



DMU 
Research
Symposium



December 5, 2013
Des Moines University
3200 Grand Avenue
Des Moines, IA

**Des Moines University's
Research Vision is to be...**
A cultivator of distinctive faculty and
student researchers who discover
and disseminate new knowledge.

**DMU Research Symposium
December 5, 2013
Des Moines University, Des Moines, IA**

Welcome

Welcome to the fourth annual Des Moines University (DMU) Research Symposium! One of DMU's four vision statements is to become "a cultivator of distinctive faculty and student researchers who discover and disseminate new knowledge." There is no event that captures this vision better than our Symposium where the entire DMU campus comes together to recognize the efforts of our students, faculty, and our colleagues from the health care and scientific community. We celebrate their success by demonstrating the critical role research plays in the advancement of health care, providing a forum for the collaboration of ideas, and fostering the production of new hypotheses. The research presented here is multidisciplinary; it is the result of countless hours of effort and has real potential for impacting knowledge across disciplines. I continue to be impressed with the ever-growing interest and participation in research and scholarship at DMU.

We are excited to have Dr. Laurel Haak, who currently serves as executive director of ORCID, a discovery and collaboration network, as our keynote speaker. Originally trained as a neuroscientist at Stanford University Medical School, Dr. Haak's career has evolved to include information technology and work on diversity in health research. Prior to her leap into information technology she worked at the National Academies where she directed workforce policy studies on international students, interdisciplinary research, women in academia, postdoctoral researchers, and innovation policy. Dr. Haak's keynote address will discuss the development of persistent identifiers to track and promote your career and consider whether race, gender and ethnicity impact the likelihood of receiving significant research funding.

I would like to thank our organizing committee for their efforts in putting together such a high quality program: Dr. Feilmeier, Dr. Nguyen, Dr. Ronnebaum, Vanessa Ross and especially our student members Kristin Kindred, DPM'16, Kelsey Randel, DO'16, and Nolan Wright, DPT'14. If you get a chance, please congratulate them. In addition, I am very grateful to the individuals who are serving as abstract judges. These individuals are instrumental in ensuring an enriching experience for the Symposiums students and residents.

DMU is striving to become a leader with our research culture and environment; this Symposium demonstrates the strong research that is occurring on campus and in our community. While attending the oral presentations and viewing the posters, I hope you will reflect on how the discoveries we are making in research today will impact the scientific and medical community and the future of our patients.

Please enjoy the Symposium and thank you for attending!

Jeffrey T. Gray, Ph.D.
Vice President for Research, Des Moines University

Agenda

Time		Location
9 a.m.	Poster Viewing	SEC First Floor (Near the Bookstore)
12 p.m.	Lunch	SEC Auditorium and Academic Center Lecture Hall 2
12:30 p.m.	Diversity, Databases, and Discoverability <i>Laurel L. Haak, PhD, Executive Director, ORCID</i> <ol style="list-style-type: none"> Analyze the impact of the relationship between race, gender and ethnicity in the likelihood of receiving significant research funding. Use effective evaluation plans in research grants, particularly those that relate to training and development programs. Use tools to pro-actively improve the effectiveness of career tracking, evaluation efforts, and utilization of mentors. Discuss professional career tracking plans to improve the discoverability of researchers and clinicians in the scientific community. 	
1:30 p.m.	Poster Presentations	SEC First Floor
2:15 p.m.	Break	
2:30 p.m.	Oral Presentations (Concurrent Sessions)	Academic Center Lecture Halls
3:30 p.m.	Break	
3:45 p.m.	Poster Presentations	SEC First Floor
4:45 p.m.	Awards Presentation	
5 p.m.	Adjourn	

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Purpose

The Research Symposium aims to recognize the research efforts of those at DMU and in the surrounding medical and scientific community by providing a forum for the collaboration of ideas, the production of new hypotheses, and to demonstrate to the attendees the critical role that research plays in the advancement of health care.

Research Opportunities

Mentored Research Program for DMU students

The mentored research program is a competitive program which encourages DMU students to work in one of the wide range of research projects at DMU. Funding for this program is provided by the research and grants committee. Each year, four students are selected to receive a \$2,000 tuition scholarship with the remaining students receiving a stipend during the program. The program began in 2002 and is a robust and active research opportunity at DMU. The eight week program also includes three lunch and learn sessions, a closing program consisting of a guest speaker, poster and power point presentations. All applications are due by March 3, 2014. Additional information can be found at <http://www.dmu.edu/research/student-research-opportunities/>.

Mentored Research Program for Undergraduate Students

The undergraduate mentored research program is committed to providing an array of research experiences to undergraduate students. Selection of applicants is based upon academic performance in the sciences, statement of career and academic goals and letter of recommendation from a biology or health science faculty member. Selected students will work with faculty researchers for an eight-week period usually in June and July, on projects in microbiology, pharmacology, physiology, biochemistry and physical therapy. Students receive a stipend of \$10.50 per hour, but no housing is provided. Students are required to work up to 40 hours per week. All applications are due by March 3, 2014. Additional information can be found at <http://www.dmu.edu/research/student-research-opportunities/>.

Keynote Speaker

Laurel L. Haak, PhD

Dr. Haak is the executive director of ORCID, an international and interdisciplinary non-profit organization dedicated to providing the technical infrastructure to generate and maintain unique and persistent identifiers for researchers and scholars. She earned a BS and MS in Biology from Stanford University, completed her Ph.D. in neuroscience at Stanford University Medical School, and conducted postdoctoral research in neuronal-glia signaling at the National Institutes of Health.

Following postdoctoral work, she served as editor of Science Magazine's NextWave Postdoc Network, a weekly publication of the American Association for the Advancement of Science (AAAS). Dr. Haak was a program officer at the National Academies, where she directed workforce policy studies on international students, interdisciplinary research, women in academia, postdoctoral researchers, and innovation policy.

Prior to joining ORCID, Dr. Haak served as chief science officer at Discovery Logic, a Thomson Reuters business, where she led the Research Evaluation division.

Dr. Haak indicated she has no financial relationships to disclose relevant to the content of this CME activity.

Target Audience

Des Moines University faculty, staff, students, residents, alumni, external researchers and health professionals from the Des Moines area and surrounding medical and scientific community are invited to participate and present. All students, faculty, and residents are encouraged to develop research projects to be presented at the Symposium.

Organizing Committee

Jeffrey Gray, PhD, Vice President for Research (Scientific Chair), Director – Master of Science in Biomedical Sciences Program, Professor – Microbiology and Immunology

Mindi Feilmeier, DPM, FCFAS, Assistant Professor – Doctor of Podiatric Medicine Program, Clinician – Foot and Ankle Clinic

Kristin Kindred, DPM'16

Marie Nguyen, PhD, Assistant Professor – Microbiology and Immunology and Master of Science in Biomedical Sciences Program

Kelsey Randel, DO'16

Julie Ronnebaum, GCS, DPT, Assistant Professor – Doctor of Physical Therapy Program

Vanessa Ross, CMP, CCMEP, Manager – Continuing Medical Education

Nolan Wright, DPT'14

The organizing committee indicated they have no financial relationships to disclose relevant to the content of the CME activity.

CME Credit

ACCME: This activity has been planned and implemented in accordance with ACCME® Essential Areas and Elements and Iowa Medical Society (IMS) policies. Des Moines University is accredited by the IMS to provide continuing medical education for physicians. Des Moines University designates this live education activity for a maximum of 3.75 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.



AOA: Des Moines University and the AOA Council on Continuing Medical Education approve this program for a maximum of 1.0 hour of AOA Category 1-A CME credits, 1.0 hour of AOA Category 2-A CME credits, 1.50 hour of AOA Category 2-B CME credits.

CPME: Des Moines University is approved by the Council of Podiatric Medical Education as a sponsor of continuing education in Podiatric Medicine. This program has been reviewed and approved for a maximum of 3.75 continuing education contact hours.

IBON: Des Moines University continuing education (provider #112) is approved by the Iowa Board of Nursing as an accredited provider. This program has been reviewed and approved for a maximum of 4.50 continuing education contact hours.

Other: This live activity was designated for 3.75 *AMA PRA Category 1 Credits™*.

Oral Presentation Schedule

Movement Science and Education
Academic Center Lecture Hall 2
Moderator: Teri Stumbo, PhD, MS, PT

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Academic Center Lecture Hall 3
Moderator: Carolyn Beverly, MD, MPH

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Neutral Position of the Subtalar Joint During Gait Using 3-D Analysis

James Mahoney, DPM, Vassilios Vardaxis, PhD, **Eric So, DPM'15**

Background: The underlying theory behind podiatric biomechanics as developed by Root maintains that foot pathology can be corrected by restoring the foot as close to subtalar joint (STJ) neutral as possible. This requires that during gait the STJ function within a range of initial pronation, through STJ neutral, and finally into supination. However, work by McPoil and Cornwall, and later by Pierrynowski, showed that during gait the STJ does not reach neutral position and the foot functions in a pronated position throughout. This 3-D motion analysis study is designed to shed more light on this controversy.

Methods: Biomechanical examinations were performed on the right foot and leg of 20 male participants in SJNR, SJNP, RCSP, and NCSP. X-ray views of the right leg and foot were taken to allow accurate assessment of skin-bone alignment. The kinematics data during self-selected and fast walking trials, as well as static captures were collected using an eight-camera Motion Analysis system (Motion Analysis Corporation, Santa Rosa, CA)

Results: During self-selected walking, the subtalar joint did not reach neutral position during midstance, and remained in an everted and abducted position with respect to all three clinically used subtalar joint neutral positions (NCSP, SJNR and SJNP).

Conclusions: The STJ during midstance in gait does not match the neutral position as maintained by Root, utilizing his exact definition of STJ neutral.

Augmentative Exercises and Manual Therapy: Effects on Clinical Outcomes and Quantitative Sensory Testing

Shannon Petersen, CE Cook, MB Donaldson, AL Hassen, AR Ellis, KE Learman
Des Moines University, Des Moines, IA
Walsh University, North Canton OH
Youngstown State University, Youngstown, OH

Background and Purpose: Manual Therapy (MT) and exercise combined have been shown to benefit patients with neck pain. Previous studies examining manipulation have included concurrent regimens of range of motion (ROM) exercises and/or strengthening exercises. What remains unknown is whether the effects of MT can be enhanced using a specific augmentative exercise program (AEP). The purpose of this study was to examine the effect of MT when combined with AEP versus general ROM on clinical outcomes and quantitative sensory testing (QST) in subjects with neck pain.

Methods: Sixty-nine subjects with neck pain were treated with MT and randomly assigned to either AEP or ROM. Self-report outcome measures for pain and disability, and QST measures were collected at baseline, post MT treatment, at ~48 hours, and at ~96 hours. Three repeated measures multivariate analyses of covariance were performed to analyze within and between group effects.

Results: There were no between group differences for pain, disability and QST measures. Significant improvements in the AEP group for global rating of change (GRoC) were found ($P < 0.01$). There were significant within group differences for both groups in pain and disability ($P < 0.01$) and trapezius pressure pain threshold ($P < 0.01$).

Discussion and Conclusion: Regardless of the assigned exercise program, subjects with neck pain benefit from MT interventions and exercise over a 96-hour period. AEP enhanced the subjects' GRoC scores but did not significantly improve pain or disability.

A Case Study on Physical Therapy Treatment of Levator Ani Syndrome

Kari Smith, DPT, BCB-PMD

Des Moines University, Des Moines, IA

Background and Purpose: Levator ani syndrome (LAS) is a pain syndrome caused from spasms of the levator ani muscle causing significant pain with sitting or defecation, each episode lasting 20 minutes or longer. Literature searches on the current treatment options have limited effectiveness in the elimination of pain and return of normal quality of life. The purpose of this case study is to identify the physical therapists role in the treatment options available for LAS.

Study Design: This study is a case report looking at the biopsychosocial model for treatment along with using current concepts from pain sciences and central sensitization.

Case Description: This patient is a 55 year old female with an insidious onset of anal pain 4 months ago. The signs and symptoms of her pain were consistent with a medical diagnosis from the Rome III classification of levator ani syndrome, dyspareunia and coccydynia.

Outcomes: This patient was seen for 13 visits over 5 months for her pelvic pain. Upon discharge, her global rating of change score improved to a 14/15 or “a great deal better”. On the pelvic floor distress inventory (PFDI-20) minimal change was noted but further analysis determined a change that resulted in an elevated rating in the pelvic organ prolapse categories since symptoms changed from pain to heaviness and dullness.

Discussion: The physical therapy interventions for a woman with an insidious onset of pelvic pain are discussed, using an interdisciplinary approach to treatment.

Changing the Mindset from Parking Lots to Cyber-Classrooms: Building Universal Accessibility into Higher Education

Denise M. Hill, JD, MPA and Devrim Ozdemir, PhD

Des Moines University, Des Moines, IA

For over 30 years institutions of higher learning and general society have incorporated accessibility for people with disabilities into the built environment of our parking lots, our buildings and other public venues. For example, a person who has limitations on their ability to walk can generally pull into a parking lot at a university and does not need to request a special accommodation to have accessible parking; it is already provided as part of the built environment. However, when it comes to higher education, access to the learning environment often requires individuals with disabilities to specifically request accommodations, even when such accommodations are common-place requests. This is particularly true for students in the health professions who will be serving a population with many disabilities. Further, many aspects of education now encompass a virtual learning environment—one that may not automatically account for the access needs of those with disabilities.

This presentation will serve as a call to action to embrace the use of universal design to provide access to all students and other stakeholders. The rationale for universal access, major principles of universal design, and the related legal/ethical obligations will all be addressed in an efficient and meaningful way. Examples of struggles faced by students with disabilities who have had their access to education limited in both the face-to-face and online classroom will also be shared. Participants should leave the presentation with an appreciation for why universal design is important and a commitment to implementing it in their own learning environments.

Learning Objectives: As a result of participating in this session, participants will be able to:

1. Define universal design.
2. Briefly explain the major principles involved with effective universal design.
3. List three (3) appropriate applications of universal design that could be incorporated into their own courses or health professional environments.
4. Describe the primary legal and ethical duties supporting universal design in health care education.

***In vitro* Physiology of RPE65 Gene Therapy for Congenital Blindness Highlights the Importance of Early Treatment**

Steven F. Stasheff^{1,4}, **Frederick R. Blodi**², Malini Shankar², Jeannette Bennicelli⁵, Jean Bennett⁵, Sajag Bhattarai³, Stewart Thompson³, Arlene V. Drack³

¹ *University of Iowa and Carver College of Medicine, Program in Neuroscience, Iowa City, IA*

² *University of Iowa and Carver College of Medicine, Departments of Pediatrics, Iowa City, IA*

³ *University of Iowa and Carver College of Medicine, Ophthalmology and Visual Sciences and the Stephen A. Wynn Institute for Vision Research, Iowa City, IA*

⁴ *University of Iowa and Carver College of Medicine, Biomedical Engineering, Iowa City, IA*

⁵ *F.M. Kirby Center for Molecular Ophthalmology/Scheie Eye Institute, University of Pennsylvania and Children's Hospital of Philadelphia, Philadelphia, PA*

Purpose: To help improve Rpe65 gene therapy for Leber's congenital amaurosis (LCA), we examined its effectiveness at the resolution of single cells and retinal circuits. Here we report substantial improvements in retinal ganglion cell (RGC) responsiveness to light *in vitro*, but also persistent background hyperactivity that may degrade the quality of visual signals. Emergence of hyperactivity was prevented only in some cases treated prior to the age of eye opening. Further understanding of underlying mechanisms may help explain the superior response of children in early clinical trials and improve treatments.

Methods: We recorded RGC activity in *rd12* (Rpe65^{-/-}) mouse retinas using *in vitro* multielectrode techniques, after subretinal viral transfection of retinal pigment epithelium (RPE) cells with normal RPE65 (AAV2/1-hRPE65). We compared spontaneous and light-evoked activity in treated and untreated eyes 7-90 days after injecting this vector at various ages.

Results: In retinotopic regions receiving gene therapy, RGC responses were robust, including multiple recognizable types of response to full field flashes and reliable receptive field mapping with pseudorandomized checkerboard stimuli in many (but not all) cells. No light-evoked responses were detected in untreated eyes. Spontaneous hyperactivity equivalent to that in untreated eyes persisted after gene therapy, unless treatment began at P4.

Conclusions: *In vitro* multielectrode recording evaluates the effectiveness of gene therapy at high resolution not possible in human patients. This provides detailed understanding of mechanisms underlying imperfect treatment responsiveness, to guide further improvements in treatment. Our current study suggests that spontaneous hyperactivity corrupts the neural code of RGCs, decreasing the precision of some RGC responses and limiting gene therapy's effectiveness unless it is initiated sufficiently early.

Some of this material was presented at the 2013 Annual Meeting of the Child Neurology Society and of the Association for Research in Vision and Ophthalmology.

***Salmonella* Vaccine to Enhance Food Safety and Reduce Environmental Contamination**

Bradley L. Bearson, PhD

USDA, ARS, National Laboratory for Agriculture and the Environment, Ames, IA

Salmonella is the leading cause of bacterial foodborne morbidity and mortality in the U.S. The variety of foods associated with *Salmonella* foodborne outbreaks is extensive including meats, cheeses, vegetables, fruits, nuts, and cereals. The annual medical costs associated with *Salmonella* infections are estimated to be \$365 million with 100,000 drug-resistant *Salmonella* infections each year. In the environment, *Salmonella* is ubiquitous and can sub-clinically colonize food-producing animals and poultry, as well as wild animals and birds. There are >2,400 *Salmonella* serovars and exposure to one serovar may not confer strong protection against other serovars. Thus, effective strategies to reduce *Salmonella* colonization in food-producing animals are needed to decrease foodborne disease. We have designed a rationally attenuated *Salmonella* vaccine to confer broad protection against multiple *Salmonella* serovars to enhance food safety and reduce environmental contamination. Vaccination conferred protection against *S. Choleraesuis*, the causative agent of severe, systemic disease and mortality in swine. Furthermore, vaccination reduced gastrointestinal colonization and fecal shedding into the environment by *S. Typhimurium*, a leading cause of human foodborne disease. It is

anticipated that a reduction in *Salmonella* colonization and shedding will have a concomitant decrease in pathogen transmission, further limiting infection of naïve animals. Our research indicates that vaccination of food-producing animals with a vaccine that confers broad protection against multiple *Salmonella* serovars should enhance food safety and limit environmental impact.

Polk County Blood Pressure Screening Pilot Program

Chris Bolander, DO'15, Carolyn Beverly, MD, MPH, Simon Geletta, PhD
Des Moines University, Des Moines, IA

The prevalence of hypertension (HTN) is the highest in African-American men as compared to men of other ethnic origins, and they, consequently, face a higher risk of cardiovascular morbidity and mortality. Key contributing factors to this health disparity include scarcities of awareness, education, and access to preventive care. Recent public health efforts have emphasized routinely accessible community sites as health resources for these high-risk populations. This study analyzed the efficacy of one such outreach program—a barbershop and church-based blood pressure screening and education project. The goal of this program was to evaluate an innovative approach to blood pressure screening, health education and referral to community-based healthcare providers. Monetary incentives were offered to those with elevated blood pressures to encourage consultation from a healthcare provider.

Patrons of partnering barbershops and church members were offered blood pressure screenings and health education by trained volunteers. Screened individuals with elevated blood pressures (“≥ hypertensive” per JNC-VII guidelines) were offered small monetary incentives (\$10) to follow up with a healthcare provider. Data was gathered from all participants on a voluntary basis. A total of 188 individuals were screened over the course of 102 Days.

Analysis of screening data reaffirms the high prevalence of HTN in the African-American community. However, healthcare follow-up was less than anticipated, which implies that future incentives would be optimal if >\$10 in value. Achieving an increase in healthcare access remains a key objective for further research. Barbershop and church communities embraced the concept of health screenings and education, which suggests that community-driven health outreach is a promising approach to reducing health disparities.

Switch What Do You Do, View, and Chew: A Multi-Ecological Childhood Obesity Prevention/Intervention

Rachel Reimer, Douglas Gentile, Amy Nathanson, David Walsh, Joey Eisenman

The purpose of this talk is to present 3 studies from the Switch intervention. Over 1,200 3rd – 5th grade children, their primary caregivers, and their teachers in Iowa and Minnesota participated in the Switch study. The switch intervention was a theory-based, multi-component, longitudinal childhood obesity prevention intervention health intervention. In study 1 will discuss the intervention methodology and results. Next, I will present results from an analysis examining the reliability and validity of multiple informants in data collection in Study 2. Finally, I will present the results from recent work examining the longitudinal effects of parental monitoring on a variety of academic, social, and physical health outcomes.

How to Read a Poster Abstract

A common approach for evaluating posters involves considering the following factors in the technical, visual and presenter categories. This tool can be used when reviewing posters at this meeting and as a helpful guide for constructing your posters in the future.

Category	Notes
Technical	
Research topic clearly described with adequate introduction and a clear hypothesis.	
Good use of the space of the poster with sections on methods, results, and discussion as appropriate.	
Conclusion section which emphasizes the relevance of the research in the field of study.	
Visual	
Title, author(s), affiliations, and contact info included.	
Poster design logical and easy to follow with appropriate visuals (methods, results, etc.).	
Text easy to read, understand and free of errors.	
Graphics clearly contribute to the overall presentation.	
Presenter	
Able to communicate in-depth technical information in an easy-to-understand manner.	
Able to interpret the data properly, and clearly answer questions related to project.	
Recognize limitations of the project's procedures.	
Courteous and professional.	

Poster Abstracts

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= Resident

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+ = Undergraduate

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Comparison of the Modified Paper Grip Test (mPGT) and Rocker Board Test (RBT) in Individuals With and Without Plantar Heel Pain (PHP)

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Introduction: Impaired foot and lower leg muscle performance has been linked to plantar heel pain (PHP). The mPGT test and the RBT clinically measure foot and lower leg muscle performance. The purpose of this study was to compare performance in the mPGT and the RBT in individuals with and without PHP.

Methods: The mPGT and RBT was performed 7 control and 18 PHP participants. Multivariate analysis and post-hoc tests were used to compare performance in the mPGT (of the great toe and lesser toes) and the RBT between the involved and uninvolved extremity of individuals with PHP and health control participants.

Results: The involved and uninvolved sides of individuals with PHP were weaker than controls in the RBT by 2.8 (95% CI 6.1, 20.3) and 3.0 (95% CI 3, 18.5) repetitions, respectively. There was no difference in the RBT between the involved and uninvolved sides of individuals with PHP ($p = .584$). In addition, no differences were found between groups for the mPGT for the great toe ($p = .163$, Power = .369) or lesser toes ($p = .072$, Power = .520), but individuals with PHP underperformed the controls by greater than the minimum detectable difference (MDD).

Discussion: Individuals with PHP were weaker in the RBT on the involved and uninvolved sides than individuals without PHP. Additional testing is needed to determine differences in the mPGT because of the low power observed in this sample. The RBT and mPGT may be used to identify weakness in individuals with PHP and to assess change using the MDD.

Reliability and Minimal Detectable Difference of the Modified Paper Grip Test (mPGT) and Rocker Board Test (RBT) for Clinical Assessment of Foot and Lower Leg Muscle Performance

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Introduction: Impaired foot and lower leg muscle performance is associated with foot and lower leg disorders, but reliable clinical measures have not been established. The purpose of this study was to assess intra and inter-rater reliability of 2 novel foot and lower leg performance tests.

Methods: Two examiners repeated testing of the mPGT and RBT in a sample of 33 individuals without and 7 with plantar heel pain (PHP). The mPGT was performed by measuring the force required to pull a business card from beneath the great toe and lesser toes. The RBT required participants to perform unilateral ankle plantar flexion on a rocker board until fatigue of the calf muscles. The intraclass correlation coefficient (ICC) and minimal detectable difference (MDD) was calculated for each test.

Results: The intra-rater ICC range for the great toe and lesser toes mPGT, and RBT was 0.669-0.958, 0.907-0.954, and 0.682-0.889, respectively. The inter-rater ICC range for the great toe and lesser toes mPGT, and RBT was 0.886, 0.824, and 0.731, respectively. Narrow confidence intervals were observed except in the examiner who tested individuals with PHP (ICC 95% CI, 0.132-0.882). The MDD for the great toe and lesser toes mPGT, and RBT was 0.8 kg, 0.36 kg, and 7.23 repetitions, respectively.

Discussion: The mPGT and RBT demonstrated acceptable clinical reliability to assess muscle performance of the foot and lower leg. Reliability was lower when testing individuals with PHP, but wide confidence intervals warrant additional testing in individuals with foot disorders (eg, PHP).

Falls Among the Elderly with Dementia

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Purpose: In 2011, there were over nine million cases of falls in the U.S. that resulted in hospitalization. As can be inferred from this statistic, falls are a serious injury problem amongst the population, especially the elderly. It has been shown that as age increases, the incidence of falls increases rather dramatically. While most falls only result in minor injuries, such as abrasions and bruising, more serious injuries such as fractures and death can occur. It has also been shown that cognitive function, including dementia, is a risk factor for serious injuries due to falls. In this study, we are investigating the association dementia has on mortality in elderly patients aged 65 and older.

Method: Data from the 2010 Illinois Discharge Dataset was collected and evaluated using a logistic regression model.

Results: We found that 1.9%, or 101 patients, who had dementia died versus 0.98%, or 849 patients, without dementia. The risk of death due to a fall with dementia was found to have a significant crude odds ratio of 1.964 with an adjusted of 0.869, which was not significant.

Analysis/Conclusion: It has been shown in previous literature that cognitive function is a risk factor for falls among the elderly; it has never been looked at in a mortality sense with such a large sample size. While our study did not show a significant association between death from falls and dementia, it does show that the elderly with dementia are a high risk population and should be cared for accordingly.

Lower Trapezius Strength Following Manual Therapy and Augmentative Exercise in Subjects with Neck Pain

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Purpose: Lower trapezius (LT) muscle weakness has been associated with neck pain (NP). Manual therapy (MT) to the thoracic spine has been shown to increase LT strength in healthy subjects, yet LT strength following MT to the cervical spine has not been examined in subjects with NP. The purpose of this study was to examine LT strength changes following MT and augmentative exercise in subjects with NP.

Methods: LT strength was assessed using a hand-held dynamometer. All subjects received MT to the cervical spine and were instructed in a home exercise to augment the specific MT intervention applied. Strength was examined immediately post intervention and again ~24 hours and ~96 hours post-intervention. Repeated measures ANOVAs were calculated for strength on sides ipsilateral and contralateral to NP.

Results: Nine female subjects and 1 male subject participated. Mean \pm SD: Age 32.9 ± 14.9 years; Symptom Duration 30.5 ± 34.1 months. Significant difference between ipsilateral LT strength and contralateral LT strength was found at baseline ($p=0.002$). Significant improvement was seen in ipsilateral LT strength between baseline and each follow-up session ($p=0.005$). No significant difference found in LT strength over time for the side contralateral to the NP (0.476).

Conclusions: Improvement in LT strength was seen over a 96 hour period following MT and augmentative exercise. Significant strength improvements were seen only on the side of NP. Results seen cannot be attributed to a single intervention since a combined approach was used and there was no control group.

Effects of an Intense Week-Long Exercise Program in Chronic CVA: A Case Series

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Background and Purpose: To assess the effects of a one-week intensive exercise program in patients with chronic stroke. Des Moines University (DMU) faculty and students in the doctor of physical therapy program participated in the week-long stroke camps held in Jamaica, during a global health trip, and on the DMU campus.

Case Description: Thirteen U.S. participants from the Des Moines community (36-76 years; mean age 63.5 years) with chronic stroke (1.3 – 23.5 years post-CVA) and twelve Jamaica participants with chronic stroke (no demographics) completed stroke camp at their respective locations. Group and individualized exercise sessions focused on balance, gait, and upper extremity function. Pre and post testing included: Berg Balance Scale (BBS), Timed Up and Go (TUG), 6-Minute Walk Test, and the Wolf Motor Function Test (WMFT). Pre and post testing at DMU stroke camp also included the Four Square Step Test (FSST), Dynamic Gait Index (DGI), and spatial/temporal gait parameters.

Outcomes: Jamaica participants improved significantly on the 6-MWT and TUG and met the Minimal Detectable Change (MDC) criteria for both outcomes (177.5 ft./ >8 sec respectively). Jamaica and U.S. participants improved significantly on the BBS and met the MDC (>5 points). U.S. participants significantly improved on the DGI but did not meet the MDC. U.S. participants significantly improved on the WMFT Complex and met the MDC (4.36 sec). No other WMFTs, US gait parameters, or FSST scores reached significance.

Discussion: A week-long individualized intensive exercise program may be beneficial for improving functional balance in patients with chronic stroke.

Modified American Spinal Cord Injury Association (ASIA) Examination for Ambulatory Patients (MAAP) Prior to OMT

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For the practicing clinician, evaluating a musculoskeletal condition, in particular prior to consideration of OMT, the MAAP is a valuable assessment tool to help identify neurological red-flag findings prior to making decisions regarding treatment.

Performing the MAAP examination in the thorough evaluation of musculoskeletal conditions can be an extremely useful guide to identify the appropriate use, or restraint, of OMT in a patient who may be neurologically compromised. It may also identify previously undiagnosed neurologic disease, and prevent untoward outcomes and avoid potential litigation from missed neurologic disease.

We present this modified examination which has been tailored to the ambulatory setting, and present several cases wherein this new examination was useful.

Utilization of Impulse to Characterize Asymmetry in Lower Limb Loading During Sit-to-Stand in Patients with Total Hip Arthroplasty

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Introduction: Total hip arthroplasty (THA) is a common treatment option for individuals suffering from hip OA and is known to reduce pain and enhance mobility. Even so, it must be noted that bilaterally asymmetrical biomechanical patterns still persist in activities of daily living (ADL) such as sitting and standing even after THA. This asymmetrical loading is viewed as a risk factor for development of OA in the non-operative leg. The present study uses a novel calculation “the impulse ratio” of the loading forces generated by the lower limbs to evaluate the asymmetrical lower limb loading in patient’s pre and post THA.

Method: Control and subject groups were assessed for loading forces using force plates during sit-to-stand motion. Participants were told to sit and stand from an armless/backless chair using only their legs. The forces were recorded using force plates located beneath the feet. 5 trials were recorded during each visit at intervals of 0 (preop), 3, 6, and 12 months. The data was then used to calculate the impulse ratio, which was later used to compare the degree of asymmetry in patients with THA.

Results: The controls all had uniform loading mechanics and produced symmetrical loading, which was noticed when the impulse ratios were seen to be equivalent to approximately 1. On the other hand, the subjects with THA showed a gradual improvement in impulse ratios that slowly approached 1, showing improvement in the loading symmetry between limbs.

Conclusion: The findings suggest that impulse ratio can be used to characterize and quantify the level of asymmetry observed in lower limb loading during sit-to-stand in patients with total hip arthroplasty. Over time, the impulse ratio in the experimental group approached steadily towards 1, indicating improvement in sit-to-stand biomechanics (equal limb loading).

Longitudinal Study of Hip Range of Motion and Strength Following Total Hip Arthroplasty

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Background: Patients suffering from hip osteoarthritis (OA) develop limitations in hip range of motion (ROM) and strength due to immobility, pain, and the natural course of hip OA. These limitations often coexist in the contralateral side and may be due to adaptations to the initial OA.

Purpose: The purpose of our study was to evaluate preoperative and post-operative ROM and strength in the surgical and non-surgical hips to see if changes occur after 12 months post-surgery.

Methods: Thirty six subjects with end stage OA underwent either a posterolateral or direct anterior approach. These two groups were combined for one cohort study. The data was collected pre-surgery and at 3, 6, and 12 months post-surgery.

Results: Hip ROM of the surgical hip improved relative to pre-surgery values in all motions of the hip. Hip ROM of the non-surgical hip increased in internal rotation, decreased in extension, and no change was noted in all other motions. An overall increase was seen in hip strength following surgery, but a decline was noted once patients returned to normal gait and activity levels. Interestingly, the non-surgical hip was significantly reduced in hip extension.

Conclusions: Overall, improvements were seen in both hips, but as patients regain function they often taper the amount of exercise completed. Decreasing exercise may then be a reason for a loss of ROM and strength. Therefore, it may be potentially beneficial to encourage patients to continue their exercise for up to a year, post-THA, to look for any long term benefits.

Balance Assessment in Patient with Hip Osteoarthritis after Total Hip Arthroplasty

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Introduction: Hip osteoarthritis occurs when inflammation and injury to the hip joint causes the breakdown of the cartilage tissue. When the hip joint becomes severely deformed physicians recommend total hip arthroplasty (THA). Osteoarthritis alone accounts for 70% of THA cases. Balance during everyday life is significantly altered by severe OA of the hip. The clinical implications of balance loss in this population is not well understood, considering its importance in the everyday tasks of walking, standing, walking up/down stairs, and transitioning from sit-to-stand/stand-to-sit. The specific aim of this study is to assess the standing balance in THA patients before and after surgery.

Methods and Measures: Twenty-three patients with unilateral THA participated in the study. All subjects were evaluated over time at PRE, 3, 6, and 12 months POST THA. The balance assessment was performed in bilateral standing position with eyes open/closed. Thirty second balance test was used, three trials per condition. The balance measures assessed were bilateral body weight support, and center of pressure (COP): path length and 95% confidence ellipse area. Two-way ANOVA repeated measures design was used to test for changes on the balance measures over time and between conditions (eyes open/close).

Results: The results of the two-way ANOVA showed significant changes in balance ability over time, specifically: enhanced weight distribution during stance ($p=0.049$), increase in the BW load supported by the operated side ($p=0.015$), and decrease in the COP path length ($p=0.001$). A significant eyes open/close condition difference was found in the 95% ellipse area ($p=0.001$). Post-hoc contrasts revealed that the significant improvements were achieved at the 12 month, with the exception of the COP path length which showed differences at six months.

Discussion and Conclusions: The findings of this project suggest that severe hip OA patients post THA have also balance deficiencies which do not improve until a year post surgery. Besides the physical deficiencies, the THA patients may also have proprioception deficits that can contribute to this postural instability.

Disclosure Statement: None of the authors of this abstract have conflicts of interest to disclose.

The Relationship Between Ultrasound Imaging and Clinical Biomechanical Measurements That Reflect Lisfranc Ligament Length Changes With Load

Nooreen Ibrahim, Dalton Ryba, Todd Jaramillo, Jim Choi, MD, Vassilios Vardaxis, PhD

Current methods of evaluating midfoot pain, with respect to Lisfranc joint, rely upon standard radiographs, but there is an alarmingly high false negative rate. This false negative rate calls for re-evaluation of current diagnostic modalities and exploration of new methods that may lead to safer, cheaper, and a more accurate diagnosis. Further investigation into the use of ultrasound imaging technology in the diagnostic protocol of midfoot pain merits exploration due to its potential viability. The overall goal of this project is to demonstrate if the dorsal Lisfranc ligament can be reliably visualized under physiologically relevant stresses and considerably deforms with load. The specific aim of this study is to explore the potential relationship between clinical measurements and the Lisfranc ligament deformation with load. Bilateral dorsal Lisfranc ligament measurements were taken from fifty healthy volunteers (25 males and 25 females), for a total of one hundred asymptomatic feet, using sonographic imaging technology under three different stress conditions (low, medium and high load). Stress load was applied using the individual's body weight (low load – seated position; medium load – equal weight bearing standing position; and high load – single leg standing). Clinical/biomechanical measurements, the Longitudinal Arch Angle and the Arch Height Index, were also taken under the same load conditions. Typically these measures are used in clinic to gauge the static foot posture and characterize the shape and structure of the foot arch. The potential relationship between imaging and clinical evaluation offers a redundancy in the diagnosis of a very challenging mid-foot injury.

Clinical Evaluation of Dorsal Lisfranc Ligament Deformation with Change in Load Using Ultrasound Imaging

Dalton Ryba, Nooreen Ibrahim, Todd Jaramillo, Jim Choi, MD, Vassilios Vardaxis, PhD

The use of ultrasound is a viable modality for medical imaging of ligamentous tissue. In a previous study we were able to demonstrate that the dorsal Lisfranc ligament can be reliably visualized with ultrasound and that we can discern load-varying ligament deformation with the images obtained. The study was limited with respect to the laboratory setting environment and the artificial loads used to apply stress on the foot using a calf raise machine. The goal of the present study was to attempt to replicate these findings under a clinical setting using physiologically relevant stresses. Bilateral dorsal Lisfranc ligament measurements were taken from fifty healthy volunteers (25 males and 25 females), for a total of one hundred asymptomatic feet, using sonographic imaging technology under three different stress conditions (low, medium and high load). Stress load was applied using the individuals' body weight (low load – seated position; medium load – equal weight bearing standing position; and high load – single leg standing). The medium load stress condition was repeated in two separate foot orientation positions (feet parallel and self-selected). Two floor imbedded force plates were used to measure the exact physiological load. Data was collected in the order of the following protocol: A) explanation of the project and consent, B) completion of a medical history questionnaire, C) collection of anthropometric measures (height, weight, etc), D) clinical foot evaluation, E) Stress and foot position orientation measurements of the dorsal Lisfranc ligament strain using ultrasound imaging.

Does Getting Sutures Wet Postoperatively Increase the Incidence of Infection? A Prospective Observation

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Purpose: Surgeons and hospitals use several means to decrease infection rates at incision sites. Foot and ankle surgeons often keep the incision site dry and covered postoperatively until the sutures and pins are removed as a means of preventing infection, despite evidence to support this practice. Our study was aimed at determining if the infection rate in the early postoperative course is altered by early surgical site exposure to showering.

Methodology: A prospective study of 111 patients undergoing elective foot and ankle surgery were allowed to shower within the first week postoperative. Apriori power analysis was used to determine the number of cases needed to determine significance. Risk factors for infection were recorded. Logistic regression was performed to determine correlations between infection rate and early showering.

Procedures: Patients were allowed to shower after their first postoperative appointment. They were evaluated at each postoperative appointment for signs of infection. Redness and swelling were considered signs of minor infection and were treated with oral antibiotics until resolved. Major infection was considered any infection altering the course of recovery or requiring admission or further surgery.

Results: The overall infection rate was 4.5%. All infections were considered mild. Logistic regression shows that none of the recorded risk factors significantly predict infection.

Discussion: The incidence of postoperative infection reported in the literature is 0.5% to 6.5% for foot and ankle surgery. This study suggests that early daily showering of a surgical site after a foot and ankle surgery does not increase the risk of infection.

The Observed Changes in Radiographic Measurements of the First Ray Following Valgus Rotation of the Hallux

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Background: The purpose of this study is to observe Anterior-Posterior (AP) radiographic changes in the first ray as the great toe position is altered.

Methods: Five fresh frozen cadaveric specimens were obtained. Screws were placed in the first proximal phalanx, and the medial and lateral sides of a platform equidistant from the hallux. Rubber bands were employed to manipulate joints into a varus or valgus position. Three AP radiographs were taken of each foot: baseline, maximum hallux valgus and maximum hallux varus. Each radiograph was evaluated for measurements of Intermetatarsal Angle 1-2 (IMA), first Metatarsal-Cuneiform Joint Angle (MCA), and Tibial Sesamoid Position (TSP).

Results: Max hallux valgus showed a significant relationship to an increase in the TSP ($p=0.016$). A significant relationship between max hallux varus and a decrease in the IMA ($p=0.02$) as well as a decrease of the TSP ($p=0.016$). Max medial cuneiform valgus displayed a significant relationship to an increase in TSP ($p=0.005$) as well as a decrease in the MCA ($p=0.028$). Cuneiform varus did show a significant relationship to a decrease in the TSP.

Conclusion: Valgus rotation of the hallux along with abduction produces an increase in TSP. This shows that the hallux could potentially drive the proximal deformity that is seen with Hallux Abducto Valgus with Metatarsus Primus Adducto Valgus.

Review of Equinus Deformity: A Proposed Prospective Study on Outcomes and Complications Associated with Surgical Treatment

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Equinus deformity, or limited dorsiflexion, is often due to contracture of the triceps surae muscles. Equinus causes changes to normal biomechanics of gait including; pronation at the subtalar joint resulting in excessive midtarsal joint movement, changes to heel rise and changes to pressure distribution throughout gait. These changes are linked to numerous foot pathologies including plantar fasciitis, metatarsalgia, flat-foot and plantar pressure ulcer formation. Conservative treatment has been shown to be ineffective in resolving equinus deformity, while surgical intervention offers true correction. Gastrocnemius or gastrocnemius-soleus recession is commonly the surgical intervention of choice. Positive outcomes include increased knee-extended dorsiflexion of 10° or more, significant reduction of pain associated with metatarsalgia, plantar fasciitis, and Achilles tendonopathy, and positive patient satisfaction. Although infrequent, complications most often mentioned in the literature include sural nerve entrapment and neuritis, scarring, weakness, pain, wound infection, subcutaneous dimpling, and deep vein thrombosis. The purpose of our proposed prospective investigation is to increase the volume of literature by assessing longer term (up to 1 year) post-operative outcomes relative to pre-operative measures in a sample powered to detect pre- to post-test differences in function, pain, range of motion, and plantar flexion torque than is currently presented in the literature. We also hope to show that patients are satisfied with the procedure and have excellent postoperative Foot and Ankle Ability Measure (FAAM) scores.

Acknowledgement and thank you to Dr. Shane M. McClinton for assistance in research design.

Cross-Validation of VO₂ Prediction Equations on Underwater Treadmill Exercise

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The purpose of this study was to determine the validity of two equations developed by Greene et al., 2011; for predicting weight-relative oxygen consumption (VO₂) during Underwater Treadmill (UTM) exercise at various treadmill velocities ($m \cdot min^{-1}$) and frontal jet resistance (% maximal force). We applied data to these equations from three previous studies that were performed at Utah State University, (Blackwell et al., 2011; Rutledge et al., 2007; Alkurdi et al., 2010) which examined VO₂ during UTM walking and/or running exercise with/without frontal jet resistance. In total we analyzed data from 52 participants with average age = 34.43, average height = 170.65 cm \pm 7.65 cm, average weight = 71.28 kg \pm 14.99 kg, and their overall fitness ranging from active/fit to inactive/obese. In our analysis the predicted VO₂ values were compared to the observed VO₂ values by examining the Pearson correlation coefficient (r), R² value (r²), standard error of estimate (SEE), total error (TE), and graphical regression analysis. The results obtained were: Eq.1 (walking): Actual Mean =15.18 \pm 5.22, Predicted Mean=10.97 \pm 3.29, r=0.77, r²=0.59, SEE=2.12, TE=25.0% \pm 17.3%. Eq.1 (running): Actual Mean=30.16 \pm 6.68, Predicted Mean=25.05 \pm 3.42, r=0.77, r²=0.59, SEE=4.29, TE=14.8% \pm 12.5%. Eq.2 (running): Actual Mean=41.41 \pm 9.02, Predicted Mean=32.40 \pm 4.82, r=0.83, r²=0.69, SEE=5.05, TE=19.9% \pm 10.5%. These results suggest that the given equations systematically underestimate weight-relative VO₂. This underestimation appears to be more prevalent in the most-fit individuals. We recommend a parameter of body composition such as body fat percentage or body mass index be evaluated for improving these prediction equations.

Does Education in TEAM STEPPS Improve Team Performance in Emergency Hand Offs for DPT Students?

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Background: With the institution of healthcare reform, there is a need to decrease healthcare dollars spent, while providing effective and safe care for patients. In order to do this, teamwork and collaboration are essential. Currently, healthcare workers possess the common goal of quality and patient safety but yet work independently. This type of atmosphere has promoted the formation of barriers to an effective functioning healthcare team and medical errors. Each discipline has its own terminology, expectations, and idiosyncrasies relative to communication. In emergency situations, communication and teamwork are key areas for successful patient outcomes. Team STEPPS provides individuals with the skills needed to improve teamwork and communication, resulting in decreased medical errors. Team skills are not innate but must be trained. The simulated environment provides the perfect atmosphere to utilize the skills learned for all professions.

Methods: Seven DPT students enrolled in the Simulation in Emergency Situations elective. Case scenarios were executed with the use of simulators and standardized patients. Each of the students participated in two case scenarios prior to team STEPPS training and then participated in two more case scenarios after the Team STEPPS training. The student's performance regarding teamwork and communication were observed during all scenarios with the Team Performance Observation Tool.

Results: Results show improvement in Mutual support, Team Structure and Communication.

Conclusion: Team STEPPS can improve teamwork and communication skills between physical therapy and nursing students in emergency situations.

Effect of Embedded Internships on Student Physical Therapy Knowledge As Measured By Performance on a Didactic-Based Comprehensive Examination

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Background: There has been considerable research to identify factors that predict successful outcomes in physical therapy programs. Outcomes that have been studied include academic achievement, clinical proficiency, and passage of the licensure examination. The type of clinical education experience (CE) that students complete has not been evaluated with regard to student academic achievement. The purpose of this study was to determine if the type of CE that is completed by physical therapy students affects their scores on a comprehensive examination.

Methods: This retrospective study examined records for 194 third year doctor of physical therapy students from an entry-level doctoral program. A multivariate analysis of variance was conducted to investigate if there was a correlation between the type of clinical education experience completed and the aggregate and section scores on a program-specific comprehensive examination.

Results: No significant difference was found between the type of CE and the scores on a comprehensive examination. ($F = .896$, $p = .569$). Positive correlations were found between academic course grades and content area examination scores and the aggregate comprehensive examination scores.

Conclusion: Results of this study suggest the type of CE experience does not have an effect on the scores of an academic comprehensive examination. A clinical education experience provides students the opportunity to integrate and utilize knowledge gained during the didactic program. Emphasis on the type of clinical education experience does not need to be the focus for a clinical education program.

Do Medical Students Need More Medical Education Training for Residency? A Medical Education Needs Assessment

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Introduction: It has become increasingly challenging for medical students to obtain their top residency choice. The total number of residency slots remains fairly constant but the total number of applicants for those slots increases every year. The goal for medical students is to find a way to become more interesting to the residency program of their choice. One of the many important roles of medical residents is to serve as educators, helping teach fellow residents, medical students and patients. As a result of this expectation, many residency programs have incorporated a teaching and research components as a requirement for graduation.

The purpose of this research project is to evaluate the importance of and need for additional medical education training during medical school and its impact on enhancing the competitiveness of medical students as applicants for residency.

Methods and Materials: The study design was an eight-question survey created using a Survey Monkey online survey poll. An email with a link to the survey was sent to the program directors of 258 internal medicine residency programs at the end of January, 2013 and the survey was closed at the end of April, 2013. Of the 258 residency programs, 41 directors completed the survey. There were five emails returned due to incorrect email address.

Results: A response rate of 16% (41 of 258) was obtained. 100% of programs indicated they placed an emphasis on medical education and teaching; however, only 20 programs (49%) have a structured teaching and education rotation. 85% (35 of 41) of programs indicated they would like to see medical schools emphasize medical education training. Teaching was the number one activity (33 responses) in which residency programs would like to see medical students receive additional training, while simulation training was second (20 responses) and research was third (13 responses). When comparing a student with additional medical education training to a similar applicant without, 59% (24 of 41 responses) of programs indicated they would

rate that student higher for resident selection. When asked to rank from highest (1) -to- lowest (4) importance with regard to applicants for their residency program, board scores received the highest overall rating (2.02) and the most number of highest (#1) scores (18 total). The second highest overall rating was class rank/GPA with an average rating of 2.09 while teaching/medical education experience had the lowest overall rating of 3.51 and the most number of lowest (#4) scores (28 total). The average satisfaction rating of the teaching skills of medical students that enter residency was 3.39, indicating a level between neutral (3) and somewhat satisfied (4).

Conclusions: Internal medicine residency programs place an emphasis on teaching and medical education. There is a need for undergraduate medical education training and a majority of residency programs would like to see medical schools emphasize such training. Having additional training, specifically teaching experience, is a desirable trait that can enhance your competitiveness as an applicant for residency programs and students should seek out teaching opportunities when available. Medical education training, while important, plays a smaller role compared to traditional categories of board scores, class rank/GPA and awards/honors (clerkship honors) regarding application for residency. The Pathways of Distinction Clinician Educator pathway provides medical students with the teaching, simulation and research experience for which residency programs are looking and serves as a highly valuable tool in preparing students for educator responsibilities in residency.

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Medical and Allied Health Professional Students Perceptions of Research Literacy Skills

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Aims: This study assessed the research literacy perceptions of health professions students at DMU.

Methods: Data was collected using a validated instrument assessing research perceptions, skills and their impact on professional development administered by an anonymous web-based survey offered to DO, DPM, PA and DPT students at DMU in 2012. Significance was determined by an $\alpha = 0.05$. This study was reviewed and approved by both institutions' IRB committees.

Results: A total of 478 (36.8%) students responded. Most had some prior research experience (45-74%), with the DO and DPM students having the most and a significantly greater interest in research (57 and 69%). Overall, 14% of students were currently involved in a research project across all programs. Students consistently expressed recognition of the relationship of research to patient care (91-94%) and the need for research methods and statistics in the curricula (62-85%). Perceptions of research skills required differed among the groups. While 64% of the DPT students felt competent in the identified skills only 39% of the others concurred. Overall, the research climate was perceived as favorable and supportive, though it differed significantly by program. Time for research was noted as an impediment by all programs.

Conclusion: The results demonstrate that student experience and interest in research outweighs participation and perceived opportunities, though there are significant differences by program. This may reflect the faculty's personal research interests, differences in research expectations by program and/or perceived role of the profession. Time is a limiting factor in all programs.

IRB #: DMU: 05-12-04, Ohio University: #09E221 and 12D008

COMLEX vs USMLE: Evaluating ACGME Internal Medicine Residency Program: Preferences and Position on Applicant Board Examinations

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Background: After completing their education in the basic medical sciences (usually two years of classroom education) medical students prepare to take the first set of board exams. Allopathic medical students are required to take USMLE (*United States Medical Licensing Exam*®) Step 1, while COMLEX (*Comprehensive Osteopathic Medical Licensing Examination*®) Level 1 is the board exam requirement for osteopathic medical students. The osteopathic medical also students have the option of sitting for the USMLE board examinations if they desire.

The latter option becomes an important consideration for many osteopathic medical students as they consider potential post-graduate training options (i.e. internships and/or residencies.) For students who consider pursuing a post-graduate position in an allopathic (ACGME: *Accreditation Council for Graduate Medical Education*) programs, the decision to sit for an additional exam can be quite stressful. Taking the USMLE in addition to COMLEX requires additional examination fees, and may require additional time commitment for added exam preparation, as well as time to take the exam.

Taking the USMLE and applying to allopathic residency programs is strictly an optional consideration for osteopathic medical students. However, this decision has been complicated by the disproportionate increase in osteopathic medical school graduates compared to osteopathic post-graduate training positions. In 2012, 5014 students graduated from osteopathic medical schools¹, while there were only 2655 first year osteopathic post-graduate training positions available². This means that only 52.95% of osteopathic graduates in 2012 could have obtained a training position in an osteopathic residency, while 2359 (47.05%) students would have had to seek training in other programs, namely allopathic residency programs.

This survey was developed with the intent of providing osteopathic medical students information regarding allopathic (ACGME) residency program views on the COMLEX compared to USMLE. This information may be utilized to potentially aid in a student's decision whether or not to take the USMLE. Due to the large number of residency programs for all specialties, the initial survey has been limited to internal medicine residency programs. Other specialties may be considered in the future.

Methods and Materials: The initial phase was creating the seven question survey. This included questions directly pertaining to program views on the COMLEX compared to USMLE, in addition to questions about board exams in general, as well as accreditation and geographic location. The survey was intentionally short, in an attempt to make it simpler and easier to complete for program representatives. This survey was sent out via e-mail and using Survey Monkey online survey tool.

The ACGME was contacted and a link to the publically accessible list of internal medicine residency programs with current e-mail addresses was provided. There are 376 total ACGME Internal Medicine residency programs and 258 had contact e-mails listed on the program list. The survey was sent to all programs with available e-mails listed on this list. The survey was open for 10 weeks, with a reminder survey request e-mail sent six weeks after the initial e-mail was sent.

Results: A total of 258 e-mails with explanation of intent and a link to the online survey were sent out to ACGME internal medicine residency programs. Nine programs (3.5%) had their e-mail address "bounce" and five programs (1.9%) opted out of the survey. Sixty programs (23.3%) began the survey, with 55 (21.3%) fully completing the survey and 5 (1.9%) partially completing it. The following data reflected the responses from the 60 programs that participated in the survey. An introductory question found that 14 (23%) programs were dually accredited by the AOA and ACGME, while 6 (10%) did not respond. The remaining 40 (67%) were accredited solely by the ACGME.

The top response for both questions was 1-10%, with 35 (58%) programs reporting this for osteopathic applicants and 30 (50%) reporting this for percentage of matched residents. No programs reported >50% for either question.

Question 3 asked programs to rate their view on the importance of board scores when evaluating applicants on a scale of 1-5. One was "no or minimal role in applicant's evaluation" and 5 being "one of the most important aspects of applicant's evaluation." Six programs (10%) had no response, with an average response of 4 for the

54 responding programs. Ten (17%) programs rated board score importance as 3, 31 (52%) ranked it as 4, and 13 (22%) ranked it as 5.

Discussion: From the information gathered, it appears that the majority of ACGME internal medicine residency programs prefer that graduates of osteopathic medicine sit for USMLE as well as COMLEX if they plan to apply to that program. It should be noted that, while many programs indicate that USMLE provides more useful information, relatively few (15%) require that applicants take USMLE in addition to COMLEX to be considered by the program.

The results also indicated that most programs felt that board scores were a significantly important aspects when evaluating an applicant. Information about each responding program's geographical location was also collected. The vast majority of programs came from the East Coast or Midwest, with relatively few responses from programs on the West Coast or Pacific Northwest regions. This indicates that the information gathered cannot necessarily be generalized to all areas of the country. The low response rate (23.3%) was another factor limiting the generalizability of the information gathered.

This study only sought to evaluate the views of internal medicine residency programs. It is highly likely that the results would vary depending what specialty was surveyed. The questions used in this survey could easily be applied to various specialties with little or no modification, with the only exception being gathering of the other program's contact information.

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The Relationship Between Academic Performance and Student Clinical Performance Self-Assessment in the Des Moines University College of Podiatric Medicine and Surgery (DMUCPMS)

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Purpose: This study aims to identify the relationship between student academic performance and third-year clinical performance self-assessment in DMUCPMS.

Method: Third-year podiatric medical students from the classes of 2012, 2013, and 2014 completed a self-assessment of their performance for each of five broad clinical podiatric objectives (Medicine, Radiology, Surgery, Biomechanics, and General/Professionalism). Each objective was rated on a five-point Likert scale. The assessment was completed after students completed the first twelve weeks of their third-year clinical rotations (PRE) and a second time at the conclusion of the third-year (POST). The mean self-assessment score for PRE and POST surveys for all combined objectives was determined for each student. This mean was compared to student's three year cumulative GPA. Student clinical experiences for the year were essentially identical.

Results: There was no statistically significant correlation identified between cumulative GPA and the PRE and POST clinical self-assessments, nor with the change between PRE and POST assessments based on the Pearson correlation test (p-values: PRE -0.024, POST -0.053, Change -0.026). Interestingly, a low significant correlation was found between PRE and POST self-assessment scores ($r=0.459$, $p=0.01$).

Discussion/Conclusion: Little has been published in medical education and no such research is available in podiatric medical education on the relationship between student academic performance and clinical performance self-assessment. Published studies in allopathic medical education has shown that students with lower GPAs tend to rate their clinical performance higher in initial clinical performance self-assessment. The results from our study may be due to the explicit description of the clinical competencies and the orientation students receive prior to the start of their clinical training.

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Geospatial Analysis of School-Based Dental Sealant Programs in Iowa

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Objectives: Dental sealants are a preventive treatment that helps protect cavity-prone teeth as a child and into adulthood. This study assessed the geographic distribution of school-based dental sealant programs (SBS) in Iowa, identified high-risk counties not currently served by a program based on socioeconomic correlates and community water fluoridation status, and determined viable expansion target locations throughout the state that could improve access to preventive oral health care services for children in Iowa.

Methods: Physical address locations of existing school-based dental sealant programs were mapped using a geographic information system. High-risk explanatory variables included: elementary, junior high, and middle schools with 40 percent or greater free and reduced-price lunch eligibility, 2012 Medicaid enrollment for children ages six to 14 years, by county, and fluoridation status of each community water system. Geospatial analyses were conducted using ArcGIS v10.1 (Environmental Systems Research Institute Inc., Redlands, CA).

Results: The SBS program analysis revealed 63 of Iowa's 99 counties had at least one SBS program serving students in an elementary school setting while 26 counties had at least one program serving students in a junior high/middle school setting. Based on the established high-risk criteria, disparities exist in rural and socioeconomically depressed counties of northeast Iowa and west to southwestern Iowa.

Conclusion: Ensuring expansion of existing SBS programs into high-need areas, working with local school leaders, and maintaining public health supervision licensing for dental hygienists could improve dental public health infrastructure and help improve access to oral health care for children in Iowa.

Broadlawns Family Health Center System Implementation for Immunizations in Children <36 Months-Midpoint Review

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Background: Childhood immunizations prevent 14 million cases of disease, 33,000 deaths, and save \$43.3 billion in health care costs per birth cohort. Broadlawns Family Health Center is in the middle of a one year system based effort to improve childhood immunizations.

Objective: To perform a midpoint evaluation of immunization rates in children less than 36 months of age and to qualitatively determine why children are behind on immunizations.

Methods: We performed an immunization audit for every pediatric patient from birth to 36 months seen at Broadlawns Family Health Center (FHC) and identified children late in receiving immunizations according to the Iowa Immunization Registry Information System (IRIS). Immunization rates were compared to results of a similar audit performed in July 2013. Caregivers were surveyed regarding their child's late immunization status.

Results: The FHC had 170 children less than 36 months old registered in the electronic medical record. Sixty (35%) children were deficient in immunizations. Seventeen (28%) caregivers were successfully contacted and surveyed. Compared to the July 2013 audit, immunization rates did not improve. Caregivers reported late immunizations were due to difficulty scheduling and being unaware of the child's status.

Conclusions: Broadlawns FHC seeks to improve childhood immunization rates through a systems based approach. Immunization rates did not improve compared to the July 2013 audit though caregiver surveys offered an explanation. Limited availability for well child visits was the primary problem and the FHC plans to expand access for these services.

Characterization of Pathways Involved in C1q-Dependent Phagocytosis

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C1q is the recognition component of the classical complement pathway and it has a well described role in enhancing phagocytic function of monocytes, macrophages and dendritic cells independent of complement activation. Deficiency in C1q leads to the development of autoimmunity due to decreased ability to engulf apoptotic cells (efferocytosis), however the mechanism leading to C1q-dependent engulfment is poorly understood. C1q is a 460 kDa soluble multimer that consists of a C-terminal globular head region and an N-terminal collagen-like tail, and previous studies have implicated the collagen-like tail in enhancement of phagocytic function. Our lab recently demonstrated that C1q triggers enhanced engulfment of apoptotic cells in mouse bone-marrow derived macrophages by upregulating expression of Mer tyrosine kinase (MerTK) and its ligand, Gas6, a well-known receptor-ligand pair required for efferocytosis. Here we demonstrate that the C1q collagen-like tails are not sufficient to elicit MerTK expression and efferocytosis despite their ability to trigger engulfment of antibody-opsonized targets. To determine if this novel C1q-dependent efferocytosis pathway was active in human monocytes, monocytes were purified from human blood using negative selection with magnetic beads. While monocytes responded to C1q with enhanced phagocytosis of antibody-opsonized targets, they failed to respond to C1q with enhanced engulfment of apoptotic cells. These data demonstrate that C1q triggers enhanced phagocytic function via multiple mechanisms and future studies are directed at further defining the biochemical pathways involved in C1q-dependent enhanced phagocytosis.

Statins have a Mevalonate Pathway Independent Synergistic Antimicrobial Effect in Combination with Aminoglycosides

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Sepsis is the 10th leading cause of death in the United States. As antimicrobial resistant bacterial strains emerge, treatment options are increasingly limited. Studies have shown that HMG-CoA reductase inhibitors, or statins, have pleiotropic effects beyond their lipid lowering capabilities. Many of these effects are attributed to immunomodulatory effects. Recent studies indicate that statins also have antimicrobial effects but at higher concentrations than typically clinically achievable. We hypothesized that statins may have synergistic effects when combined with traditional antimicrobials. This study investigated the potential antimicrobial effects of statins in combination with antimicrobials on *Staphylococcus aureus* and the mechanism behind this phenomenon. In combination with statins, only aminoglycosides demonstrate a synergistic antimicrobial effect on *S. aureus*. While all statins showed a synergistic antimicrobial effect, fungal derived statins (simvastatin and lovastatin) are more potent than synthetic statins (atorvastatin and fluvastatin). Interestingly, the prodrug forms are more potent than active acid statins. These effects were not reversed by the addition of mevalonate. Upregulation in mevalonate kinase expression was also not observed in *S. aureus* post treatment with inactive simvastatin and/or gentamicin, as observed when HMG-CoA reductase is inhibited in *S. aureus*. Thus these effects are mevalonate pathway independent. Based upon morphological changes and the decreased rate of autolysis, we hypothesize that statins damage the cell wall of *S. aureus* by nonlethal means, allowing for better uptake of gentamicin. Further exploration is required to fully understand the mechanism of action of statins, as they may aid in treatment of invasive *S. aureus* infections.

Antiviral Effect of MST-312 on Herpes Simplex Virus

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Herpes simplex virus (HSV) is a double stranded DNA virus that causes cold sores and genital herpes. In between outbreaks, the virus remains latent in neuronal cells. Although there are effective treatment options available for HSV disease, antiviral resistance can occur. Therefore, there is a need to identify new antiviral targets. One such target may be the cellular enzyme telomerase. Telomerase is the enzyme that prevents the shortening of telomeres. Previous research has shown that telomerase activity is increased during HSV infection. Our lab has recently determined that treatment with the telomerase inhibitor MST-312 dramatically reduced HSV replication when added to the infected cells prior to 6 hpi. The goals of this study were to characterize the effects of MST-312 on cell viability and virion stability. Trypan blue exclusion was used to measure cell toxicity in HEp-2 and hTERT-HME1 cells treated for 24 hours with 2-100 μ M of MST-312. There was no statistically significant increase in cell death when MST-312 treated cells were compared to DMSO control. To determine the effects of MST-312 on HSV virions, HSV was treated with 20- 100 μ M of MST-312 for 30-90 minutes. The MST-312 in the samples of HSV was then diluted to a concentration below the lowest dose shown to affect HSV-infected cells; and infectious virus was measured using plaque assay on VERO cells. MST-312 treatment led to a 30 – 95% reduction in the ability of HSV to form plaques. Therefore, we conclude that MST-312 can have a direct antiviral effect on HSV.

Neuropil Distribution in the Anterior Cingulate and Primary Visual Cortex of Cetartiodactyla, Primates, and Afrotheria

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Previous studies of the cerebral cortex have utilized the neuropil space as a proxy for connectivity, highlighting structural differences between cortical areas. The following study aims to investigate the distribution of neuropil space across 18 mammalian orders in two cortical areas, sampled from the frontal and occipital lobes. Results indicate a significant difference in neuropil space between cortical areas and species. The anterior cingulate cortex maintained a higher neuropil fraction than the primary visual cortex among all species studied.

Anatomic Variations of the Aortic Arch Branching Pattern

M.A. Khan, PhD and Nolan J. Rudder, DO'16

The aortic arch branching pattern was examined in 39 cadaver specimens. The classic branching pattern of the aortic arch consists of the brachiocephalic trunk, left common carotid, and left subclavian arteries. The left and right vertebral arteries are normally branches of the left and right subclavian arteries, respectively. The present study demonstrates variant occurrence of the left common carotid and the left vertebral arteries. The left common carotid in one cadaver originated from the base of the brachiocephalic artery, crossed to the left side anterior to the trachea and then ascended on the left side of the cervical region. This anomaly can have various effects on the hemodynamics of the cerebral circulation and should be identified before performing any surgical procedures involving the aortic arch. In a separate cadaver, the left vertebral artery originated from the aortic arch, approximately 5mm posterior to the origin of the left subclavian artery. The anomalous left vertebral artery measured 7.34mm in diameter, while the right vertebral artery measured 7.26mm. The origin of the left vertebral artery from the aortic arch is significant as it has been associated with a higher incidence of arterial dissection than a left vertebral artery of subclavian origin. Anomalies in the aortic arch branching pattern are likely due to atypical development of the embryonic aortic arch system. A complete understanding of the normal aortic arch branching pattern, as well as its possible variations is vital to successful surgical and medical management of vascular pathologies.

Endogenous D-serine Enhances Glutamatergic Transmission and Network Activity in Cortex

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The prefrontal cortex (PFC) is involved in working memory and other cognitive functions. Medial PFC (mPFC) pyramidal neurons exhibit characteristic prolonged membrane depolarization that often leads to sustained firing. NMDA receptors are thought to be critical in maintaining the sustained activity. We are interested in how the sustained activity is modulated by D-serine, a glia-derived co-agonist of NMDA receptors and highly enriched in the mPFC region (2119±204 nmol/g). Evoked sustained activity in layer 5 pyramidal neurons exhibited a significantly longer duration in low Mg²⁺ (0.1 mM), and the duration was further increased by 10-100 μM D-serine. Application of the NMDA receptor blocker abolished the sustained activity. However, the enhancement of sustained activity by D-serine was not significant in a mutant mouse lacking functional D-amino acid oxidase (DAO-). Similarly, the addition of D-serine failed to enhance NMDA receptor mediated synaptic currents in DAO- mice. Taken together, these data suggest that D-serine in mPFC might serve as a modulator of NMDA receptors, influencing the level of sustained network activity.

Maintenance of the Transcriptional Repressor Tup1 During the Morphological Transition in *Candida albicans*

Nichelle Hackert, Micheal Boyer, Martin Schmidt

The yeast *Candida albicans* is a normal member of the human gastrointestinal microbiome that can convert into an opportunistic pathogen. Upon stimulation by environmental factors, *C. albicans* acquires considerable virulence by switching from a unicellular to a hyphal morphology. This yeast-to-hyphae transition is controlled by positive and negative transcriptional regulators that mediate the induction of a hyphal growth program. It has been shown that boric acid (BA) is an effective agent to control *C. albicans* infections, possibly because it inhibits the yeast-to-hyphae transition. The molecular mechanism behind this action is unclear. A chance observation in the model yeast showed that BA inhibits protein degradation, raising the possibility that BA inhibits the timely degradation of the repressor of filamentous growth, Tup1. A reporter strain expressing a Tup1-GFP fusion was constructed by the short-flanking homology PCR method and the localization of the fusion protein to the nucleus was confirmed by fluorescence microscopy. The fluorescence intensity of cells expressing the Tup1-GFP fusion was examined by flow cytometry in order to characterize the degradation of the Tup1 repressor in the presence and absence of BA. It was found that the fluorescence intensity of reporter strain nuclei did not change during the transition to filamentous growth or in the presence of BA. We conclude that the amount of nuclear Tup1-GFP neither fluctuates during the yeast-to-hyphae transition nor responds to exposure to BA.

Regulators of Hyphal Growth Determine Boric Acid Resistance in *Candida albicans*

Martin Schmidt, Alexander Hjelmaas, Celia Venezia, Michael Boyer

Boric acid (BA) has a poorly understood broad antibiological activity. In the dimorphic yeast *C. albicans*, BA inhibits the yeast-to-hypha transition – a property that may explain the effectiveness of BA in the treatment of vaginal yeast infections (De Seta *et al.*, 2009. *J Antimicrob Chemother* 63(2), 325). We established that hypha formation is universally inhibited by BA in clinical isolates of *C. albicans*, even in problematic multidrug resistant strains. Furthermore, it became evident that the inhibition of hyphal formation occurs at BA concentrations too low to have a negative effect on colony formation, indicating that the suppression of invasive growth is rather specific and not the result of a general growth inhibition. *We hypothesize that BA inhibits the expression of proteins required for the induction of the filamentous growth program in C. albicans.* In order to characterize the mechanism of action of BA on hypha formation, we examined the influence of BA on viability and morphology of selected *C. albicans* deletion mutants. We focused our studies on mutants with known defects in stress response pathways and abnormalities in the induction of hyphal-growth.

Influence of Boric Acid on Histone Acetylation During the *Candida albicans* Morphological Transition

Ben Pointer, M. Boyer, M. Schmidt

Acetylation of histones H3 and H4 is recognized as an important factor in the regulation of gene expression during both normal growth and the response to environmental clues. In the opportunistic pathogen *C. albicans*, acetylation of lysine 56 is a hallmark of freshly synthesized histone H3 that is required for the survival of genotoxic stress. Boric acid (BA) induces histone acetylation in *S. cerevisiae* and suppresses the transition from yeast to hyphal growth in *C. albicans*. The present study examines the relationship between BA treatment, chromatin modification and the morphological transition in heat/serum stimulated cultures of *C. albicans*. The experiments show that the presence of 0.1% BA completely inhibits the induction of germ-tubes in *C. albicans* and reduces the degree of H3K56 acetylation while not significantly affecting H4K12 acetylation. We propose that the observed reduction in H3K56 acetylation reflects a general inhibition in protein synthesis and has wide-ranging effects on *C. albicans* gene expression.

Purification and Characterization of a Putative Invertase from *Trichomonas vaginalis*

Michael Dirkx, Michael P. Boyer, Andrew Brittingham, Wayne Wilson

Trichomonas vaginalis, a flagellated protozoan, is the agent responsible for trichomoniasis, the most common nonviral sexually transmitted infection worldwide. A reported 200 million cases are documented each year with far more cases going unreported. However, *T. vaginalis* is disproportionality under studied, especially considering its basic metabolism. It has been demonstrated that *T. vaginalis* does not grow on sucrose. However, the *T. vaginalis* genome contains some nine putative sucrose transporters and a putative β -fructofuranosidase (invertase). Thus, the machinery for both uptake and cleavage of sucrose appears to be present. We amplified the β -fructofuranosidase from *T. vaginalis* cDNA and cloned it into an *Escherichia coli* expression system. The expressed, purified protein was found to behave similarly to other known β -fructofuranosidases. It had a similar K_m and V_{max} to previously characterized enzymes using sucrose as a substrate, was also active towards raffinose, but had no detectable activity towards inulin. Thus, *T. vaginalis* has the coding capacity to produce an active β -fructofuranosidase capable of hydrolyzing di- and trisaccharides containing a terminal, non-reducing fructose residue. Since we cloned this enzyme from cDNA, we know that the gene in question is transcribed. Therefore, the reason why *T. vaginalis* is unable to effectively grow on sucrose remains to be determined.

The Cloning, Recombinant Expression, and Characterization of Glycogen Synthase from the Parasitic Protozoan *Trichomonas vaginalis*

Nayasha Madhan, Prajakta Pradhan, Andrew Brittingham, Wayne Wilson

Trichomonas vaginalis is a protozoan parasite transmitted by sexual contact. Worldwide, it is the most common non-viral, sexually transmitted infection. In females, *T. vaginalis* infection may result in vaginal discomfort and a characteristic discharge. In males, the infection is typically asymptomatic. Although often considered nothing more than a nuisance, *T. vaginalis* infection predisposes an individual to infection with HIV and other sexually transmitted diseases. The genome of *T. vaginalis* has been sequenced but many questions remain regarding this pathogen's core metabolism. Previous work has demonstrated the presence of substantial glycogen stores within the organism and that the *T. vaginalis* genome contains sequences believed to encode glycogen synthase and glycogen phosphorylase activities. Here we report our attempt to clone the gene encoding this putative glycogen synthase, express recombinant protein in *E. coli*, and begin biochemical analyses of its enzymatic activity. Our preliminary data suggests that we have successfully produced recombinant glycogen synthase in *E. coli* that is functionally active. We are currently beginning the large-scale purification of recombinant protein to allow for a more detailed analysis of its enzymatic activity. These studies may shed light on the mechanisms involved in carbohydrate acquisition and utilization by *T. vaginalis* and other pathogenic protists.

Transcriptional Regulation of Glycogen Phosphorylase in *Saccharomyces cerevisiae*

Mirza M. Baig, Michael P. Boyer, Wayne A. Wilson

We have a longstanding interest in understanding the control of glycogen storage in the budding yeast, *Saccharomyces cerevisiae*. Glycogen is used as a form of energy storage across many species. Glycogen degradation can be accomplished by the action of glycogen phosphorylase. Glycogen phosphorylase is the product of the *GPH1* gene. Expression of *GPH1* is induced in cells that approach stationary phase, and it is believed that the increase in the expression of this gene requires the activity of the cAMP-dependent protein kinase (Protein kinase A; PKA). *TPK1*, *TPK2*, and *TPK3* encode three isoforms of the catalytic subunit of PKA. PKA is involved in phosphorylating various cellular targets, and each isoform has distinct sets of targets. The purpose of this study was to examine the effect of each *TPK* gene on glycogen phosphorylase expression. To address this question, mutant yeast strains were generated. The glycogen phosphorylase gene was replaced with the gene encoding green fluorescent protein (GFP). Gene replacement was carried out in wild type yeast and in yeast lacking the *TPK1*, *TPK2* or *TPK3* gene. The various yeast strains were then grown in batch culture and the intensity of green fluorescence measured as an indicator of *GPH1* promoter activity. Preliminary data indicate that the *TPK2* gene product may have the greatest impact on phosphorylase expression, an observation consistent with previous data indicating reduced phosphorylase enzyme activity in a strain lacking functional *TPK2*.

DNA Repair Deficiencies in PARP1 Knockout Cells

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BRCA-deficient breast cancers have proven difficult to treat due to the variability in gene expression between tumor types. In recent years, clinical trials with patients who have BRCA-deficient breast cancers have been shown to positively respond to PARP (poly ADP-ribose polymerase) inhibitor treatments. Unfortunately the molecular mechanism(s) underlying the way these inhibitors work has not been elucidated. PARP1, one of 17 PARP-like genes in the human genome, plays a key role in DNA repair and is the likely physiological target of PARP inhibitors. PARP1 is an important mediator of alternative non-homologous end joining (A-NHEJ), base excision repair, and is required to restart stalled replication forks. PARP1's major role in DNA repair was presumed to occur mainly through the A-NHEJ pathway, but my work has proven otherwise. By generating PARP1-deficient HCT116 human colorectal cancer cells by recombinant adeno-associated virus-mediated gene targeting, I have shown that PARP1 is crucial for restarting stalled replication forks, and hypothesize that this defect also results in shortened telomeres. This genetic approach has phenocopied at least some of the effects observed with PARP inhibitors and strongly support the contention that PARP1 is the biologically important target of PARP1 inhibitors. These studies should help in the development of new approaches to treat BRCA-deficient tumors.

Decreased Arrhythmic Burden Following Exercise is Associated with a Decrease in Cx43 Phosphorylation Specifically at Serines 368 and not Serines 255 and 279/280

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Cardiovascular diseases are the leading cause of death globally for the last decade. Cardiac arrhythmias are a common serious outcome of these diseases which can be caused by gap junction dysfunction. Gap junction proteins (GJP) are located between cardiac myocytes. This allows for intercellular current flow, and coordinated propagation of electrical signals. One possible cellular mechanism for signal propagation is the expression and

phosphorylation of Cx43. Connexin 43 (Cx43) is the main GJP in the left ventricle. Exercise training simultaneously increases cardiac parasympathetic tone, while decreasing cardiac sympathetic tone⁶. Several studies have linked Cx43 phosphorylation and expression with chronic exercise training¹. This has prompted us to further investigate that relationship. Previously we have examined the relationship between Cx43 phosphorylation and arrhythmic response to acute myocardial ischemia, and determined if this effect is modulated by chronic exercise training. Rats underwent 8 weeks of exercise conditioning or remained sedentary controls. Rats were then subjected to 20 minutes of myocardial ischemia and electrocardiograms were recorded. Arrhythmias detected during this period were identified according to the Lambeth Convention guidelines². Following the ischemic period the heart and hindlimb muscles were dissected and flash frozen. Expression of Cx43 phosphorylation in the left ventricle was examined by Western Blot analysis. There was significant decreased phosphorylation of Cx43 at S368 in the exercised animals when compared to sedentary controls. To further analyze the phosphorylation status of Cx43 we studied arrhythmic susceptible sites S255 and S279/282. No significant difference of phosphorylation was observed at those sites.

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The G Protein-Coupled Estrogen Receptor 1 Regulates Endothelial Ca²⁺ Efflux

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The novel G protein-coupled estrogen receptor 1 (GPER) has been demonstrated to have a vast array of cardiovascular effects. We have tested the hypothesis that the G protein-coupled estrogen receptor 1 (GPER) is involved in the regulation of calcium efflux in the vasculature. In primary vascular endothelium, the specific GPER agonist G₁ dose-dependently inhibits the activity of the plasma membrane calcium-ATPase (PMCA) measured dynamically in living cells. PMCA and GPER form a complex during Ca²⁺ signals triggered by the SERCA pump inhibitor thapsigargin in cells pretreated with or without 17β-estradiol. Knockdown of GPER in endothelial cells using antisense directed against GPER is associated with a ~ 40% enhancement of PMCA activity compared to scrambled antisense. Heterologous expression of human GPER in fusion with the fluorescent protein DsRed2 in HEK 293 cells results in a 38% reduction of PMCA activity. In cells expressing fluorescent reporters constructed based on individual sub-membrane domains (SMDs) of GPER, endogenous PMCA coimmunoprecipitates with SMDs 1, 3, and 4 of GPER, but not with SMD2, at the peak of a typical Ca²⁺ signal triggered by emptying of endoplasmic reticulum Ca²⁺ store. These data suggest that GPER regulates Ca²⁺ efflux in endothelial cells by interacting with PMCA through the receptor's sub-membrane domains 1, 3, and 4 and inhibiting the pump's activity partly via this mechanism.

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Novel Biosensor-Based Approach Identifies Three Distinct Calmodulin-Binding Domains in the G Protein-Coupled Estrogen Receptor 1

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The new G protein-coupled estrogen receptor 1 (GPER) has been demonstrated to participate in many important cellular functions, but its regulatory inputs are not clearly understood. Here we describe a new approach that identifies GPER as a novel calmodulin-binding protein, locates its binding sites and characterizes their binding properties. GPER coimmunoprecipitates with calmodulin in primary vascular smooth muscle cells treated acutely with either specific ligands or a Ca²⁺-elevating agent. To confirm direct interaction and locate the calmodulin-binding domain(s), we designed a series of FRET biosensors that consist of enhanced variants of cyan and yellow fluorescent proteins as the energy donor and acceptor, respectively, flanking each of GPER's submembrane domains (SMDs). The responses of these biosensors showed that submembrane domains 2, 3 and 4 directly bind calmodulin. Additional biosensors with modified linker lengths identified domains that display the strongest calmodulin-binding affinities and largest biosensor dynamics, including a.a. 150-175, 242-259, and 330-351, corresponding respectively to SMDs 2, 3 and the juxtamembrane section of SMD4. These biosensors bind calmodulin in a strictly Ca²⁺-dependent fashion and with disparate affinities in the order SMD2>SMD4>SMD3, K_d values being 0.44 ± 0.03, 8.01 ± 0.29, and 1.47 ± 0.16 μM, respectively. Interestingly,

simultaneous determinations of biosensor responses and suitable Ca^{2+} indicators showed separate Ca^{2+} dependencies for their interaction with calmodulin in a different order of $\text{SMD4} > \text{SMD2} > \text{SMD3}$, $\text{EC}_{50}(\text{Ca}^{2+})$ values being 2.38 ± 0.13 , 5.15 ± 0.25 , and 0.75 ± 0.05 μM , respectively. These data clearly indicate that calmodulin may regulate GPER-dependent signaling at the receptor levels. The use of FRET-based biosensors represents a simple method to identify unknown calmodulin-binding domains in G protein-coupled receptors and to quantitatively assess binding properties.

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Regulation of Store-Operated Ca^{2+} Entry in the Vascular Endothelium by the G Protein-Coupled Estrogen Receptor 1

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The novel G protein-coupled estrogen receptor 1 (GPER/GPR30) has been found to participate in numerous cardiovascular functions. Store-operated Ca^{2+} entry (SOCE) is an essential mechanism that is required for many endothelial cell functions. We found that activation of GPER using the GPER specific agonist G1 causes a dose-dependent inhibition of SOCE in primary vascular endothelial cells. Heterologous of GPER in HEK 293 cells is associated with substantial decreases in the total Ca^{2+} signal triggered by thapsigargin, and a 40% decrease in the rate of SOCE. Knockdown of GPER in endothelial cells using antisense directed against GPER increases SOCE by approximately 50% compared to cells transfected scrambled oligo. Interestingly, the GPER specific antagonist G15 increases SOCE stimulated by thapsigargin, an agent that activates classic SOCE independently of estrogen action. In primary endothelial cells, GPER forms a complex with the stromal interaction molecule 1 (Stim1), an essential molecular switcher of SOCE. Interestingly, SOCE measured in cells stably expressing fusions between EYFP and individual sub-membrane domains (SMDs) 1 – 4 of GPER does not differ from internal controls. These data indicate that GPER may be an important regulatory input of store-operated Ca^{2+} entry via its interaction with Stim1. Since the EYFP-SMD fusions are all cytoplasmically expressed, the data may also suggest that proper membrane docking (PM or ER) of full-length GPER is required for it to exert its effect on SOCE.

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Identification and Characterization of Calmodulin-Binding Domains in the Angiotensin II Receptor Type 1A

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Angiotensin II receptor type 1A (AT1R) is a G protein-coupled receptor responsible for the many important effects of angiotensin II (AngII). In vascular smooth muscle cells, AngII induces contraction via a Ca^{2+} /CaM-dependent process. We have begun to test the idea that signaling via AT1R involves CaM also at the receptor level. In vascular smooth muscle cells, AT1R coimmunoprecipitates with CaM upon stimulation by AngII or thapsigargin, a specific SERCA inhibitor that triggers classic store-operated Ca^{2+} entry. To identify all CaM-binding domains in AT1R, we have generated a series of biosensors that consist of each of the four sub-membrane domains (SMDs) or a fragment thereof in AT1R flanked by enhanced variants of yellow and cyan fluorescence protein. We named these biosensors BSAT1R_x, with x denoting the amino acid numbering of the linker. In response to purified Ca^{2+} -saturated CaM, BSAT1R₁₂₅₋₁₄₁, BSAT1R₂₁₅₋₂₄₂ and BSAT1R₃₀₉₋₃₂₇ display drastic disruption of FRET formed between ECFP and EYFP. These changes are characteristic of conformational changes caused by direct binding of CaM to SMD2, SMD3 and the juxta-membranous segment SMD4 in human AT1R. These changes are reversed upon chelation of Ca^{2+} . BSAT1R₅₃₋₆₄, corresponding to SMD1, does not respond to Ca^{2+} -CaM. Titrations of purified Ca^{2+} -saturated CaM yielded dissociation constants of $\sim 46.2 \pm 0.35$, 0.36 ± 0.07 , and 0.5 ± 0.01 μM , respectively for SMD2, 3, and the juxta-membranous segment of SMD4. The respective Ca^{2+} sensitivities of these interactions were $\sim 3.01 \pm 0.49$, 0.18 ± 0.002 , and 1.36 ± 0.07 μM , determined by monitoring concurrent responses of the respective BSAT1R_x and a suitable Ca^{2+} indicator (indo-1 or XRhod-5F). These data strongly suggest that CaM is involved in AngII signaling via direct interactions with multiple domains in AT1R. Given the drastic differences in affinity and Ca^{2+} sensitivities of the interactions, it is likely that these domains interact with CaM in distinct physiological scenarios.

Fusions Between Nuclear Estrogen Receptors and Red Fluorescent Protein

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The reduction in circulating estrogen concentration in post-menopausal women is associated with a substantial increase in risk and incidence of cardiovascular disease. Hormone replacement therapy is expected to restore the cardiovascular protection conferred by estrogen but has not shown to provide the desired effects. Our central hypothesis is that specific targeting of estrogen receptor subtypes could produce better outcomes and prevent undesirable effects. We have previously observed that chronic estrogen treatment substantially upregulates in the vasculature the expression of total cellular calmodulin, a ubiquitous yet limiting signaling molecule. Data presented in this poster is part of studies identifying the estrogen receptor(s) (ER α , ER β , or the novel G protein-coupled estrogen receptor (GPER)), responsible for the effect of 17 β -estradiol to upregulate cellular CaM. ER- α and ER- β were PCR amplified from existing plasmids encoding the respective human sequences. The fluorescent protein DsRed₂ was then fused to the C-terminus of each receptor. The fusion DNAs were then introduced into a mammalian plasmid. The plasmids were then transiently transfected into human embryonic kidney HEK 293 cells. Intracellular imaging contrasting DsRed₂ and loaded fura-2/AM fluorescence revealed nuclear expression for ER α -DsRed₂ and ER β -DsRed₂ fusions, consistent with the functional role of ER α and ER β as nuclear receptors. The successful heterologous expression of these fusion proteins allows subsequent for evaluation of total CaM expression following chronic treatment with 17 β -estradiol.

Novel Fluorescent Reporters for the Stromal Interaction Molecule 1

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The stromal interaction molecule 1 (Stim1) is a Ca²⁺ sensor in the endoplasmic/sarcoplasmic reticulum whose Ca²⁺ sensing triggers its oligomerization and subsequent activation of store-operated Ca²⁺ entry via direct interactions with Ca²⁺ channels at the plasma membrane. We have generated a set of fluorescent reporters based on the intraluminal domain of Stim1 where dimerization and Ca²⁺ binding take place. These fluorescent reporters consist of a FRET pair (ECFP-EYFPc) flanking the Ca²⁺-binding loop of the canonical EF hand, the entire canonical EF hand, the hidden EF hand, and the sterile α motif (SAM), or a combination of these fragments. All reporters display enhanced FRET upon Ca²⁺ binding and FRET disruption upon Ca²⁺ chelation from a Ca²⁺-saturated state. Reporters generated from the unmodified canonical EF domain and the Ca²⁺-binding loop of this domain display the largest dynamic range in Ca²⁺-dependent responses. However, double-loop or triple loop chimeras of the linker yield significant improvement in the dynamic range of the biosensors upon interaction with Ca²⁺. Analyses of spectrofluorometric Ca²⁺ titrations yielded apparent dissociation constants in the millimolar range for these reporters. To investigate the role of the negative charges in the Ca²⁺-binding loop of Stim1, we generated D to K substitutions at position 2 & 3, or 2, 3, 5, and 7 in the Ca²⁺-binding loop and introduced these into the triple loop biosensor configuration. The D76/77K substitutions reduces affinity for Ca²⁺ binding, whereas D76/77/81/83K quadruple substitutions completely abolished Ca²⁺ binding. These reporters allow highly quantitative assessment of factors controlling the Ca²⁺-sensing capability of Stim1. The data indicate that negative charges in the Ca²⁺-binding loop play an essential role in the interaction between Stim1 and Ca²⁺.

The Effects of Moderate Intensity Exercise Training on the Incidence of Supraventricular Arrhythmias and Atrial Connexin 40 and Connexin 43 Expression in Young and Aged Rats

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Supraventricular arrhythmias are the most prevalent of all arrhythmias, with the elderly being at the greatest risk. Exercise training has been repeatedly shown to reduce supraventricular arrhythmic susceptibility. Connexin 40 (Cx40) is known to be the primary regulator of conduction between atrial cardiomyocytes and alteration of its expression has been associated with atrial arrhythmia development. Recent evidence also suggests that Connexin 43 (Cx43) assists controlling atrial electrical conduction. We hypothesized exercise reduces atrial arrhythmic susceptibility in young and aged animals and would be accompanied by increased atrial Cx40 and Cx43 expression. Groups of young and aged F344 rats underwent treadmill exercise training or sedentary handling. Subcutaneous electrocardiographic leads were then implanted following the respective exercise or sedentary protocols. The arrhythmic index (AI) was calculated using a modified scoring system totaling supraventricular arrhythmias during a baseline period (BL), sympathoexcitation (ISO), and psychological stressor (BR). AI was significantly reduced during BL and ISO periods in young exercise animals compared to sedentary counterparts. Western blot analysis showed significantly greater atrial Cx40 expression in young exercise compared to young sedentary rats, while there was no significant change in the aged animals. Interestingly, a significant increase was observed in atrial Cx43 expression in aged exercise rats compared to sedentary counterparts. These preliminary results indicate moderate exercise is cardioprotective in a young animal model by reducing supraventricular arrhythmias and increasing atrial Cx40 expression while a similar aged model resulted in no changes in arrhythmic susceptibility but did increase in atrial Cx43 expression.

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