of hippocampal mitogenesis is greater in the ghrelin-treated group than in the placebo group.

Conclusions: Preliminary results indicate that the 500-pM dosage of ghrelin may produce the most profound changes in immobility time in the FST and that treatment with ghrelin increases the rate of hippocampal mitogenesis. We are testing whether ghrelin treatment also increases the rate of neurogenesis.

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Keywords: depression; juvenile; ghrelin; neurogenesis; hippocampus
Background: The importance of cholinergic activity in proper memory function has been well documented. It has been reported that an improvement in memory in mice is associated with improved hippocampal cholinergic activity and neurogenesis. In the mouse Alzheimer’s disease (AD) model, the TgCRND8 mouse demonstrated a disruption in corticothalamic pathways of the prefrontal cortex, suggesting that AD was associated with a loss of intact cholinergic function. In addition, many drugs, such as benedryl (diphenhydramine) possess significant anti-muscarinic action, an action that can produce cognitive impairment in mice. Diphenhydramine is also useful as a mild sedative in some patients.

Methods: This study tested memory changes by use of a Barnes Maze (BM), a nonstress cognition system measuring the ability of mice to remember the location of an escape compartment. Naive mice were divided into 5 cohorts (C) and trained using the BM. Cohorts received either no drug (Control, C-1), or oral administration of GDW (Sham, C-2), atropine (ATR, 0.5 mg/kg, C-3), diphenhydramine (DPH, 0.5 mg/kg, C-4) or DAU 5884 (0.25 mg/kg, C-5).

Results: Results indicate there is a decrease in the ability of mice treated with ATR and DPH to find the escape compartment, shown by increased time to escape and increased distance travelled to escape. Only the ATR treated mice travelled a greater distance to the escape compartment, but both the ATR and the DPH treated mice took more time to find the escape compartment. In addition, the ATR mice were clearly more aggressive when handled compared to mice in all other cohorts. The results are compatible with previous studies and there is suggested clinical relevance associated with the data. There is concern that drugs with anti-muscarinic activity may target M1 receptors in the central nervous system, potentiating cognitive decline. Clinically this is relevant when treating overactive bladder disease. It is important to choose the anti-muscarinic that is least likely to cause cognitive function decline, especially in the elderly.

Conclusions: Our study supports previous studies indicating that use of selective anti-muscarinic agents, such as DAU 5884 and darifenicin for treatment in patients with overactive bladder produce improved quality of life with minimal risk of cognitive decline.

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Keywords: DAU 5884, darifenicin, overactive bladder
[056-FS] Using Specific Blockers to Identify TTX-S Naᵥ Channel Subtypes in Rat Muscle Afferent Neurons

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Background: Muscle pain is transmitted by group III and IV afferents, but our knowledge of the Naᵥ channel types that generate the action potentials is incomplete. Previously we demonstrated that tetradotoxin-resistant (TTX-R) Naᵥ1.8 channels dominate the Naᵥ current in muscle afferent somata. Using immunohistochemistry, we have demonstrated expression of tetradotoxin-sensitive (TTX-S) Naᵥ1.6 and Naᵥ1.7 channels in the somata and axons of group IV neurons, but the contribution of these channels to Naᵥ current is unknown.

Methods: We used patch clamp electrophysiology to test the blockers in isolated, cultured rat group III and IV neurons (diameter ≤38 µm).

Results: We tested Naᵥ channel-selective blockers to determine the contribution of Naᵥ1.6 and Naᵥ1.7 current to the TTX-S current. For Naᵥ1.6 current we used 4,9-Anhydrotetrodotoxin (AnTTX, 30 nM, IC₅₀ = 7.8 nM) and found an average of 18 ± 15% (SD) block of the TTX-S current (n=9). The Naᵥ1.7 component current was probed using ProTx-II (100 nM; IC₅₀ = 0.3 nM), Ssm6a (100 nM; IC₅₀ = 25 nM) and ICA-121431 (ICA, 1 µM, IC₅₀ = 19 nM). However, both ProTx-II (n=6) and Ssm6a (n=4) failed to block Naᵥ current. ICA did block to yield a 61 ± 21% inhibition of the TTX-S current (n=18, p < 0.05).

Conclusions: Based on the published IC₅₀s we expected all three Naᵥ1.7 channel blockers to produce similar effects, and do not yet understand reason for the absence of block by ProTx-II and Ssm6a. However, the toxin IC₅₀s were derived from human (h)Naᵥ1.7 channels. It has been demonstrated that hNaᵥ1.7 and rat (r)Naᵥ1.7 channels respond differently to ICA, with hNaᵥ1.7 channels being insensitive to the blocker. Perhaps rNaᵥ1.7 channels are insensitive to ProTx-II and Ssm6a. Based on the ICA and AnTTX results, we tentatively conclude that ~60% of the TTX-S current is generated by Naᵥ1.7 channels and ~18% is contributed by Naᵥ1.6 channels in muscle afferent neurons. The remaining ~20% of TTX-S current is generated by another TTX-S Naᵥ channel type, perhaps Naᵥ1.1 and/or Naᵥ1.3.

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Keywords: dorsal root ganglia, voltage gated sodium channels, electrophysiology
Blunted Respiratory Responses in the STZ-Induced Rat Model of Alzheimer’s Disease

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Background: Alzheimer’s disease (AD) is a debilitating disease of the central nervous system that results in a drastic decline in cognition and memory. In addition, respiratory dysfunction is frequently observed in AD patients, as shown by altered breathing during sleep and blunted minute ventilation during heightened oxygen demand with peak exercise. The combination of AD symptoms leads to a decrease in day-to-day function and increased mortality. At this time, the mechanisms behind the respiratory alterations are widely unknown.

Methods: For this study, an AD rat model was induced by injecting 1.5 mg/kg Streptozotocin (STZ) in the lateral ventricle to trigger pathological changes consistent with sporadic AD. We used plethysmography to analyze the peripheral and central chemoreflex in response to hypoxia (14 - 8% O2, equilibrated with N2) or hypercapnia (5% CO2, equilibrated with O2), respectively. We compared respiratory parameters before and after injection of STZ or vehicle (aCSF). Morphological changes in the brainstem and hippocampus were immunohistochemically analyzed using an antibody against S-100B for astrocytes.

Results: Similar to the inflammation in the CNS of AD patients, microinjection of STZ induced astrogliosis in the CA1 region of the hippocampus. We also found reactive astrocytes in the commissural part of the nucleus tractus solitarii, an important center for the control of respiration and responses to low oxygen conditions. Analyzing the respiratory pattern, we found an expected age-dependent decrease in minute ventilation in our control group. This age-dependent decrease was absent in the AD group, indicating elevated minute ventilation following STZ administration. Peripheral chemoreflex activation with hypoxia showed significant alterations in the AD group, as observed by a blunted elevation of respiratory rate and minute ventilation. Central chemoreflex activation with hypercapnia only decreased respiratory rate following STZ.

Conclusions: We show that the STZ-induced AD rat model displays significant respiratory dysfunction at rest and in response to hypoxia. Thus, this study provides the first model to elucidate the mechanisms behind respiratory dysfunction of sporadic Alzheimer’s disease.

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Keywords: chemoreflex, hypoxia, hypercapnia, ventilation, nucleus tractus solitarii, brainstem, astrocytosis, streptozotocin
[058-U] Investigating Modulators of the Protein kinase R-like ER kinase (PERK) pathway of the ER Stress Response.

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Background: We have an ongoing project in which we are investigating the modulators of the PERK pathway associated with ER stress caused by the accumulation of misfolded proteins. PERK is a stress sensing molecule located in the membrane of the ER that detects the accumulation of misfolded and acts to shutdown global protein synthesis by phosphorylating eIF2a, thus inactivating it. In the short term, this pathway is adaptive, but prolonged activation of this pathway becomes maladaptive in that the cells resort to apoptosis. This pathway has been heavily implicated Alzheimer’s disease as well as other neurodegenerative diseases. Our study focuses on how the protein synthesis shutdown can be reversed such that in the face of chronic PERK pathway activation, the cell can continue to synthesis essential proteins. We are testing the ability of the molecule ISRIB to reverse the shutdown of protein synthesis. This study is being done in a Xenopus oocyte model.

Methods: ER stress is induced by treating Xenopus oocytes with Tunicamycin (Tm) to activate PERK (and phosphorylate eIF2a) and Salubrinal (SAL) to inhibit phosphatases of eIF2a. Xenopus oocytes are made to express CFTR by injecting the RNA into the oocytes. We use the expression of CFTR channels in Xenopus oocytes to assess the level of protein synthesis. Whole cell voltage clamping is used to study the expression of the CFTR channels by looking at the conductance of chloride ions. We also perform western blots to study differences in expression of CFTR among the treatment groups.

Results: Electrophysiology experiments showed that oocytes treated with the stress inducer Tm and eIF2a phosphatase inhibitor SAL, and ISRIB resulted in CFTR expression levels that were higher than the oocytes treated with Tm and SAL -but lower than oocytes that had received no treatment.

Conclusions: ISRIB has shown some ability to restore protein synthesis and hence has a potential to delay apoptosis. Its ability to restore protein synthesis could also help mitigate the memory deficits characteristic of Alzheimer’s.

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Keywords: ER stress; Alzheimer’s disease; unfolded protein response; ISRIB; eIF2a; eIF2b.
Output Characterization of Clinically Applied Diode Laser Systems for Management of Chronic Periodontal Disease

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Background: Portable diode-laser devices are increasingly being used in the management of chronic periodontal disease patients. However, it is difficult to predict the output characteristics for these systems in a clinical setting, as the laser tip is manipulated. The purpose of this benchtop study is to characterize output from two diode lasers intended for use in a chronic periodontal disease management clinical study. Both systems – ezlase® (940 nm), and Alta®-ST (980 nm), have similar operating wavelengths. However, the functional conditions of the two systems are distinct, Alta-ST having a unique tip initiation technique to attain a controlled tip carbonization prior to use. The distinct output characteristics of the two systems are studied in order to correlate their respective potential clinical performance to source conditions.

Methods: Total laser power as well as 2-dimensional beam profiles were measured by mounting the laser sources and a thermopile sensor or 2-D beam profiler on a breadboard (Ophir Optronics), with position adjusted using a micrometer. Each laser with a 400-micron fiber was operated at 2 W, in CW or pulsed mode (50% duty cycle). Measurements were made with the bare fiber tip or with fiber tip activated for each device, and repeated three times.

Results: Total measured output power in CW mode for bare-fiber tips was approximately 10-20% lower than the displayed power for each system. With tip activation, the measured total power was lower by 30% compared to the power readout. The beam profile of the ezlase system was much sharper, compared to a more uniform flat-topped beam profile for the Alta-ST. On tip activation, in each case, the beam profiles were much broader and the peak amplitude measured much lower compared to the bare tip maxima, under same drive conditions.

Conclusions: Output characteristics of two dental diode lasers under anticipated conditions for use in clinical procedures were compared during benchtop testing. Total power output characteristics are distinct for the two systems, among other factors, depending on the recommended technique for tip activation. These measurements can potentially help correlate clinical response from individual laser systems.

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Keywords: dental lasers, Diode lasers, laser output, laser beam map, periodontal disease
Ketones Alleviate Neuroinflammation through Modulation of Metabolic Sensors

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**Background:** Inflammation is a major pathogenic process underlying disease progression that is ubiquitous to both dental and systemic disease. Despite the advent of diverse anti-inflammatory drugs, there are still clinical demands for more effective therapies. Recently, β-hydroxybutyrate (BHB), a metabolic substrate of the ketogenic diet (KD), has shown the anti-inflammatory properties. However, the mechanism(s) of this interaction has yet to be elucidated. The purpose of this study was to determine whether ATP-sensitive potassium (K\textsubscript{ATP}) channels underlie the anti-inflammatory actions of the KD or BHB alone against lipopolysaccharide (LPS) induced inflammation.

**Methods:** Using C3H mice and BV2 microglial cells following application of either KD or BHB with LPS, we measured changes in inflammatory mediators (TNF-a, NFkB, IL-1b, IL-6) and K\textsubscript{ATP} channel expression. Samples from hippocampi and BV2 cells were used to evaluate the expression profile of RNAs proteins, and nitric oxide (NO).

**Results:** Intraperitoneal injection of 10 mg/kg LPS in mice stimulated microglial cell activation and gene expression of inflammatory mediators. In contrast, these responses were markedly suppressed by KD administration. Under BHB-treated BV2 cell with 1 mg/ml LPS, 1 mM BHB significantly reduced expression level of inflammatory mediators and NO in conjunction with upregulation of the K\textsubscript{ATP} channel. This action was inversely correlated with pretreatment of a K\textsubscript{ATP} channel blocker, glibenclamide.

**Conclusions:** The data provides evidence for anti-inflammatory properties of both the KD and BHB. BHB may closely correlate with the mechanism underlying KD-driven inflammation control, which may be in part a consequence of K\textsubscript{ATP} channel modulation.

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**Keywords:** ketogenic diet; neuroinflammation; beta-hydroxybuterate; lipopolysaccharide; neurodegenerative disease
ORAL HEALTH

[063-G] Oral Microbiome Analysis using Ion Torrent Next-Gen Sequencing Technology

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Background: Little is known about the changes in the oral flora during pregnancy or whether pregnancy provides some selective advantage to microbial strains which have been shown to affect pregnancy outcome. *P. gingivalis* strain A7A1-28 is a strain of interest as it appears to be associated with adverse pregnancy outcomes but not severe periodontitis. The focus of this project is to explore changes in the oral microbiome due to *P. gingivalis* strain A7A1-28 infection and pregnancy. This will be accomplished by creating a 16S microbiome profile of rats which will describe both the microbial diversity and abundance of the total microbial population sampled. Through this focus, we endeavor to answer the question: What oral flora changes occur in relation to a *P. gingivalis* strain A7A1-28 infection in an *in vivo* pregnancy setting?

Methods: The Next-Generation Sequencing workflow focuses on targeting seven of the nine variable regions of the 16S bacterial rRNA gene to determine the type and abundance of bacteria present in each sample. The 16S rRNA gene is well conserved across bacteria except for these nine variable regions which can be sequenced to determine the specific bacteria present down to the genus and, possibly, species levels. 33 oral specimens were collected on either a nylon cytology brush or rayon swab from the Sprague-Dawley rats at set time points. DNA extracted from these samples was enriched for microbial DNA by removing eukaryotic DNA. Using the microbial genomic DNA as the template, the 16S gene was PCR amplified at seven of the nine variable regions. These sample amplicons were then processed to create uniquely barcoded libraries which were pooled at equal molar concentrations. The pools are now currently being templated using the Ion OneTouch 2 System and sequenced using the Ion Torrent Personal Genome Machine.

Results: DNA has been extracted from samples and the microbial DNA separated from the eukaryotic DNA. The 16S variable region PCR amplification has led to consistent results between samples. The adaptor ligation resulted in uniquely distinguishable libraries when sequenced. Lastly, the first sequencing completed resulted in data collection in the fragment length and chip coverage desired.

Conclusions: This project is currently in progress and has thus far proven successful. The final templating and sequencing steps are being completed. Once finished, the data will be analyzed to create the desired microbiome profiles.

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Keywords: microbiome profile, 16S rRNA gene, Next-Gen sequencing, Ion Torrent
[071-U] Relationship of Fat-Free Mass and Fat Mass to Body Weight in College Football Players

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Background: College football is a sport dominated by size and typically classified in terms of height and body weight. Less frequently evaluated is the compartmentalization of body weight into its chief components of fat-free mass (FFM) and fat mass (FM). FFM is the functional component as it is closely associated with maximal voluntary strength. In contrast, FM plays an important role in energy balance and may coincidentally serve a shock absorption role with respect to football. With the ever increasing emphasis on body mass associated with football, the question begins to focus on the limits FFM and FM accumulation. The present purpose is to determine the relationship of FFM and FM to height and body weight across the range of height and body weight typically observed in college football players.

Methods: Fifty-seven NCAA D-II football players (age = 20.1 ± 1.2 y) volunteered to serve as subjects in this correlational study. Body composition was assessed using dual-energy x-ray absorptiometry (DEXA). This technique provides compartmentalized and regional estimates of lean (bone, muscle, etc.) and fat tissue from which FFM and FM are determined.

Results: FFM and FM were significantly related to height (r = 0.74 and 0.65, respectively) and body weight (r = 0.93 and 0.97, respectfully). The relationship between body weight and FM was significantly greater than with FFM. FM accounted for 70.2% of the variance in body weight, while FFM accounted for only 29.8%. The relationship between FFM and FM was significant (r = 0.85), but curvilinear, showing a great accumulation of FM at higher body weight.

Conclusions: FFM increases linearly with height, but appears to reach an asymptote with respect to body weight suggesting that players are approaching a theoretical limit of FFM accumulation. In contrast, the accumulation of FM follows height, body mass and FFM with an apparent limit of accumulation beyond the anthropometric and energy balance characteristics of this present sample of players.

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Keywords: fat-free mass accumulation, DEXA X-ray, body mass compartments
EXERCISE SCIENCE

[072-G] Time-Dependency of Fatigue is Independent of Blood Pressure and Heart Rate Variability Response

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Background: Previously we observed dissociation of skeletal muscle activation and recovery of force generation in sustained maximal voluntary isometric contractions. Fatigue was specifically related to reduced muscle activation within bouts; yet, incomplete recovery of force between bouts occurred in the face of maximal muscle activation. This suggests interference in excitation-contraction coupling. The present purpose is to repeat previous experiments while estimating central drive from changes in heart rate (HR) and blood pressure (BP); previous experiments suggested similarly differential effects.

Methods: Subjects (n=6) performed two bouts (B1, B2) of sustained maximal voluntary isometric handgrip contractions separated/followed by 10-min recovery periods. HR (Lead II ECG), and BP (auscultation), and force (dynamometer during bouts) were collected continuously throughout the 35-min experiment. HR variability was analyzed using time-domain ((RR interval standard deviation (SDRR); RR range (dRR)) and frequency-domain (FFT of decomposed Lead II signals to spectral density of high- (0.15-0.4 Hz), low- (0.04-0.15 Hz), and very low- (0.003-0.04) frequency) analyses.

Results: Isometric force declined similarly in B1 and B2 (75 and 72%); yet B2 initial force was less than B1 (20%). Fatigue progressed in two-phases; fast mechanical response was similar in both bouts despite differences in initial force (B1: y=-2.14x+224 N; B2: y=-0.182x+17.9 N). Slow-phase inflection occurred at 75-sec (B1) and 60-sec (B2); being earlier in B2 at the same level of initial force (68 and 67%, respectively). Slow-phase force and mechanical response was similar in B1 (y=-0.323x+110.7 N) and B2 (y=-0.216x+88.5 N). SDRR and dRR were reduced during each contraction bout; recovering to pre-contraction levels between bouts. High-frequency band decreased while low-frequency increased; reversing rapidly during recovery. HR and BP increased rapidly during each bout; returning to pre-contraction levels by 1-min post contraction.

Conclusions: The two-phase mechanical response and delayed recovery are similar to previous observations. Changes in HR, BP and time- and frequency- domain analyses of HR variability suggest a similar pattern of response and recovery not related to delayed recovery of muscle force. Experiments will continue; to include investigation of sex-specific differences in mechanical and neural response to contractions and recovery.

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Keywords: muscle force, sympathetic drive, heart rate variability, fast-phase fatigue, slow-phase fatigue
Comparison of Techniques for Tracking Body Composition Changes Across a Basketball Season

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**Background:** Assessing body composition is a significant part of an athlete’s year-round training program. Various methods are used to estimate percent body fat (\%fat). In particular, bioelectrical impedance analysis (BIA) has gained popularity due to cost, ease and speed of use in estimating \%fat. BIA is based on tissue electrical conductance, which is altered by training, thus, selected models have an “athlete” setting that purports to enhance measurement accuracy. Limited information is available regarding accuracy of various methods to track body composition changes over a competitive year cycle as compared to clinical standards. The purpose of the study was to validate various methods of tracking body composition across a college basketball season.

**Methods:** Fourteen NCAA D-II women (age = 20.1 ± 1.2 y) with 4-8 yrs of competitive experience were subjects. Each player was evaluated pre-season (T1), after pre-season conditioning (T2), mid-season (T3), and post-season (T4). Dual-energy x-ray absorptiometry (DXA) was the criterion measure. Height, weight, and skinfolds (SKF), bioelectric impedance analysis (BIA), and DXA \%fat were measured. SKF sites included biceps, triceps, subscapular, suprailiac, abdomen, and thigh. Site were measured 3 times and averaged for prediction of \%fat using the Jackson-Pollock (JP) and Durnin-Wormsley (DW) athlete-specific equations. Two BIA models (hand held; HBIA or foot scale model; FBIA) with athlete settings were used to estimate \%fat.

**Results:** A method x trial factorial ANOVA of \%fat with repeated measures over the second factor indicated JP, HBIA, and FBIA were not significantly different, FBIA and DXA were not significantly different, and DXA and DW were not significantly different. Across trials, T1 was significantly greater than T2 but did not differ from T3 or T4. Correlations between DXA and the other methods were high (ICC=0.95–0.97). Rank-order correlation of DXA with the other methods indicated HBIA (rho=0.67–0.78) and FBIA (rho=0.62–0.77) were the only acceptable techniques; both SKF equations had lower correlations (rho=0.46–0.73).

**Conclusions:** Compared to the DXA standard, the FBIA device may provide adequate relative tracking of \%fat across a basketball season. Skinfold equations do not provide adequate patterns for tracking \%fat, with the JP equation offering the closest parallel pattern of change but significantly lower \%fat values.

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**Keywords:** DXA, skinfolds, bioelectrical impedance analysis, women athletes
[074-G] Gait Transition Not Related to Kinematic or Metabolic Input in Humans

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Background: Human bipedal locomotion is characterized by two distinct gait patterns; walking and running. Gait transition is directly related to horizontal velocity, since humans cannot accelerate beyond a certain velocity while maintaining double limb support; definition of walking. Adopting a running gait allows quicker, more energetically efficient travel than high velocity walking. Gait transition is influenced by factors other than horizontal velocity; our purpose is to investigate the role of kinematic and metabolic factors in gait transition.

Methods: Walk-run (WRTS) and run-walk (RWTS) transition speed was determined in subjects (n=6 to date) during treadmill bouts separated by a 20-min rest period. WRTS: treadmill speed is increased from 3.5 mph in 0.1 mph increments every 30-sec until assuming a running gait. RWTS: treadmill speed is decreased from 5.5 mph in 0.1 mph decrements until assuming a walking gait. Each bout continues for 2-min after transition. Kinematic data is recorded with an infrared timing device. Pulmonary function includes peak expiratory flow rate (PERF) and maximal voluntary ventilation (MMV) determined prior to each bout. PERF, minute ventilation (VE), and heart rate (HR) are recorded throughout each bout. Sense of effort (Borg CR-10 scale) is recorded at the end of each 30-sec period.

Results: WRTS was 4.3±0.4 mph with increasing stride length (StL:149±9-168±10) and decreasing stance time (746±42-457±52 ms) at transition; not changing following transition (StL=162±13; stance=393±46 ms). Sense of effort increased from onset of walking (weak, 2±0.5) to transition (strong, 6±2). HR (114±19-149±23), breathing frequency (F; 18±6-26±5 b/min), VE/MVV (0.20-0.31), PERF_bout/PERF (0.22-0.27) increased as transition. RWTS was 4.3±0.2 mph with decreasing StL (188±25 to168±18) and increasing stance time (368±30-580±37 ms) at RWT; not changing following RWT (StL=173±13; stance time=530±110 ms). Sense of effort decreased from onset of running (strong, 6±1) to transition (weak, 2±0.5). HR (153±21-144±26) and f (29±5-26±2 b/min) did not change, but VE/MVV (0.41-0.36) and PERF_bout/PERF (0.34-0.29) increased at RWTS.

Conclusions: WRTS and RWTS were similar; however, the absence of hysteresis is notable. The magnitude of pulmonary response, but not HR appears dissociated from sense of effort. Lack of change in these and kinematic variables suggests they play no role in gait transition. Data collection continues.

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Keywords: stride length, run-walk transition, sense of effort, walk-run transition, ventilation
[075-FS] Biological Variation and Bilateral Asymmetry of Human Gait

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**Background:** Human gait is believed to be symmetrical and regular. In contrast, emerging evidence shows gait to be asymmetrical and random, but constrained; variable. Motor pathologies lead to variability, asymmetry, dysfunction and/or injury by destabilizing balance and altering gait dynamics. A current lack of understanding and quantification of gait asymmetry and variability leads to difficulty differentiating normal and pathological gait. Such understanding is an important step in establishing reliable diagnostic protocols and is the purpose of the present investigation.

**Methods:** In a retrospective analysis, subjects (n=30) had completed gait testing; walking on a treadmill for 5 minutes at 3 mph with data collected during the final 1-min. The retrospective analysis led to the present study design. In the ongoing study, subjects (n=5 to date) complete two, 8-min bouts of walking on two days, separated by 5-days. Same-day bouts are separated by 20-min of passive rest. Anthropometric assessment includes leg length and circumferences. Kinematic data are collected using an infrared optical timing system. Subjects are fitted with 3-dimensional accelerometers (each ankle and dorsum of the pelvis) from which kinetic variables are derived. Asymmetry index is calculated as: \((L-R)/(0.5*(L+R))\).

**Results:** Our retrospective gait analysis revealed notable asymmetry (AI) for step length (SL) (among other variables) and 3 groups (G) emerged. Asymmetry in G1 (n=5), post-ACL surgery showed SL AI of ±25% oriented towards the involved limb. G2 (n=11) reported no history of lower body injury with SL AI ± 15% without dominance. G3 (n=14) reported a history of injury/surgery >2 years post event without symptoms; SL AI ±20% without dominance. Preliminary data from the ongoing study show a similar, repeatable SL AI (±5–15%) with apparent dominance in some cases. Previous and preliminary data analysis suggests a biological variation for SL asymmetry of ±5%. Poincare plots are used to define the range variability from retrospective and new data revealing a potential means for identifying an aberrant gait.

**Conclusions:** Biological variability and asymmetry in gait requires quantification towards understanding. The test-retest design and longer duration of gait trials in the ongoing study will allow for identification of biological variation and asymmetry of kinematic and kinetic data and initial attempts to use non-linear dynamics for assessing gait variability.

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**Keywords:** asymmetry index, step length, gait variability

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Introduction: Bilateral asymmetry has been observed in muscular strength/power movements and has been linked to poor performance and/or risk of injury. The present purpose is to investigate bilateral asymmetry during jumping in men.

Methods: Athletes (A, intercollegiate sports; n=13) and physically active (C, n=11) men gave informed consent to participate in this university approved study. Subjects completed repeat trials of a 2-leg (2L) and single-leg (1L; left and right leg) squat jump without countertormovement; data averaged across trials. Jumps were conducted on individual force plates (2L) or singularly for 1L. Jump height (JHt) was calculated from jump impulse (IMPₐ) determined from ground reaction force and from flight time (Δt). Asymmetry index was calculated as (L-R)/(0.5*(L+R)). Bilateral facilitation/deficit was determined from jump performance as (1L+1R)/2L). ANOVA was used to evaluate differences with significance accepted and reported with p<0.05.

Results: 2L (A: 36.7±0.4 cm; C: 33.7±0.8 cm) and 1L (left & right: A: 17.6±0.3 & 16.6±0.4 cm; C: 16.4±0.6 & 16.3±0.4 cm, respectively) JHt were similar between groups. An extreme bilateral asymmetry (AI range 37 to -58%) was noted in IMPₐ during 2L; individual leg IMPₐ was not related to JHt (r=0.13 left; r=0.14 right). To accomplish the same 2L JHt both groups produced a greater jump impulse in one leg (A: 135.1±25.4 N; C: 108.3±24.1 N) vs the other (A: 111.6±19.7 N; C: 89.1±11.9 N); accounting for asymmetry. 2L performance was associated with a bilateral deficit (n=4) or facilitation (n=15); yet, neither bilateral asymmetry nor deficit/facilitation impacted performance directly. The top 5 jumps (>40cm) were recorded from 2 A and 3 C with a bilateral asymmetry of 10-40% and bilateral deficit (2-19%) or facilitation (5-12%). 1L JHt was also poorly related to IMPₐ (r = 0.58 left and 0.50 right); likely due to poor balance indicated by pattern (slope, appearance of plateaus, flat peak, etc) of force expression.

Conclusion: Performance of a 2-leg squat jump is associated with extreme IMPₐ bilateral asymmetry (range ±45%) and is independent of training status. Expression of bilateral facilitation or deficit does not appear to impact jump effectiveness. 1L jump performance is limited in its ability to explain 2L jump performance, bilateral asymmetry, or neural strategy (bilateral deficit/facilitation) likely due to balance issues.

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Keywords: asymmetry index, bilateral facilitation, bilateral deficit, jump impulse, velocity
Cardiac Structure-Function and Aerobic Capacity in a Cross-Section of College Athletes.

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Background: Athletes (A) conduct intense physical training to attain peak performance. Intense training is associated with cardiac remodeling, altered blood pressure regulation, and cardiac electrical abnormalities. These changes have been linked to sudden cardiac death in A. Our purpose is to investigate the relationship between structural changes and electrical abnormalities in the heart to aerobic capacity (Vo$_{2}$max) in collegiate athletes and controls.

Methods: A cross-section of NCAA athletes (A; n=9) and healthy men and women (C; n=7) volunteered for this Institutional Review Board approved study. Measurements included anthropometric assessment (DEXA body composition), resting ECG, and a graded exercise test (GXT) with cardiac echocardiography/Doppler ultrasound performed before and immediately following the GXT (>85% of maximal predicted heart rate). The GXT was conducted on a treadmill (6 mph) with increasing grade (2-min intervals, 0%, 4%, then 2%/interval) to Vo$_{2}$max. Respiratory gas measurements (Vo$_{2}$, etc.) were collected during the GXT with an open-flow, indirect calorimetry system.

Results: At the same height, A had greater body mass and surface area with greater fat-free mass (A=63.1±10.8 kg; C=41.3±18.6 kg) bone mineral density (A=1.325±0.17 g cm$^{-2}$; C=1.16±0.08 g cm$^{-2}$) and lesser fat mass (A=12.2±3.5 kg; C=17.9±7.07 kg). Resting heart rate (A=59±10; C=63±9) and blood pressure (A=115/72±15/6; C=111/68±7.7/7.9) were not different. There were no differences in resting stroke volume or cardiac output (A=4.79±1.43 l min$^{-1}$; C=4.85±1.46 l min$^{-1}$). Ultrasound measurements left ventricular (LV) end-diastolic dimension and posterior and septal wall thickness provide evidence of cardiac remodeling (n=3) and eccentric hypertrophy (n=1) in A. ECG analysis showed PVC's (n=1), voltage criteria for LV hypertrophy (n=2), and evidence of peaked T-waves (n=3), J-waves (n=4), and U-waves (n=3) in A. Vo$_{2}$max (A=50.0±8.6 ml kg$^{-1}$ min$^{-1}$; C=43.5±5.9 ml kg$^{-1}$ min$^{-1}$) and maximal heart rate (A=186±11 b min$^{-1}$; C=187±8 b min$^{-1}$) were not different. Post-exercise cardiac output (A=15.26 l min$^{-1}$; C=9.17±5.02 l min$^{-1}$) and stroke volume (A=87.86±31.9 ml beat$^{-1}$; C=55.17±29.84 ml beat$^{-1}$) were greater in A.

Conclusions: ECG abnormalities are considered normal and benign according to Seattle ECG criteria for A. Interestingly, these preliminary results show no relationship between post-exercise cardiac output and Vo$_{2}$max. Future direction: continue data collection.

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Keywords: echocardiography, electrocardiography, ventricular mass
Introduction: Previous research indicated that upper-body muscular strength gains from resistance training may be greater in individuals with higher initial fat-free mass (FFM). Further results also suggest that individuals with lower initial strength levels gain significantly more than those with higher strength levels. However, strength and size factors have not been analyzed simultaneously to determine the interactive effect of these components. The purpose of the study was to evaluate the improvement in upper-body muscular strength resulting from resistance training using free weights (FW) and machine weights (MW).

Methods: College men (n = 150) and women (n = 133) enrolled in a required wellness course volunteered to participate. Each participant was measured before and after 12 weeks of periodized resistance training for 1RM on free-weight (FW, n = 160) or machine weight (MW, 123) bench press and fat-free mass (FFM) predicted from skinfolds assessment. Mode-specific bench press training was supplemented with auxiliary upper- and lower-body exercises were performed in 3 sets of 6 repetitions. Bench press was periodized with progressively heavier loads and reduced repetitions designed to achieve maximum strength improvement.

Results: A gender x training mode ANOVA indicated men had significantly more FFM than women but there was no significant difference in FFM between FW (62.3 ± 9.6 kg) and MW (60.8 ± 9.9 kg) groups. A gender x training mode ANCOVA holding initial muscular strength and FFM constant indicated that men gained more strength (9.1 ± 5.7 kg) than women (5.9 ± 5.5 kg), the MW group (9.5 ± 5.4 kg) gained more upper-body muscular strength than the FW groups (6.2 ± 5.7 kg), and there was no significant interaction between the factors.

Conclusions: When differences in initial FFM and strength are accounted for, training on MW produce a significantly greater increase in upper-body strength compared to FW. It might be wise for beginning lifters to utilize machine weights to make greater improvements in upper-body strength before moving to free weights.

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Keywords: resistance training, free weights, machine weights
[079-U] Accuracy of Bench Press Load and Repetitions-to-Failure for Tracking Changes in 1RM Bench Press in College Women

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Introduction: Previous research has shown submaximal loads and repetitions-to-failure (RTF) in the bench press can predict one-repetition maximum (1RM) with acceptable accuracy. However, limited information exists on the ability of this approach to track change in upper-body strength following resistance training in previously untrained women. The purpose of this study was to evaluate the accuracy bench press submaximal load and RTF to predict changes in upper-body muscular strength (1RM) following training in college women.

Methods: Untrained college women (n = 276) enrolled in a wellness course volunteered to participate. Each participant was measured for free-weight 1RM and one RTF trial using one randomly selected submaximal load (55-95% 1RM) before and after 12 weeks of resistance training. A linear periodization training program was conducted 3 times per week using 6 free-weight exercises.

Results: Pre-training (Eq 1: 1.10 Rep Load + 0.40 RTF + 0.54) and post-training (Eq 2: 1RM (kg) = 1.22 Rep Load + 0.46 RTF – 3.2) prediction equations were developed on the validation sample using repetition load and RTF. Eq 1 and Eq 2 had similar multiple correlations (R = 0.86 and 0.87, respectively) and slightly different standard errors of estimate (SEE = 3.3 and 3.8 kg, respectively) but similar coefficients of variation (11.0 and 10.5%, respectively). Eq1 predicted 53% of the pre-training cross-validation sample within ±10% of their actual 1RM. Eq2 predicted 71% of the post-training cross-validation sample within ±10% of their actual 1RM. Using Eq1 to predict post-training 1RM resulted in 72% of the sample within ±10% of their actual 1RM. In all 3 equations, the greater the actual 1RM, the more under-predicted the values were (r = -0.53, -0.30, and -.48, respectively).

Conclusions: Bench press repetitions using a submaximal load maybe an acceptable alternative to actual 1RM bench press testing before or after resistance training in the majority of college women but may underpredict stronger individuals.

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Keywords: bench press repetitions, college women
[081-G] Comparison of Ultrasonography Utilization in Rural Versus Urban Emergency Departments Across the State of Missouri

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Background: Point-of-care ultrasonography is a powerful tool for emergency situations because it can assist diagnosis and reduce costs, but the availability of equipment and training for the use of this technology vary across hospitals of different sizes. In Missouri, there are 136 hospitals with emergency departments: 48 are in rural areas, 59 are located in urban areas, and 29 are in intermediate areas between rural and urban. Considering the increasing role of ultrasonography for the evaluation of multiple patient scenarios within the emergency department, our study investigated the role of bedside, point-of-care ultrasonography in various-sized hospitals across the state of Missouri.

Methods: All Missouri hospitals with an emergency department were contacted via phone to participate in a three-question, electronic survey hosted on Google Forms. Only emergency department directors or supervisors were asked to complete surveys. The survey asked respondents: 1) if the emergency department uses ultrasonography; 2) what types of scans the department employs; and 3) what factors would increase the usage of ultrasound. Answer choices were predefined. Questions two and three allowed a write-in response for “Other.”

Results: Fifty-six hospitals responded. Thirty-seven of these (66%) indicated they use ultrasound in the emergency department. A strong association was found between the hospital size and use of ultrasonography using a Chi-Square test (P=0.0002). Vascular access, trauma-related, and pregnancy-related scans were found to be the most common uses for ultrasonography in emergency departments across all categories. More than half of all rural, urban, and intermediate hospitals agreed more training would increase its use. Lack of available equipment was also noted as a factor to increase use for rural and intermediate-sized hospitals but was noted less for urban hospitals.

Conclusions: While the advantages of the use of ultrasonography in the emergency department are clear, our results indicated that training and equipment availability remain challenging for smaller Missouri hospitals.

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Keywords: point-of-care ultrasound; rural healthcare; emergency department; ultrasound equipment; ultrasound training
HEALTH CARE

[082-G] Respiratory Effects of the Eruption of Momotombo Volcano in Chacraseca, Nicaragua

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Background: Aside from the initial eruptive risks, ashfall deposits from volcanoes can remain in the local environment for years and are hazardous to respiratory health. New respiratory conditions can be observed, such as asthma and silicosis, in addition to the worsening of chronic conditions. Chacraseca, Nicaragua is a farming community east of Leon, Nicaragua and within 81 kilometers of the Momotombo Volcano, which has been intermittently erupting after over 100 years of dormancy since December 5, 2015. These community members experience poor living conditions and health care, placing them at risk for environmental exposure.

Methods: A retrospective survey was modified from the European Community Respiratory Health Survey to fit the educational level of participants. The survey was orally performed by qualified translators as part of a medical history questionnaire distributed at a medical outreach project organized by Power of a Nickel with support from the Nicaraguan Ministry of Health in May 2016.

Results: Out of 747 participants, results were analyzed overall and for two specifically at risk populations, those with previous respiratory issues as well as infants and children under five years old. 146 reported previous respiratory problems, however, less than a third (21.9%) of those participants reported worsening of problems since the eruption. Of the infants and children under five years old, 14 out of 141 (9.9%) reported respiratory problems since the eruption. However, all 14 reported a worsening of symptoms since that time period. Overall, 87 out of 747 (11.6%) participants reported symptoms since the eruption, with 60 of the 87 (69.0%) also reporting a worsening of symptoms.

Conclusions: This survey did not support an overall worsening in the respiratory health of the people of Chacraseca, Nicaragua due to the recent eruption of the Momotombo Volcano. However, it is pertinent to note that all symptomatic infants and children under five years old contributed worsening of symptoms to the eruptive period as well as a majority of the total participants reporting symptoms since the eruption. Additional studies such as soil and air quality analyses would be needed to correlate these results to volcanic ash and exclude the many other health hazards these people face.

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Keywords: volcanic eruption, respiratory health, Nicaragua

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**Background:** Real world evidence from Phase IV (impact) and development studies addresses questions: “How does a new therapy, drug, or treatment system impact, disseminate, and express in actual practice and application? Does such an innovation improve personal and public welfare? Is it being used as prescribed? Or is it seriously misused, under-used, or over-used and thus creates unintended consequences to overwhelm potential benefits? Quasi-experimental data may be collected from patient surveys of symptoms and side effects, economic behaviors, and unobtrusive measures. Data might be macro to personal levels in non-randomized field observations. For such data, conventional statistics do not apply. Quasi-experimental methods (QEM) have been developed from the 1950’s through 1960’s for program evaluation and other inquiry where random selection and assignment are not practical. RCT remains the gold standard, yet lacks some external validity. Quasi-experimental methods may have statistical power comparable to some experimental methods in translating RWD to RWE. Here we focus on a particular QEM: the regression discontinuity design (RDD).

**Methods:** Demonstrate the use of regression discontinuity design in examining econometric data of the impact of a smoking ban in Flagstaff, Arizona in 2009. Also used are data from the Pueblo, Colorado smoking ban study on acute myocardial infarction.

**Results:** The effect of a smoking ban in Flagstaff, AZ on bar patronage was minimal. The effect of a smoking ban on acute MI in Pueblo, CO was dramatic.

**Conclusions:** The regression discontinuity design adds compelling evidence for cause and effect when randomized experiments are not feasible. Other quasi-experimental methods can be used for translating real world data into real world evidence.

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**Keywords:** methodology, statistics, Phase IV, impact studies, real-world evidence.
[084-G] Survey of Community Knowledge about Zika virus in Chacraseca, Nicaragua

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Background: As part of the DOCare International/Power of a Nickel trip to Nicaragua in May/June 2016, we developed a survey to assess knowledge and understanding of Zika virus disease, symptoms, transmission, and prevention in the communities of Chacraseca. The survey also explored knowledge of associated birth defects in relation to sexual practices.

Methods: 51 patients were interviewed by members of the medical teams from ATSU-KCOM and CCOM/MWU through Power of a Nickel. Patients were interviewed while they were waiting to be seen at the clinics set up by the teams in communities around Chacraseca. Interviewers were provided a script in both English and Spanish for data collection. Survey included 14 yes/no questions and 2 open-ended questions. All patients interviewed were provided a handout with information about Zika virus and prevention after the survey.

Results: Most patients were aware of the virus and its presence in Nicaragua, but not everyone. While almost everyone knew that mosquitoes can transmit Zika, there were many misconceptions about food and water also being sources of infection. Most patients were aware of the association with birth defects, and a few have changed their plan for pregnancy because of the risk, but a significant percentage of patients do not use birth control to prevent pregnancy.

Conclusions: Public health education about Zika virus would be beneficial to the community, especially regarding transmission and prevention. The use of birth control in relation to Zika virus needs further study.

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Keywords: Zika virus, public health survey, Nicaragua
[091-G] Biophysics of the Varanid Tympanic Membrane

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Background: Monitor lizards (Varanus) have internally-coupled ears in which the contralateral tympanic membranes are linked by patent passageways through the skull. Recent bio-physical models of this system have treated tympanic membranes as uniform vibrating disks. Whether or not the tympanum is actually homogeneous in its response to sound is unknown. In animals with internally-coupled ears, changes in pharyngeal pressure (e.g., swallowing, yawning) would affect tympanic baropressure, thus possibly affecting its auditory capacity. In humans the tympanic membrane is divided into a stiff pars flaccida that functions in baropressure regulation, and a flaccid pars tensa for vibratory response. No such division has been reported in any reptile including varanid lizards. By investigating the biophysical properties of the Varanus tympanum, we intend to answer the following questions: 1) is the current model of ICE an accurate representation of the actual tympana, and 2) is the varanid tympanum functionally similar to that of mammals?

Methods: Two hatchling and two sub-adult water monitors (Varanus salvator) were anesthetized with isoflurane and placed in an acoustic isolation chamber. Acoustic stimuli were applied, and the vibrational response of selected sites on the tympanic membrane was quantified. The tympanum of three sub-adult V. salvator was excised. Stress/strain curves were generated using a custom tabletop tensiometer. These biomechanic trials were performed on the dorsal and ventral portions of each tympanum separately.

Results: The Young’s modulus of the stress/strain curves from the dorsal and ventral regions are significantly different. The dorsal portion of the membrane is more pliable and the ventral portion is stiffer. Several variations of the tympanic vibrational response trials were performed, and they all report that the ventral portion of the tympanic membrane vibrated significantly more than the dorsal portion.

Conclusions: The clear differential vibrational and biomechanic responses of the tympanic membrane of Varanus salvator suggest that the recent biophysical models of internally-coupled ears are incomplete. The results of the present study suggest that Varanus salvator has evolved a tympanic membrane that is analogous to the mammalian system in being functionally segregated into vibrational and baropressure regions.

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Keywords: Varanus salvator; internally-coupled ears; tympanic heterogeneity; biophysics
[092-U] Effects of a Cyclophilin 1 Mutation on *Drosophila* Locomotion

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**Background:** Cyclophilin 1 (*Cyp1*) codes for peptidyl-prolyl isomerase (PPlase), which is an enzyme in the cyclophilin family of proteins that catalyze the conversion of cis and trans protein isomers. This occurs during protein folding where most proteins tend toward the trans isomer; PPlase allows proteins to be folded into cis isomers at an equivalent rate. In *Drosophila melanogaster*, the functions of Cyp1 are undefined and its molecular interactions unknown. However in humans, PPlase proteins catalyze protein-folding, mediate cardiovascular disease, facilitate viral replication, and contribute to cancer malignancy. An insertion of a P-type transposable element was found within the N terminus of *Drosophila Cyp1*. The effects of this *Cyp1* mutation on animal behavior were assessed using a larval locomotion assay.

**Methods:** For the larval locomotion assay, third instar larvae are placed in the middle of an agar plate and allowed to freely roam for a 2 min period. The larvae are then removed and the plate illuminated to view the larvae’s path, which is then measured for distance traveled, number of ‘searches’, and overall trajectory.

**Results:** Compared to its genetic control, the *Cyp1* mutation altered larval locomotion by increasing the number of ‘searches’ (mean number of searches, number of animals; genetic control: 1, N=30; *Cyp1*: 5, N=30). Larval ‘searches’ are instances in which the animal veers off of its path, changing the direction of locomotion but then reverses itself to continue along the original path or to travel along a new path. Changes in larval searching might arise from changes in the development of the central or peripheral sensory or motor circuitry. Current experiments are examining other *Cyp1* alleles for a similar locomotion phenotype. In addition, we are looking for defects in synapse formation between motoneurons and larval body wall muscles using immunohistochemistry to identify presynaptic terminals and boutons. We are also beginning to use RNAi transgenes against Cyp1 to identify which tissues are altered in the mutant to affect larval searching.

**Conclusions:** This is the first characterization of mutations affecting the *Drosophila Cyp1* gene. Further genetic work in *Drosophila* could be useful for identifying the molecular pathways used by cyclophilin family members in healthy cells and during human disease.

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**Keywords:** *Drosophila melanogaster*, protein folding, Cyp1, locomotion, peptidyl-prolyl isomerase
Overall winner: Austin J. Shackelford, BA, for his poster in the Oral Health category: Ketones Alleviate Neuroinflammation through Modulation of Metabolic Sensors

Sigma Xi (undergraduate) winner: Maria Kondrashova, for her poster in the Cancer Biology category: Investigation of Affinity at Binding Site Between Human Epidermal Growth Factor Receptor 2 (HER2) and Herceptin

Student winners:
Andrew M. Diaz, BA, for his poster in the Cancer Biology category: TGFB Engages MEK/ERK to Differentially Regulate Benign and Malignant Pancreas Cell Function
Charles A. Taylor, BS, MS, for his poster in the Cancer Biology category: Heparin Sulfate 3-O-Sulfation Increases Progenitor Cell Expansion
Erika Y. Choi, OMSII, for her poster in the Neuroscience category: Effects of Amentoflavone on the Aggregation and Disaggregation of Amyloid B
Caleb Bischoff, for his poster in the Exercise Science category: Squat Jump Performance Is Not Related to Bilateral Asymmetry or Training State in College-aged Men

Faculty/Staff winners:
Brett Berke, PhD, for his poster in the Neuroscience category: Target-dependent retrograde signaling mediates synaptic plasticity at the Drosophila neuromuscular junction
Renuka Ramachandra, PhD, for her poster in the Neuroscience category: Using specific blockers to identify TTX-S Nav channels subtypes in Rat muscle afferent neurons
William F. Brechue, PhD, for his poster in the Exercise Science category: Biological Variation and Bilateral Asymmetry of Human Gait
Zane Starks, MS, for his poster in the Musculoskeletal category: Effect of Postural Sway and Breathing on Postural Measurements using Surface Topography
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