DES MOINES UNIVERSITY
OFFICE OF RESEARCH

Mentored Student Research Program
July 18, 2016
Des Moines University, Des Moines, IA

Dear Mentored Research Students

On behalf of the Research and Grants Committee, welcome to the Des Moines University (DMU) Mentored Student Research Program closing program. This event represents and celebrates the culmination of your summer research experiences. We know you have worked hard over the last seven weeks; tackling challenges in the laboratory; learning new skills; and building new professional relationships. We were able to see firsthand the engagement, inquisitive minds, and commitment that each of you brought to this year's program and we are thoroughly impressed. Many of you will continue to work on your respective research projects over the coming academic year, and we encourage you to do so.

The goal of the DMU Mentored Student Research Program is to provide opportunities for students to develop their skills as researchers by receiving coaching and mentorship from faculty. Dissemination of new knowledge, by faculty and student researchers, supports Des Moines University's mission. You have contributed to the fulfillment of this mission by your participation in the Mentored Student Research Program. We encourage you to continue to develop as a researcher, and thank you for your hard work this summer.

This program would not be possible without the support of many individuals and departments across campus. The University has invested in this program financially, researchers across campus have taken the time to deliver research talks, and your mentors have invested time in your professional growth and education. Please take the opportunity to thank your mentors for their investment this past summer.

Keep asking questions and searching for answers! We wish you the best of luck in your future endeavors.

Sincerely,

Jeffrey Gray, PhD
Vice President for Research and Professor of Microbiology and Immunology, Des Moines University
Jeffrey.Gray@dmu.edu

Mindi J. Feilmeier, DPM, FACFAS
Assistant Professor, College of Podiatric Medicine and Surgery, Des Moines University
Chair, Des Moines University Mentored Student Research Program
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Agenda

Time	Agenda	Location
8:30 am	**Registration, Breakfast, and Poster Viewing**	**SEC Square**
9 am	**Welcome** Jeffrey Gray, PhD, Vice President for Research and Professor of Microbiology and Immunology, Des Moines University	**SEC Auditorium**
9:15 am	**Keynote Address: Advancing Cancer Therapy by Manipulating Metabolic Oxidative Stress** Bryan G. Allen, MD, PhD, Assistant Professor of Radiation Oncology, University of Iowa Carver College of Medicine • Define oxidative stress. • Describe anti-oxidants and pro-oxidants. • Describe how therapies that manipulate metabolic oxidative stress may enhance cancer therapy. • Describe the process of translating a therapy from the bench to the bed side.	
10:15 am	**Poster Viewing**	**SEC Square**
10:45 am	**Hallux Abducto Valgus Outcomes Longitudinal Project** Rachel Ellen Egdorf, DPM'19	**SEC Auditorium**
11 am	**A Comparative Genetic Analysis of the Leucine Degrading Enzymes in T Lymphocytes and EL-4 Lymphoma Cells** Michelle Brenner, DO'19	
11:15 am	**Group Picture**	**Outside SEC Auditorium**
11:30 am	**Poster Viewing**	**SEC Square**
12:20 pm	**Lunch**	**SEC Auditorium**
12:30 pm	**Contribution of Sleep Related Deaths to Infant Mortality in Iowa: An Opportunity for Improvement** Kelsey Coy, DO'20	
12:45pm	**Sensitization-Induced Modification of RAAS Components in Kidneys of Rats** Cara Cahalan, University of Nebraska-Lincoln	
1 pm	**Adjourn**	

Keynote Speaker

Bryan G. Allen, MD, PhD
Assistant Professor of Radiation Oncology, University of Iowa Carver College of Medicine

- BS, Major in Biology; Minor in Chemistry, University of Utah
- MD, Medicine, University of Iowa
- PhD, Biochemistry, University of Iowa
- Internship, University of Iowa
- Residency, University of Iowa

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

Dr. Allen's keynote slides can be found online at

https://cme.dmu.edu/Allen2016

Continuing Education Credit

- **DPM:** Des Moines University (DMU) is approved by the Council on Podiatric Medical Education as a provider of continuing education in podiatric medicine. DMU has approved this live activity for a maximum of 3.0 continuing education contact hour(s).
- **MD:** This activity has been planned and implement in accordance with the accreditation requirements and policies of the Iowa Medical Society (IMS). Des Moines University (DMU) is accredited by the IMS to provide continuing medical education for physicians. DMU designates this live activity for 3.0 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.
- **DO:** Des Moines University (DMU) is accredited by the American Osteopathic Association (AOA) and approves this live activity for 2.0 AOA Category 2-A CME credit(s) and 1.0 AOA Category 2-B CME credit(s).
- **Other:** This live activity is designated for 3.0 *AMA PRA Category 1 Credit(s)*™.

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Hallux Abducto Valgus Outcomes Longitudinal Project

Paul Dayton, DPM, MS, FACFAS, Mindi Feilmeier, DPM, FACFAS, **Rachel Egdorf, DPM'19**

College of Podiatric Medicine and Surgery, Des Moines University, Des Moines, IA

Currently over 130 different procedures are cited in the literature for the treatment of Hallux Abducto Valgus (HAV). HAV surgery is highly unpredictable with a high recurrence rate. This research study will be the first of its kind, multicenter, prospective, nationwide assessment of HAV surgical outcomes. This study will involve creation of a secure database to house data regarding short and long-term outcomes of the most popular surgical techniques. Pre-operative assessments of patients will include patient age, sex, BMI, smoking status, Diabetes/HgbA1C, previous foot surgery, additional foot deformities, and current health status. The pre-operative evaluation will include a standardized visual analog scale, 1st metatarsophalangeal joint ROM, radiographic findings, and scores from two subjective surveys. Intraoperative evaluation will include laterality, operative time, unusual findings, if a release of the first MTPJ was performed, joint preparation technique, bone debridement, capsular thinning, fixation construct and presence/size of a lateral facet. The post-operative outcome evaluations of these surgeries would include VAS, radiographic findings, activity resumption, recurrence, additional surgeries (if needed), satisfaction, and complications (bone or soft tissue). With the post-operative evaluations, certain subpopulations (sex, age, activity level) will be analyzed for trends. The post-operative assessments of these surgeries will be conducted after 3 months, 6 months, 12 months, 2 years, 5 years, and 10 years. With over 300,000 bunion surgeries performed yearly, our work identifying the best surgical procedure(s) for HAV will be one of the most beneficial studies of its time for the field of podiatry and allow improved outcomes of surgery patients.

A Comparative Genetic Analysis of the Leucine Degrading Enzymes in T Lymphocytes and EL-4 Lymphoma Cells

Michelle Brenner, DO'19 and Elitsa Ananieva, PhD

Biochemistry and Nutrition Department, Des Moines University, Des Moines, IA

Cancer and immune cells use leucine to support their biosynthetic and energy demands. The cellular concentrations of leucine are regulated by leucine degrading enzymes such as the cytosolic and mitochondrial branched-chain aminotransferases (BCATc and BCATm) and the branched-chain α-ketoacid dehydrogenase complex (E1α and E2 enzymes). The gene regulation of these enzymes is largely unknown but important to understand how immune and cancer cells interact in the tumor microenvironment.

Previous work determined that the transcription factor NFAT (nuclear factor of activated T cells), the oncogene c-Myc, and complex 1 of the mTOR pathway (mTORC1) impacted the protein expression of BCATc, BCATm, E1α, and E2 enzymes in T lymphocytes and their cancerous counterpart, EL-4 lymphoma cells. Utilizing quantitative RT-PCR, this study explored the mRNA expression of the above enzymes utilizing cyclosporine A (CsA), rapamycin, and 10058-F4, which inhibit NFAT, mTORC1, and c-Myc, respectively.

Rapamycin inhibited the mRNA expression of BCATc and E2 while 10058-F4 inhibited all genes. Thus, mTORC1 stimulates the gene expression of BCATc and E2 while c-Myc stimulates all genes examined. CsA differentially inhibited all genes in T lymphocytes suggesting a T lymphocyte-specific gene regulation of the leucine degrading enzymes by NFAT. A bioinformatics analysis of the promoter regions of the studied genes confirmed that all genes bind c-Myc and NFAT. Deciphering the gene regulation of the leucine degrading enzymes will aid in manipulating leucine metabolism in a direction that provides an advantage to immune cells to better combat cancer cells in the tumor microenvironment.

Contribution of Sleep Related Deaths to Infant Mortality in Iowa: An Opportunity for Improvement

Kelsey Coy, DO'20[1] and Simon Geletta, PhD[2]

[1]*College of Osteopathic Medicine, Des Moines University, Des Moines, IA*
[2]*School of Public Health, Des Moines University, Des Moines, IA*

In this study we examined trends in the incidence of infant deaths due to uncertain or less-understood underlying causes – as documented in the death certificates – that occurred in Iowa over nine years. We compared trends within the state to regional and nationwide trends. We specifically targeted sleep-related deaths; as such incidences have been consistently linked to a number of modifiable risk behaviors and factors, and thus are potential targets for public health interventions.

While the infant mortality rate (IMR) in Iowa is consistently below national and regional rates, infant sleep-related deaths exceeded national averages a third of the time and thus had a larger than expected impact on overall IMR. Additionally, an erratic pattern of improvement and retrogression in both IMR and sleep-related infant death rates during the study period suggests that rates have varied in the absence of focused and consistently applied interventions.

According to an Iowa Child Death Review Team report summarizing findings from 2004-2012, 79% of sleep-related infant deaths during this period occurred while the infant slept outside of an approved crib, <50% of the infants were placed to sleep on their back and in only 25% of cases was the infant confirmed to have been sleeping alone.

The American Academy of Pediatrics has issued guidelines stating that infants should be placed on their backs on a firm and unshared sleeping surface but clearly, adherence is less than complete. The trends observed suggest there is opportunity for an innovative and focused public health intervention in Iowa.

Sensitization-Induced Modification of RAAS Components in Kidneys of Rats

Cara Cahalan[1] and Sarah Clayton, PhD[2]

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[2]*Department of Physiology and Pharmacology, Des Moines University, Des Moines, IA*

Although one in three American adults has hypertension, the underlying cause in most patients is not known. The renin angiotensin aldosterone system (RAAS) has been implicated in many experimental models of hypertension and pharmacological agents that target this pathway are used extensively in the clinic. The complete RAAS has both a pro-hypertensive arm, consisting of angiotensin Type-I receptor (AT1R) and Angiotensin-converting enzyme (ACE) and the anti-hypertensive (AT2R and ACE2). Short sensitization periods can have long lasting neuroplastic effects and may impact the development of hypertension. Understanding how sensitization affects gene expression of RAAS components was the goal of this study. We hypothesized that sensitization increases the expression of pro-hypertensive RAAS components and decreases anti-hypertensive components when compared to un-sensitized controls. Laboratory animals were subjected to sensitization with angiotensin II (Ang II) or aldosterone (ALDO) then given 2% saline to induce hypertension. Because the kidney is pivotal in overall blood pressure regulation, we used RT-qPCR to evaluate gene expression in the kidneys of these animals. We found a decrease in the expression of ACE2 and a trend towards a decrease in AT2R expression in sensitized animals. Therefore, our sensitization protocol has reduces the anti-hypertensive arm of the RAAS. This may increase the effect of the pro-hypertensive arm in these animals. Understanding the mechanism of sensitization in the brain and peripheral sites (e.g. the kidney) will provide insight into possible causes of hypertension and elucidate better treatment strategies.

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♦ 2 ♦

Genetic Influences on Obesity in Male Twins - The National Heart, Lung, and Blood Institute Twin Study

Abigail Krone[1], Terry Reed[2], Jun Dai, PhD, MD, MSc[3]

[1]Mentored Student Research Program, Department of Public Health, Des Moines University, Des Moines, IA
[2]The Department of Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, IN
[3]Master of Public Health Program, Department of Public Health, Des Moines University, Des Moines, IA

Background: Body mass index (BMI) is influenced by heritable factors. We aimed to investigate whether genetic factors contributed to obesity.

Methods: In 1969, the National Heart, Lung, and Blood Institute (NHLBI) initiated a longitudinal study of 514 middle-aged, white veteran twin pairs (254 monozygotic and 260 dizygotic twin pairs). Data on height, weight, and BMI was available at the military induction (1943) and baseline exam of the study (1969-1973, exam 1). Obesity was defined as BMI≥ 30. Probandwise concordance, Falconer's heritability, and the environmental contribution were calculated.

Results: At the military induction, the prevalence of obesity was 1.07% in the total twin population (0.4% in monozygotic and 1.73% in dizygotic twins). Approximately 28 years later, at the baseline exam, the prevalence was increased to 8.28% in the total twin population (8.51 % in monozygotic twins and 8.05% in dizygotic twins). The probandwise concordance rate was 0 for both monozygotic and dizygotic twins at the military induction. At the baseline exam, the probandwise concordance rate was 65% for monozygotic twins, and 43% for dizygotic twins. The Falconer's heritability for obesity was 0 at the induction and 0 at exam 1. The common environmental influences on obesity was 11% at the induction and 26% at baseline. The unique environment influences was 89% at the induction and 74% at baseline.

Conclusions: The prevalence of obesity was increased sevenfold over 28 years and the broad heritability did not influence obesity. Both common and unique environmental factors have great influences on obesity.

♦ 3 ♦

Insight into Patient Beliefs about Health Care Professionals' Recommendations Regarding HPV Vaccination

Shruti Nadkarni, DO'20[1] and Rachel Reimer, PhD[2]

[1]Mentored Student Research Program, Department of Public Health, Des Moines University, Des Moines, IA
[2]Department of Public Health Chair/Master of Public Health Program Director, Department of Public Health, Des Moines University, Des Moines, IA

Objective: HPV is the most common sexually transmitted infection in the United States and globally.[1] Though multiple vaccines are available, the rates for vaccination in the United States are low. While there are several factors associated with low vaccination rates; one key factor is health care professionals' vaccination recommendation. There is evidence that physician recommendations may differ by racial and ethnic group affiliation.[1,2] The purpose of this study was to analyze data from the Health Information National Trends Survey (HINTS), to examine the associations of participants' sex, race, and ethnicity with patient experiences of health care provider recommendations.

Methods: A series of logistic regressions, with a jackknife procedure for variation estimation to handle the nationally representative sampling, were used. There were two dependent variables analyzed from the survey set, participants' reports of healthcare professionals' HPV recommendation and patients' recall of patient-provider discussion regarding HPV vaccination. The independent variables were gender, race, age, trust of a healthcare professional, and the link between the HPV vaccine and a reduced likelihood of cervical cancer.

Results: Gender, and the belief that HPV causes cervical cancer were both significantly associated with having discussed with, and received, a physicians' recommendation for the HPV vaccine. There are discrepancies of understanding HPV related cancers and physician recommendations for different races and ethnicities. In the future, additional steps must be taken to enhance HPV vaccination uptake and completion rates.

1. Kolar, S., Wheldon, C., Hernandez, N., Young, L., Romero-Daza, N., & Daley, E. (2015). Human papillomavirus vaccine knowledge and attitudes, preventative health behaviors, and medical mistrust among a racially and ethnically diverse sample of college women. Journal of Racial and Ethnic Health Disparities, 2(1), 77-85. doi:10.1007/s40615-014-0050-2
2. Rickert, V. I., Rehm, S. J., Aalsma, M. C., & Zimet, G. D. (2015). The role of parental attitudes and provider discussions in uptake of adolescent vaccines. Vaccine, 33(5), 642-647. doi:10.1016/j.vaccine.2014.12.016

♦ 4 ♦

Feasibility and Usability of a "My Walking Health" Brochure to Provide Meaningful Health Information to Older Adults

Emilie Johnson[1], Taylor Woods[2], Wesley Farrington, DPT'16[3], Alex Krajek[3], Kristin Lowry, PhD[3], Kathy Mercuris, PT, DHS[3]

[1]Iowa State University, Department of Kinesiology, Ames, IA
[2]Grandview University, Department of Biology, Des Moines, IA
[3]Des Moines University, Department of Physical Therapy, Des Moines, IA

Background: Measures of gait speed (GS) and gait variability (GV) have been successful in assessing function, health, and risk of falls[1-4] and can serve to identify a need for rehabilitation[4]. Gait speed is a simple measurement tool, and can be calculated by timing ambulation over a 4m or 8m area. However, findings from previous research indicate that some individuals are at risk for falls even with normal GS[1]. To provide a more comprehensive assessment of fall risk, it is also important to examine GV (stride length, step width, and timing consistency)[1,2,4]. The objective of this project was to assess the feasibility of creating and using a "My Walking Health" brochure that provides older adults with their own GS and GV scores.

Methods: Sixty older adults participated in two different events where GS and GV were measured using an instrumented walkway (Protokinetics, Inc.). At each event, participants walked across the walkway four times at their comfortable pace, their data was processed online, and a "My Walking Health" brochure was created for the individual. A qualified professional discussed the individualized GS and GV results with each participant.

Results: The process in the methods section required 10 minutes. There was positive verbal feedback from participants and it has been reported that several participants have taken their results to a physical therapist and their physician to take preventative measures.

Conclusion: Gait speed and variability are feasible to measure in a clinical setting and can be used by the clinician and patient for preventative care.

♦ 5 ♦

Experimental Comparison of the Clinical Measurement of Ankle Joint Dorsiflexion and Radiographic Tibiotalar Position

Paul Dayton, DPM, MS, FACFAS, Mindi Feilmeier, DPM, FACFAS, Kalani Parker, DPM'17, Riane Otti, DPM'18, Rachel Reimer, PhD, Merrell Kauwe, DPM, **Jake Eisenschink, DPM'19,** Joshua Wolfe, DPM'18

College of Podiatric Medicine and Surgery, Des Moines University, Des Moines, IA

Equinus is an anatomic abnormality that leads to many pathological compensations in the lower extremity and is the cause of a variety of foot and ankle disorders. Standardization of the clinical measurement of ankle dorsiflexion is necessary to allow for accurate diagnosis and selection of appropriate treatments. Many of the techniques proposed to measure ankle dorsiflexion lack reliability and reproducibility which may lead to misdiagnoses and therefore errors in treatment. Specifically, many clinical methods do not account for foot movement during passive dorsiflexion and therefore do not accurately assess tibiotalar motion.

Research questions:

1. Is there a clinically significant difference in the measure amount of dorsiflexion when the foot is supinated, neutral or pronated?
2. What effect does foot position have on actual tibiotalor position measured on x-ray?
3. What is the reliability of clinical measurement of ankle dorsiflexion?

To answer these questions 50 subjects (100 extremities) were enrolled and clinical assessment of passive ankle dorsiflexion (three positions each) using a digital goniometer by three clinicians. A lateral radiograph was taken in the three positions to assess true ankle position.

We found a large variation in AJ DF measurement with the foot in a pronated position compared to neutral or supinated and that neutral and supinated showed only a small difference. The changes in AJ position on x-ray were negligible between Supinated , pronated and neutral which indicates that when we are clinically measuring AJ dorsiflexion we are to a large extent measuring foot movement not purely ankle movement.

♦ 6 ♦

Electromyographic Activity Variation Between and Within Gleno-Humeral Joint Muscles During Flexion in Four Different Body Orientation Positions

Russell Kamps, DO'19, Traci Bush, DPT, OTR/L, DHS, David Stapleton, Vassilios Vardaxis, PhD

Purpose/Hypothesis: Fundamental aspects of resistance training may be strategically modified in systematic ways when pursuing particular program results.[1-3] This study assessed the effect of body orientation on muscle activation characteristics during shoulder flexion. We hypothesized that individual shoulder muscle demands would be affected, with respect to peak activation level and corresponding joint angle, by altering body position.

Number of Subjects: Eighteen (18)

Materials/Methods: Subjects performed shoulder flexion to 100° in 4 positions: seated, side-lying, supine, and prone. Arm movement was monitored using 3D motion capture. Muscle demand in each position was assessed using peak activation, expressed as a percentage of activation elicited via manual muscle testing (%MMT), and joint angle at the time of peak. Surface EMG electrodes were placed on: posterior, middle, and anterior deltoid, upper trapezius, pectoralis major, biceps brachii, triceps brachii, and latissimus dorsi.

Results: Peak activation (averaged across deltoids and trapezius muscles) was higher in prone and seated (34 & 49 %MMT, respectively), and had a higher corresponding joint angle versus supine and side-laying positions (16 & 17 %MMT, respectively). While low, peak activation for the pectoralis, biceps, triceps, and latissimus dorsi varied between positions—displaying highest values when prone or seated and lowest when supine or side-laying.

Conclusions: Changing the plane of motion alters the gravitational effect on joint forces.[2,4] Consequently, muscle activation varies between positions in order to effectively carry out the flexion task, providing an opportunity to strategically focus loading on a particular muscle in order to improve performance, or reduce muscle imbalances.[1,3,4]

1. Edwards P, Ebert J, Joss B, Bhabra G, Ackland T, Wang A. Exercise rehabilitation in the non-operative management of rotator cuff tears: A review of the literature. *Int J Sports Phys Ther*. 2016;11(2):279-301. Accessed July 8, 2016.
2. Giphart JE, Brunkhorst JP, Horn NH, Shelburne KB, Torry MR, Millett PJ. Effect of plane of arm elevation on glenohumeral kinematics: A normative biplane fluoroscopy study. *J Bone Joint Surg Am*. 2013;95(3):238-245. Accessed July 8, 2016. doi: 10.2106/JBJS.J.01875.
3. Kisner C, Colby LA. *Therapeutic exercise; foundations and techniques.* 6th ed. F.A. Davis: Philidelphia; 2012.
4. Gaunt BW, McCluskey GM, Uhl TL. An electromyographic evaluation of subdividing active-assistive shoulder elevation exercises. *Sports Health*. 2010;2(5):424-432. Accessed July 8, 2016. doi: 10.1177/1941738110366840.

♦ 7 ♦

The Figure-of-8 Walk Test: Does Variability Matter?

Taylor Woods, RA, Emilie Johnson, RA, Alex Krajek, RA, KayLynn Bland, SPT, Aimee Dahlhauser, SPT, Wesley Farrington, DPT, Kristin Lowry, PT, PhD

Department of Physical Therapy, Des Moines University, Des Moines, IA

Background: The Figure-of-8 Walk Test (F8WT) requires both straight- and curved-path walking. Older adults completing the F8WT ≤ 8 seconds (F8L) have better mobility than those completing the F8WT in > 8 seconds (F8H)[1]. Gait variability (stepping consistency) indicates impaired mobility during straight-path walking[2], but is necessary for efficient turning during curved-path walking. The purpose of the study was to determine if better F8WT performance was associated with higher gait variability.

Methods: Thirty-two older adults (mean age 72.06 yrs ± 9.26) walked a figure-of-8 around 2 cones 5 feet apart on an instrumented walkway (Protokinetics, Inc.). Number of steps and time to complete F8WT (stopwatch) were recorded. Walkway measures were: 1) F8WT gait speed, 2) gait variability - standard deviations of step length (SLV) and stride width (SWV). Two groups (F8L: n= 16, F8H: n=16) were formed based on time to complete F8WT. Group differences in SLV and SWV were determined with ANOVAs. Associations between gait variability and F8WT performance were examined using Pearson r correlations.

Results: There were group differences for SLV and SWV (SLV: F8L = 22.2, F8H= 18.2, p=.024; SWV: F8L = 23, F8H = 17.2, p<.001). There were negative associations between variability measures and F8WT time (SLV, r= -.40, SWV r=-.70), and number of steps (SLV, r= -.42, SWV r=-.80).

Discussion: Participants who had higher spatial variability effectively executed the F8WT. These data suggest that practice of curved-path walking and active adjustment of step length and width may be an important part of functional mobility training.

1. Brach, J. S., Lowry, K., Perera, S., Hornyak, V., Wert, D., Studenski, S., VanSwearingen, J.M. (2015). Improving Motor Control in Walking: A Randomized Clinical Trial in Older Adults With Subclinical Walking Difficulty. Archives of Physical Medicine and Rehabilitation. 96, 388-394. doi: 10.1016/j.apmr.2014.10.018
2. Brach, J.S., Studenski, S., Perera, S., VanSwearingen, J. M., Newman, A.B. (2007). Stance time and step width variability have unique contributing impairment in older persons. Gait & Posture. 27, 431-439. doi: 10.1016/j.gaitpost.2007.05.016

♦ 8 ♦

Literature Review of Mobility During Pregnancy with Pelvic Girdle Pain

Dana Bray[1], Catherine Stevermer, PT, PhD, GCS[2], Kari Smith, DPT, BCB-PMD[2]

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Introduction: Pelvic Girdle Pain (PGP) is a prevalent issue within the pregnant population, causing pain and disability. This condition may have a significant effect on this population and how they perform certain functional tasks, as compared to pregnant woman without PGP. PGP during pregnancy may lead woman to reduce physical activity and become sedentary, which may pose both maternal and fetal risks.

The purpose of this review was to identify how pregnant woman with PGP perform the functional tasks of sit to stand, gait, and stair climbing compared to those who do not have PGP.

Methods: Three databases, (EBSCO host, Scopus, and PubMed), and previously collected articles from the research team were searched for results. Key terms such as “pelvic girdle pain”, “pregnancy”, “gait”, “stairs”, “sit to stand”, and all combinations of these terms were used.

Results: A review of literature identified altered movement parameters, during sit to stand activities and stair climbing in pregnancy, including reduced speed and amplitude of movement. Additionally, pregnant woman demonstrate changes in stance time, step lengths, and walking velocity during gait tasks. However, there is only some evidence surrounding movement parameters during these functional tasks for a PGP population.

Conclusion: This review provides a summary of the literature on the effects of PGP, within the pregnant population. There is little evidence on quantifiable movement parameters for pregnant woman experiencing PGP, which warrants further research to aid in determining objective changes in this population during physical therapy interventions.

♦ 10 ♦

High Altitude Effects on Cranial Size and Nasal Cavity Morphology

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High altitude dwelling individuals (<2500M) are subject to a number of environmental stressors including low temperatures, low humidity, and low levels of oxygen. Previous studies have shown that these stressors have caused anatomical and physiological adaptations. Our study aimed to determine how these factors influenced the craniofacial size and nasal cavity morphology of high altitude individuals. 113 skulls of regionally paired high and low altitude individuals were studied. 3D renderings were generated from CT scans before being landmarked. These landmarks were used to determine linear distances and sizes. The distances were then compared against all populations using analysis of variance (ANOVA) followed by Tukey pairwise tests (significance P <0.05). We found that when looking at all populations, cranial size did not differ but nasal cavity size did. Measurements of nasal cavity length varied the most, specifically facial length, nasal length, and nasal floor length. The pairwise tests showed that the vast majorities of these differences occurred when comparing high altitude populations to low altitude populations. Although significant differences between high and low altitude populations are apparent, additional studies are needed to determine which specific factors (altitude, temperature) are contributing to these differences. Our next phase of the study will be to collect internal nasal and maxillary sinus measurements to help determine the question of which specific factors influence these structures.

♦ 11 ♦

Making Sense of Variation in Brain Size, White Matter Volume and Metabolism in the Domestic Dog

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Domestic dogs exhibit a tremendous range of variation in body size, shape and color, the mechanisms of which are of great informational value as we seek to understand the processes that control the limits on morphological variation. The following study was aimed at assessing the range of variation in brain and associated white matter volume in a sample of domestic dogs (N = 10, breed = mixed beagle; age range = 243-1634 days). Using quantitative magnetic resonance imaging (qMRI), we derived *in situ* cortical white matter volumes and brain volumes and compared these using allometric analyses to evaluate the range of variation. Using previously published data on the volume-specific glucose metabolic rate based on the internal capsule, corpus callosum and whole brain (Karbowski, 2007) we calculated the predicted glucose utilization rate for our sample of domestic dogs. These results indicate a proportional increase in white matter volume with increases in brain volume and predict that despite wide ranges in brain and body size in domestic dogs (e.g., 200 lbs great Dane versus 6 lbs Chihuahua), the metabolic requirements of white matter and cortical brain volume remain bound within a narrow range across all canines to support the wide range of brain sizes observed in this species. While preliminary, this data suggests that domestication may have allowed for greater variation in morphology by uncoupling the relationship between metabolism and brain or body size, thus keeping metabolic requirements largely invariable across members of the same species.

♦ 12 ♦

Neuropil Space and Body Size in the Nile Crocodile (*Crocodylus niloticus*)

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While historically understudied, the reptilian nervous system promises much for our understanding of the conserved evolutionary and morphological relationships that characterize the vertebrate brain. Of particular interest, has been the observation that the central nervous system of the Nile crocodile (*Crocodylus niloticus*) is quite unique in that it appears to undergo continuous growth throughout the animal's lifespan, the basis for which might offer insight into possible treatments options for neurodegenerative diseases, while also adding much needed informational value on the crocodilian brain. To this end, we used a quantitative image analysis approach to survey the neuropil space in three regions of the crocodilian nervous system (i.e., dorsal ventricular ridge, dorsal cortex, and optic tectum) and explored correlative relationships with body size in four crocodiles ranging in size from 343.5 grams to 10 kilograms. The neuropil space is well known as a robust proxy for connectivity, as it comprises that region of cortex characterized by the dendrites, axons and synapses. While preliminary, our results indicate strong evidence of a negative allometric relationship, indicating that larger crocodiles tend to have smaller neuropil space, perhaps indicative of ongoing increases in neuronal size or packing density as the entire organism continues to grow throughout lifetime.

♦ 13 ♦

C1q and Adiponectin Regulate Mouse Macrophage Activation

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Complement component C1q upregulates the macrophage-mediated phagocytosis of apoptotic cells and inhibits macrophage production of proinflammatory TNFα. In more than 90% of cases, a deficiency in C1q leads to the development of the autoimmune disease systemic lupus erythematosus, which is associated with a failure to engulf apoptotic cells and a dysregulation of inflammatory cytokine production. C1q is similar in structure to adiponectin, an important regulator of metabolism. These proteins are called "defense collagens" and contain a globular head region and collagen-like tails. Both defense collagens have been shown to upregulate expression of Mer tyrosine kinase (Mer), a kinase required for efficient engulfment of apoptotic cells. This suggests that C1q and adiponectin signal through a shared pathway for phagocytosis, but little is known about the shared mechanisms leading to regulation of inflammatory cytokine production. LAIR-1, a collagen receptor found on leukocytes, has been shown to mediate C1q-dependent inhibition of proinflammatory cytokines in human phagocytes. The aim of this study was to (1) determine if adiponectin, like C1q, inhibits TNFα production in mouse macrophages and (2) determine if LAIR-1 is required for C1q/adiponectin dependent signaling in macrophages. TNFα production and expression of Mer was compared in wild type and LAIR-1 deficient mouse macrophages in the presence or absence of C1q or adiponectin. Macrophages showed an adiponectin-dependent decrease in TNFα production similar to C1q. In the absence of LAIR-1 this inhibition was also apparent and Mer expression was not affected. These data further define the shared functions of C1q and adiponectin.

♦ 14 ♦

C1q Regulates TLR Signaling in Mouse Macrophages

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Macrophages are professional phagocytes which eat apoptotic cells and can promote or inhibit inflammation through the production of various cytokines. Complement protein C1q has been shown to promote the resolution of inflammation by regulating macrophage activity. In previous studies, macrophages stimulated with lipopolysaccharide (LPS), an agonist for the cell's Toll-Like Receptor (TLR) 4, in the presence of C1q produced significantly less pro-inflammatory cytokines (1.) We hypothesized that C1q may be regulating down-stream signaling through the other eight TLRs found on the macrophage as well. In our experiment, mouse bone marrow-derived macrophages (BMDM) were activated with a single agonist specific to one of the nine TLRs found on macrophages, in the presence or absence of C1q. BMDM cultured on only human serum albumin (HSA) or C1q, and BMDM stimulated with TLR4 agonist LPS served as our controls. TNF-alpha production was quantified by ELISA for nine individual samples of BMDM corresponding to activation of each of the nine TLRs. Our results showed that activation of mouse BMDM TLRs in the presence of C1q compared to HSA resulted in a decrease in TNF-alpha production with the exception of TLR2 and TLR5. This suggests that in mouse macrophages, C1q regulation occurs via a common signaling pathway downstream of TLRs and ultimately affects the transcription and production of TNF-alpha.

♦ 15 ♦

Inhibitors of Rho GTPases Inhibit Proliferation of the Aggressive Natural Killer Cell Leukemic Cell Line YT-INDY

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Aggressive Natural Killer Cell leukemia (ANKL) is a rare form of large granular lymphocyte leukemia. Due to its innate resistance to chemotherapy, ANKL typically causes death within months after diagnosis. An effective treatment plan for ANKL has yet to be introduced; however, recent research has shown that statin drugs, commonly used to lower cholesterol, have an anti-tumor effect on the proliferation of leukemic natural killer cells by inhibiting the mevalonate pathway. It is well known that the mevalonate pathway is responsible for the biosynthesis of cholesterol, but the pathway plays a role in the synthesis of other molecules important to cellular function, including GTPases. In this study, the effect of Rho family GTPase inhibitors on proliferation and cell cycle was investigated using the ANKL cell line YT-INDY to determine which of the Rho family GTPases were important for YT-INDY proliferation. Using cell proliferation assays, it was determined that Cdc42 GTPase inhibitors ML141 and ZCL278 showed minimal to no inhibition of proliferation at sub-toxic concentrations. However, RAC1 GTPase inhibitors EHT 1864 and NSC 23766 and Rho-associated kinase (ROCK1 and ROCK2) inhibitors GSK429286A and Y-27632 showed significant dose-related inhibition of proliferation, with GSK429286A showing the most profound inhibition at the lowest concentrations. These results suggest that some Rho family GTPases are critical for the proliferation of YT-INDY. This knowledge may help direct the development of targeted pharmacologic therapies against this devastating cancer.

♦ 16 ♦

EGCG and Telomerase Inhibitor MST-312 Reduce Herpes Simplex Virus-2 Protein Accumulation in HEp-2 Cells

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Herpes simplex virus (HSV) can manifest as disease ranging from mild lesions to potentially fatal infections of the CNS. Approximately 16% of the population is infected with HSV-2, which is the leading cause of genital herpes. Genital herpes increases the risk of HIV transmission and may lead to the spread of HSV-2 to neonates during childbirth. This risk of fetal transmission is present, even with maternal compliance with high dose antiviral medications or cesarean surgery. Therefore, efforts towards new targets for antiviral therapies for HSV-2 are needed. Epigallocatechin gallate (EGCG) is a natural compound extracted from green tea that has demonstrated antiviral activity towards HSV-1. MST-312, a chemical analogue of EGCG, has shown similar effects. Previous work demonstrated that 40 μM MST-312 reduced the capacity of HSV-2 to produce progeny virions. Here, the antiviral properties of both EGCG and MST-312 were further assessed in HSV-2 infected HEp-2 cells via immunoblot assays. A decreased accumulation of the viral immediate early protein ICP27 and the late proteins VP22, gC, and gD was found when infected cells were treated with 100 μM MST-312 and EGCG. The magnitude of inhibition was greater with MST-312 compared to EGCG. The presence of as low as 20 μM MST-312 during infection resulted in a dose-dependent reduction in the accumulation of ICP27, VP22, gC, and gD. EGCG treatments as low as 70 μM led to reduced accumulation of gC and gD. Further assessments of these compounds may provide possible targets for the development of new HSV-2 antiviral medications.

♦ 17 ♦

The Telomerase Inhibitor MST-312 Inhibits Herpes Simplex Virus Replication in Cells that Use ALT for Telomere Maintenance

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Herpes simplex virus (HSV) often results in painful ulcerative lesions, such as cold sores and genital herpes, with lifelong recurrent outbreaks. Antivirals for HSV exist but drug resistance is an increasing concern, thus prompting the search for novel antivirals. Targets for novel anti-herpetic therapies includes cellular factors required for the viral replication. One potential target is the cellular enzyme telomerase, which replicate the ends (telomeres) of the cellular chromosomes.

Our previous studies have determined that an inhibitor of telomerase, MST-312, inhibits the HSV life cycle. MST-312 is a cell-permeable, synthetic, reversible telomerase inhibitor whose structure was patterned after a natural compound found in green tea, Epigallocatechin gallate (EGCG). The studies on the antiviral activities of MST-312 and EGCG were done in cancer cell lines which overexpress the telomerase enzyme. Further investigation was required to determine whether telomerase independent activities of MST-312 were responsible for the antiviral effects.

Toward this aim, we investigated the antiviral effects of MST-312 on an osteosarcoma cell line, U2OS, which uses the alternative lengthening of telomeres (ALT) pathway rather than telomerase overexpression to maintain telomere length. MST-312 treatment of HSV-infected U2OS cells caused a reduction in the accumulation of late viral proteins in a dose-dependent manner, although there was little to no change in immediate early viral proteins. Furthermore, viral replication was significantly suppressed by MST-312. Together, these results indicate that MST-312 can inhibit the HSV life cycle in cells with low telomerase activity and suggest that MST-312 can confer its antiviral properties through telomerase-independent mechanisms.

♦ 18 ♦

Trichomonas vaginalis Glycogen Synthase Can Functionally Complement the Respective Yeast Mutants

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Trichomonas vaginalis is a protozoan parasite responsible for the widespread sexually transmitted disease trichomoniasis. Like many cells, *Trichomonas vaginalis* uses glycogen as a storage form of carbon and energy, possessing enzymes such as glycogen synthase to properly polymerize glucose into glycogen. A glycogen synthase candidate in *Trichomonas vaginalis* is encoded by the TVAG_258220 open reading frame. Specifically, the C-terminal third of the predicted protein is similar to plant starch synthases and bacterial glycogen synthases. The N-terminal two-thirds of the protein is not homologous to any known protein and its function is unknown. We have previously shown that full length TVAG_258220 is functional as a glycogen synthase by complementation of yeast glycogen synthase mutants and through in vitro studies using recombinant protein produced in an *E. coli* expression system. However, we were wondering if expressing only the C-terminal third of the TVAG_258220 protein would be sufficient to function as a glycogen synthase. In order to answer this question, we constructed plasmids expressing this domain and transformed them in to strains of yeast and *E. coli* cells. We found that glycogen synthase deficient yeast strains as well as *E. coli* strains gained an ability to express glycogen synthase activity and make glycogen when complemented with the *Trichomonas vaginalis* C-terminal glycogen synthase domain. Thus we theorize that this specific domain of the TVAG_258220 protein is a functional glycogen synthase.

♦ 19 ♦

The Effect of the α-glucosidase Inhibitor, Acarbose, on the Growth of Pathogenic Trichomonads

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Trichomoniasis caused by the parasitic protist *Trichomonas vaginalis* is the most common non-viral sexually transmitted disease. Currently, only two drugs, tinidazole and metronidazole are approved to treat the infection. Both medications are from the same drug class, and drug resistance is increasing among *T. vaginalis*. Consequently, there is a need for more therapies. *T. vaginalis* requires carbohydrates for growth. Glucose polymers and oligomers, especially glycogen, are the most abundant source of carbohydrate in the vagina. Previous studies have shown that *T. vaginalis* secretes both alpha and beta amylases that can break down these polymers and oligomers. A related species, *Trichomonas foetus* causes a disease in cattle that is similar to human trichomoniasis. Our studies aimed to determine the effect of an alpha glucosidase inhibitor, acarbose, on the growth of these trichomonads *in vitro*. Studies were performed growing *T. vaginalis* and *T. foetus* in the presence of the carbohydrates glucose, maltose, or glycogen with or without the addition of acarbose. Cell counts were then collected over a growth period of four days. Preliminary results show that the addition of acarbose caused a decrease in the growth of both species in the presence of maltose and glycogen. There was no decrease in growth of either species when grown in glucose in the presence of acarbose, suggesting that the action of acarbose was directly related to the ability of the protist to breakdown and metabolize glucose polymers. This data suggest that glucosidase inhibitors may be a novel therapeutic approach to treating trichomoniasis.

♦ 20 ♦

Influence of Boric Acid on Increase ATP within *Candida albicans*

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Purpose: To evaluate the effects of boric acid on energy metabolism of *Candida albicans* in the exponential and stationary phases of growth.

Methods: One agar plate of *Candida albicans* (SN152) culture was used to start all samples. Four different concentrations of boric acid and the control were tested over 4 separate time intervals. Also cells in the stationary phase were collected after addition of 0 and 0.2% boric acid. The same collecting, storing, extraction and plating protocol was followed for each experiment. Numerical values were reached by measuring the amount of luminance and converting it into moles of ATP. The size of exponential and stationary SN152 cells were measured and converted into femtoliters.

Results: After extraction and reading of four separate sample groups of exponential cells, a significant p-value was noted for the increase ATP concentration throughout the different time intervals. There was not a significant p-value for the stationary cells collected. There was no significant size difference between exponential and stationary SN152 cells.

Conclusions: The study showed that within, exponentially growing, *Candida albicans* the amount of ATP increased over time as the concentration of boric acid increased. However, this increase in ATP concentration did not correlate with an increase in the size of the cells. Also, when these cells enter their stationary phase the increase in ATP concentration was no longer noted.

♦ 21 ♦

The Plot Thickens: Clarification of the Roles Played by *Acinetobacter nosocomialis* M2 T6SS Toxin *asi1* and Anti-Toxin *ase1* in Bacterial Competition

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Acinetobacter spp. are gram-negative bacteria of clinical interest due to their increasing multidrug resistance and role in nosocomial infections, particularly in the case of ventilator acquired and surgical site infections.

Multiple *Acinetobacter* species possess a type VI secretion system (T6SS). T6SS enable contact-dependent killing of bacterial competitors, giving *Acinetobacter* a competitive advantage when colonizing surfaces. Like the T6SS of other gram-negative bacteria, the *Acinetobacter* T6SS injects a toxic effector across prokaryotic cell membrane. *Acinetobacter* are protected from their effectors by a corresponding antitoxin protein. Previously, we hypothesized that two adjacent genes in *Acinetobacter nosocomialis* strain M2, *ase1* and asi1, corresponded with a T6SS toxin and antitoxin, respectively. These proteins could serve as targets for novel chemotherapeutics for *Acinetobacter* that reduce the bacterium's killing of competitors and increase its killing of sister cells.

To test the genes' proposed identities, strains in which *ase1* or *ase1* and *asi1* were knocked out though in-frame deletions and complemented were constructed. Mutants and complements were tested using *in vitro* competition assays to determine if loss of *ase1* or *ase1* and *asi1* affected killing of *E. coli* or survival when competed against wild type M2. Our data is consistent with the proposed roles of each gene, although mutants lacking only *ase1* killed *Escherichia coli* at a similar rate as wild type M2. These and other data from our lab are consistent with the idea that *asi1* is an immunity protein and that while *ase1* is a T6SS toxin, it is likely not M2's only T6SS toxin.

♦ 22 ♦

Acinetobacter T6SS Toxin Asi1: Determining the Location of Action via Heterologous Expression

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Acinetobacter spp., a group of gram negative bacteria, are implemented in severe infections of the immunocompromised population as well as those on ventilators. With mortality rates high, research on *Acinetobacter* has begun to focus on how this group of bacteria cause disease and how to combat their multi drug resistance.

Our lab has previously shown that *Acinetobacter* use a Type VI Secretion System (T6SS) to help them compete with other bacteria in their environment. This has been shown previously using competition experiments with *Escherichia coli*. This system allows the bacteria to inject what we presume to be a toxin into neighboring cells killing them. Along with the toxin gene, it is believed that *Acinetobacter* poses an antitoxin gene protecting from self-infection and infection from related bacteria.

Although it is not known exactly where the toxin acts, our lab believes the toxin gene is made in the cytoplasm and then injected into the periplasmic space of target cells via the T6SS where it is active against peptidoglycan. In order to further study the toxin gene, 11435, we cloned this gene into an expression plasmid, pCOLA-Duet, with or without the OmpA leader peptide. This peptide signals the toxin to be sent to the periplasmic space. Comparing cultures with/without induction with/without the leader peptide allowed us to determine if the toxin is toxic in the cytoplasm, periplasm or both. These data are to be the first investigation of the location of action of an *Acinetobacter* T6SS toxin.

♦ 23 ♦

Phenotypic and Physiologic Changes in the Ovariectomized Rat

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In the United States, hypertension significantly affects the quality of life of many Americans. While this disease has been shown to be less prevalent in premenopausal women compared to males of a similar age, postmenopausal women develop hypertension at the same rate as their male counterparts. While multiple reasons have been proposed for this occurrence, estrogen seems a likely contributor based partially on its ability to attenuate the development of hypertension in postmenopausal patients. However, the precise mechanisms in which estrogen provides this protection has not been fully elucidated. The purpose of our project was to determine the phenotypic and physiologic changes that result from a decrease in estrogen synthesis and release in Long-Evans rats. These data will be used to establish a postmenopausal model that will be used in future studies to test the overarching hypothesis that estrogen decreases blood pressure by attenuating the activity of hypertension-inducing cytokines. To accomplish this study, we utilized ovariectomized Long-Evans rats. Our physiologic data demonstrated a significant increase in blood pressure in the ovariectomized rats compared to the control at two and four weeks post-surgery. Additionally, at four weeks, we found a significant increase in renal sympathetic nerve activity in the ovariectomzied rats. Our phenotypic data demonstrated a significant increase in weight gain, food intake, and total fat distribution in the ovariectomized rat at both two and four weeks. Overall, these data demonstrate the phenotypic and physiologic outcomes that occur in the absence of estrogen.

♦ 24 ♦

Role of Carotid Body Chemoreceptors in Renal Inflammation, Oxidative Stress, and Fibrosis in Chronic Heart Failure

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Renal impairment occurs in approximately 25% of patients with chronic heart failure (CHF) and is associated with higher morbidity and mortality. Decreased renal blood flow (RBF), inflammation, and oxidative stress are thought to contribute to renal fibrosis and decline in renal function in CHF. Previous studies indicate that decreased RBF in CHF is mediated in part by tonic increases in carotid body chemoreflex (CBC) control of renal sympathetic nerve activity. The extent to which CBC activity affects renal inflammation, oxidative stress, and development of fibrosis is undetermined. We hypothesized that CBC-mediated reductions in RBF in CHF would result in increased superoxide levels, increased expression of pro-inflammatory cytokines, and development of fibrosis.

Chronic heart failure was induced by coronary artery ligation in rats. Selective CBC denervation (CBD) was performed to remove CBC drive in the CHF state. CBC sensitivity was assessed as the ventilatory response to isocapnic hypoxia (Hx) and RBF was measured using ultrasound. At the end of the experimental period, renal cortical tissue was assayed for superoxide levels using electron paramagnetic resonance (EPR), and for protein expression of SOD-1 and IL-1β (western blot). Tri-chrome stain of kidney sections were performed to determine renal collagen content.

Ventilatory responses to Hx were enhanced in CHF and abolished after CBD. RBF was decreased in CHF and was improved in CHF-CBD. Superoxide levels, IL-1β, and renal collagen content (indicative of fibrosis) were increased in CHF. Superoxide levels and collagen content were attenuated in tissue from CHF-CBD animals.

♦ 25 ♦

Inhibition of BMP2-Inducible Kinase (BMP2K) Reduces Hypoxia/Reoxygenation Injury and Decreases Autophagic Flux in H9c2 Cells

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Background: A small percentage of the 518 kinases in the human genome are known to play important roles in the pathophysiology of ischemia/reperfusion (I/R) injury in cardiomyocytes. However, there are many understudied kinases that may impact the damage to cardiomyocytes caused by I/R.

Methods and Results: H9c2 cardiomyocytes were subjected to a 0.2 % oxygen environment and nutrient starvation followed by reoxygenation (hypoxia/reoxygenation [H/R]). Control cells were incubated in complete nutrient medium in normal atmospheric oxygen levels for the duration of the experiment**.** Using affinity chromatography and quantitative mass spectrometry, we determined that H/R increased the activity of BMP2-inducible kinase (BMP2K) in H9c2 cells. To test the hypothesis that reducing BMP2K expression protects H9c2 cells during H/R, we silenced BMP2K in H9c2 cells with siRNA and subjected them to H/R. Immunoblotting results from cell lysates suggested that silencing BMP2K significantly reduced apoptosis. Additionally, overall cell death was significantly decreased in BMP2K knockdown cells when compared to control cells transfected with non-target siRNA. Because BMP2K has previously been implicated in autophagy regulation in cancer cells, we investigated the role that BMP2K plays in autophagy in H9c2 cells. Finally, we performed immunofluorescence microscopy to visualize BMP2K localization in cells.

Conclusion: Data from our kinome-profiling experiments suggest that H/R increases BMP2K activity in H9c2 cells. Silencing BMP2K in H9c2 cells decreases both cell death and autophagic flux in response to H/R. Thus, our data suggest that BMP2K is potentially a promising therapeutic target to reduce cardiomyocyte damage caused by myocardial infarction.

♦ 26 ♦

Intersectional Strategies for Genetic Labeling of Mouse Central Nervous System

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The brain is composed of many neuronal and non-neuronal cell types. The connectivity and interactions between these cells are critical to the brain's function. Thus the ability to selectively label and further manipulate specific cell types is crucial. However, cell-type specificity is rarely defined by a single gene. An increasingly effective method is to use intersectional genetic targeting of protein-based promoters in order to achieve more specific labeling of the desired cell types.

This study observed the intersectional labeling patterns of the mouse hippocampus using Cre and the Cre/Flp double recombinase system driver lines in conjunction with the tdTomato reporter. 60 micron coronal slices were cryo-sectioned and then imaged using fluorescent microscopy. The following promoters were used: somatostatin (SOM), parvalbumin (PV), Purkinje cell protein 2 (PCP2), and human red/green pigment (HRGP). The intersections, SOM-PV and PCP2-PV, were studied.

We expected SOM and PV to have general genetic labeling of GABAergic interneurons. The intersection was expected to label fewer cells as only cells that expressed both promoters should have been labeled. PCP2 is expected to be specific to Purkinje cells in the cerebellar cortex and retinal bipolar cells. However, we observed bright labeling in the hippocampus. The intersection of PCP2 and PV are also expected to label fewer cells than either PCP2 and PV individually.

In conclusion, further characterization and establishment of both driver and reporter lines are necessary for the successful application of intersectional strategies.

♦ 27 ♦

Regulation of pH Homeostasis in Human Osteosarcoma Cells

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Cancerous cells of all origins have an aberrant regulation of pH dynamics across the cell membrane and the Na^+/H^+ exchanger-1 (NHE1) is a primary mediator of pH dysregulation in tumors. Specifically, the maintenance of pH balance is vitally important to bone biology and might be compromised in bone neoplastic progression. This study aims to investigate the regulation of pH homeostasis in osteosarcoma, a malignant tumor of the bone. NHE1 activity was measured by spectrofluorometry in a human osteosarcoma cell line (143B). The isoform of the NHE protein family expressed in 143B cells was identified by treatment with Zoniporide, a highly selective NHE1 inhibitor. Zoniporide inhibited NHE activity in a concentration-dependent manner; a 10 nM Zoniporide treatment completely blocked NHE activity (-94%) with a 50% inhibition (IC_{50}) of 0.537 nM. This suggests that NHE1 is the

main isoform expressed in 143B cells. The metabolic microenvironment of a tumor is characterized by low levels of growth factors, and these conditions were mimicked by the removal of growth factors (serum deprivation). NHE1 activity was significantly inhibited by serum deprivation in non-cancerous cells; while, it was not affected by 24 or 48 hours serum deprivation in 143B cells. In summary, pH homeostasis was regulated in osteosarcoma cells by NHE1, and NHE1 activity was not influenced by serum deprivation. Future research aims to identify the signaling molecules that control NHE1 activity in osteosarcoma cells. Accomplishment of these studies will aid in determining the potential of targeting NHE1 activity as novel and selective anti-cancer therapeutic treatment.

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Egdorf, Rachel, DPM'19	Oral	5
Eisenschink, Jake, DPM'19	5	14
Gist, Galen, Simpson College	18	21
Grulke, Luther, Augustana College	15	19
Hemphill, Chase, DO'19	14	19
Hitt, Nathaniell, DO'19	24	24
Hybarger, Andrew, DO'19	24	24
Johnson, Emilie, Iowa State University	4	13
Kamps, Russell, DO'19	6	14
Klocke, Ross, DO'19	10	17
Knauf, Victoria, DPM'19	11	17
Krone, Abigail, Iowa State University	2	12
Leber, Stacey, DO'19	22	23
Li, Rachel, University of California, Berkeley	26	25
Locey, Lisa	12	18
McLean, Anthony, Grinnell College	21	22
Meyer, Hannah, DO'19	23	23
Mills, Cally, MBS'21	13	18
Nadkarni, Shruti, DO'20	3	12
Tokarski, Alexander, DPM'19	19	21
Woods, Taylor, Grand View University	7	15