WAYNE STATE
Eugene Applebaum
College of Pharmacy
and Health Sciences

19TH ANNUAL
COLLEGE RESEARCH DAY

October 12, 2022
Detroit, MI

ABSTRACTS / POSTER LOCATIONS

HEALTH SCIENCES

DOCTOR OF PHARMACY

PHARMACEUTICAL SCIENCES

POST-DOCTORAL

UNDERGRADUATE

AGENDA

- **8-9 a.m.** Poster setup in the Commons
- **9-10:55 a.m.** Poster presentations
- **11 a.m.-noon** Keynote and student award presentations in the auditorium
- **12-3 p.m.** Continued poster viewing

KEYNOTE SPEAKER

Andrew King, MD, associate clinical professor of emergency medicine, Wayne State University; attending physician, Sinai Grace Hospital, Detroit Receiving Hospital and Children's Hospital; toxicologist and medical toxicology fellowship director, WSU School of Medicine Michigan Poison & Drug Information Center. Dr. King will be discussing opioid use disorder, including approaches to treatment and his experience in Detroit.

AWARD CATEGORIES

- Health Sciences master's and doctoral students
- Pharmaceutical Sciences master's and doctoral students
- PharmD students
- Postdoctoral scholars
- Undergraduate students

WSU APPLEBAUM RESEARCH COMMITTEE

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Aya Abusalah

Taking Community Engagement to the Next Level: Collaborative Care with a Virtual from an In-Person Interprofessional Team Visit

Authors: Aya Abusalah, DPT; Shayne Billmeyer, DPT; Jessica Chapie, DPT; Kara Hecker, DPT

Faculty mentor: Martha Schiller

Abstract

Introduction. The Interprofessional Team Visit (IPTV) Program is an interprofessional educational team experience at Wayne State University for students of physical therapy (SPT). Due to the COVID-19 pandemic, the IPTV program changed the format from an in-person to an online virtual environment.

Objective. The purposes of this study were to:
1) Assess SPT attitudes, behaviors, and beliefs of collaborative care in a virtual and in-person IPTV environment using the Interprofessional Socialization and Valuing Scare (ISVS)
2) Determine if there is a difference between the two modes
3) Assess participant balance confidence and provide fall prevention education

Method. This study compares SPT data from in-person in Winter 2020 (n=38) and virtual in Fall 2021 (n=36). Teams consisted of 3-4 students of different disciplines and a community-dwelling adult participant. SPT perceptions were assessed before and after the IPTV using the ISVS. During the visit, SPTs completed the Activities-specific Balance Confidence Scale, Chair Rise Test and provided fall prevention education.

Results. Wilcoxon signed-rank test determined significant change ($p<0.05$) in the pre and post ratings for all 18 responses of the ISVS when the IPTV was conducted in-person, and only 4 responses when done virtually. There was a significant difference in pre-total ISVS scores for the virtual data, however, no significant differences in the post-total ISVS scores when comparing the virtual and in-person IPTV. PT assessments resulted in similar scores for both modes of delivery and some clients were in the fall risk categories when comparing to normative data.

Conclusion. Both in-person and virtual IPTV resulted in significant changes in student's beliefs, attitudes, and behaviors in relation to interprofessional socialization. Greater impact was seen with the in-person mode of delivery. Clients benefited from the PT assessments and patient education. Overall, IPTV is a valuable experience for both students and adult participants.

Kelly Clarkson

Michigan Older Caregivers of Emerging Adults with Neurodevelopmental Disabilities (MI-OCEAN) Family Support Project's Impact on Caregiver Well-Being

Authors: Kelly Clarkson, MOT student; Marcella Yaldo, MOT student; Christine Azzo, MOT student; Preethy S. Samuel, PhD

Faculty mentor: Preethy S. Samuel

Abstract

Introduction: Research has shown that family caregivers of adults with neurodevelopmental disabilities (NDD) are at risk for poor health and well-being due to the demands of lifelong caregiving. Aging families of adults with NDD face several barriers in accessing health and disability services and emerging evidence suggests that peer mentoring is useful in training caregivers to navigate complex care systems. Therefore, the objective of this study was to evaluate if MI-OCEAN, a peer mediated family support project implemented in Michigan from May 2019- Dec 2020, was beneficial to the quality of life (QOL) of older caregivers (50+) of adults with NDD (18+) and their families.

Methods: A pretest-posttest design was used to evaluate if project participation led to decreased caregiver depression, stress, and burden when measured by Patient Health Questionnaire (PHQ-9), Perceived Stress Scale (PSS-10), Zarit Burden Inventory (ZBI-12) respectively; and increased the caregiver's QOL and family QOL (FQOL) using World Health Organization's brief QOL scale (BREF-QOL), and international FQOL survey (FQOLS-2006).

Results: Paired sample t-tests indicated a statistically significant decrease in caregiver depression ($t = -3.54$, $p < .001$), stress ($t = -4.21$, $p < .001$), burden ($t = -5.91$, $p =< .001$) and increase in global FQOL ($t = 3.56$, $p < .001$), after participating in the project that required each family to develop and implement an individualized action plan (IAP) with 3 goals each.

Conclusion: Findings indicate that equipping participants with skills to access desired services for all family members including their adult child with disabilities can improve caregiver and family well-being. The observed increases during the pandemic when disability services were interrupted is remarkable and underscores the need to sustain this family support program for emerging adults and adolescents to prepare them for their futures.

Niharika Dantuluri

Cross-Sectional Relationship Between Grip Strength And Cognitive Function Across the Age Spectrum

Authors: Dantuluri N, Dargis J, Schlipphak J, Toal C, Fritz NE, Ph.D., P.T., D.P.T., N.C.S., Adamo DE, Ph.D., M.S., OTR

Faculty mentors: Dr. Diane Adamo, Dr. Nora Fritz

Abstract

INTRODUCTION: Previous findings showed an association in physical and cognitive function in middle aged adults. To build on previous knowledge, this study investigated the relationship between grip strength and cognition in three age groups. It was hypothesized that stronger grip strength would be associated with better cognitive performance in middle and older age groups only.

METHODS: A cross-sectional design was used to determine differences in grip strength and cognitive between young (20-30 years), middle (45-65 years) and older (65+ years) adults. All groups performed grip strength and cognitive measures (Trails A and B, Stroop Test, Controlled Oral Word Association (COWAT). An ANOVA with post-hoc testing was used to determine group differences. Bivariate correlations determined associations between physical and cognitive measures.

RESULTS: Young participants showed higher right and left grip strength than middle aged ($F(2,157) = 40.7$, $p<.001$) and older groups ($F(2,158) = 38.2$, $p<.001$). The young group had faster scores for Trails A (21.8 ± 7.31s) than middle (30.1 ± 12.84s) and older (40.1 ± 22.93s) groups ($F(2,158) = 32.5$; $p<.001$) and Trails B (42.5 ± 12.55s) than middle (70.7 ± 56.61s) and older (130.6 ± 73.85s) groups ($F(2,157) = 36.4$; $p<.001$). Similar findings were found for Stroop scores. In the middle age group stronger grip was associated with more correct answers on the COWAT ($r = 0.370$, $p = 0.009$) and faster completion of Trails A ($r = -0.394$, $p = 0.006$) and B ($r = -0.318$, $p = 0.028$).

DISCUSSION: Despite significant differences in outcome measures by age, an association between grip strength and cognition was only found in the middle-aged group. Further studies are needed to determine how other factors such as physical activity influence the rate of decline in associations between grip strength and cognition.

Tessa Diaz

The Impact of COVID-19 on Stress of Graduate Healthcare Professional Students

Authors: Tessa Diaz, SPT, Breanna Konowalski, SPT, Sean Meagher, SPT, Jennifer Dickson, PT, DPT, OMPT, Sara Maher, PT, PhD

Faculty mentors: Jennifer Dickson, Sara Maher

Abstract

INTRODUCTION: Graduate students face high stress levels, which may have been compounded by the arrival of COVID-19. OBJECTIVE: The study's purposes were to: 1.) analyze overall stress levels of graduate students from five healthcare programs, 2.) assess utilization of mental health service pre-and amid the pandemic, 3.) examine whether nurse anesthesia students had different perceived stress than other students, and 4.) determine which stress domains impacted nurse anesthesia students most.

METHODS: A cross-sectional repeated measure design was used. Students from five programs in a Midwestern University (n = 346) completed an online Qualtrics survey at three data collection points. The survey included demographic information and the Modified Stress Questionnaire (MSQ), a tool designed to measure stress perceptions in eight domains. Descriptives and frequencies were used for demographic information. One-way ANOVAs were conducted to determine if differences existed in perceived stress levels between participants, with post-hoc analysis conducted using Hochberg's GT2.

RESULTS: Perceived stress increased across five domains (academic, feedback, world, failing, environment) and decreased for three domains (faculty interactions, time, economic). Utilization of mental health services increased for all participants. Nurse anesthesia (NA) students had significantly lower perceived stress in seven domains compared to other students. NA students' perceived stress increased upon arrival of COVID-19 for environmental and decreased for economic, academic, and time.

CONCLUSION: Increased stress may have occurred due to navigating on-line learning and mandates to reduce virus transmission. Stress reductions might have been due to no commute time to campus, fewer interactions with faculty, and saving money due to business closures. For NA students, perceived stress only increased for the environmental domain which might reflect increased work hours, disruption in clinical rotations, and worry about delayed graduation. Understanding changes in student's stressors from external events may assist faculty and programs in supporting graduate students during these periods.

Teresa Diehl

Listening To Music Pre-Task On Neuromuscular Fatigue During Exercise: Preferred Vs. Non-Preferred Music

Authors: Teresa L. Diehl, SPT, Jennifer N. Yu, SPT, Frank M. Storer, SPT, and Moh H. Malek, PhD

Faculty mentor: Moh H. Malek, PhD

Abstract

Introduction: Studies indicate that listening to music can elicit various physiological responses ranging from distracting the subject from the sensation of fatigue to changes in specific regions of the brain. Indeed, the use of music, as an ergogenic aid, to improve human performance has been shown to be a powerful tool. Many studies on the effect of music on human performance have had subjects listen to music in-task (i.e., during the activity). There is, however, a growing interest to determine the role of listening to music pre task (i.e., prior to the activity) on exercise outcomes. In addition, it is important to consider the subject's music preference as that may influence the target outcome variable(s).

Objective: Therefore, the purpose of this study was to determine whether listening to preferred music pre-task influences the physical working capacity at the fatigue threshold (PWCFT). We hypothesized that listening to preferred music pre-task will increase the estimated PWCFT compared to the control condition which is listening to non preferred music.

Methods: Nine healthy college aged men [mean ± SEM: age, 23.4 ± 0.4 y; weight, 71.6 ± 2.5 kg; and height, 1.81 ± 0.02 m] volunteered for the present study. Each subject visited the laboratory on two occasions separated by seven days. In a randomized manner, subjects listened to their preferred music for 30 mins prior to the exercise test for one visit, whereas for the other visit subjects listened to their non preferred music 30 mins prior to the exercise test. Exercise outcomes were recorded for both visits and analyzed using a paired samples t-test.

Results: The results indicated no significant ($p > 0.05$) mean differences for maximal power output (mean ± SEM: 60 ± 4 W vs. 60 ± 4 W), PWCFT (25 ± 3 W vs. 29 ± 2 W) or heart rate at end-exercise (153 ± 8 beats/min vs. 155 ± 7 beats/min) between listening to non preferred versus preferred music 30 min prior to the exercise activity.

Conclusion: These findings suggest that listening to music pre-task does not influence neuromuscular fatigue during the exercise workbout.

Kayla Durbin

The effects of isometric ankle training with visual feedback in individuals with chronic stroke

Authors: Kayla Durbin, SPT; Brandon Katona, SPT; Angela Nappo, SPT

Faculty mentor: Dr. Victoria Pardo, PT, DHS; Dr. Sara Maher, PT, PhD, DScPT, OMPT

Abstract

Introduction: The NuStep Transitt recumbent stepper allows subjects to work on limb movements required for ambulation while in a safe seated position. The Transitt has a tablet display with real-time feedback of performance during the Paddle Ball game that is controlled with isometric ankle dorsiflexion and plantarflexion.

Objective: To determine the effect of isometric dorsiflexion-plantarflexion training through the NuStep Transitt Paddle Ball game on gait, functional mobility, strength, balance, coordination, visual scanning, and endurance in patients with chronic stroke. Methods: Thirteen participants (8 female, 9 right hemiparesis, mean age 59.46±11.03) with chronic stroke completed pre- and post-evaluations, which included gait on the GAITRite, Dynavision, knee and ankle maximum voluntary contractions, Lower Extremity Functional Scale, Four-Square Step Test (FSST), Five Times Sit to Stand (5xSTS), 6-Minute Walk Test (6MWT), and the lower extremity Fugl-Meyer assessment. Participants completed eight 45-minute training sessions on the Transitt twice a week, using isometric DF and PF to control the paddle. Demographic data were analyzed using descriptive statistics. Wilcoxon signed ranks were used for the 5xSTS, FSST, 6MWT, and Dynavision measures. Holm-Bonferroni post-hoc adjustments were conducted for all significant findings.

Results: There were significant improvements for 5xSTS ($p < 0.001$), 6MWT ($p = 0.008$), FSST ($p = 0.016$), Dynavision average reaction time ($p = 0.006$), total number of hits ($p = 0.009$), upper hemiplegic quadrant average reaction time ($p = 0.010$), and upper non-hemiplegic quadrant average reaction time ($p = 0.017$).

Conclusion: Decreased use of the hemiparetic ankle is a common problem for individuals post-stroke. Ankle training with visual feedback using the Transitt Paddle Ball game had clinically relevant effects on 5xSTS, FSST, 6MWT, and Dynavision total score and average reaction time which may translate to improved functional mobility and visual scanning for individuals with chronic stroke.

Jennie Feldpausch

Validation and Psychometrics of a Fatigue Assessment for Progressive Multiple Sclerosis

Authors: Emily Meyers, BS; Jennie Feldpausch, BS; Prudence Plummer, PhD, PT, BPhysio(Hons); Zade Abou-Rass; Nora Fritz, PhD, PT, DPT, NCS

Faculty mentor: Nora E. Fritz

Abstract

Introduction: Approximately 92% of persons with multiple sclerosis (MS) report symptoms of fatigue, such as lack of energy, exhaustion, or worsening of symptoms. Fatigue is common in both relapsing remitting (RRMS) and progressive (PMS) subtypes, yet currently available measures have been primarily tested in RRMS. While recent work has developed and examined psychometrics of fatigue specifically for persons with RRMS (FSIQ-RMS), the validity and MDC of this measure is unknown in PMS. Furthermore, concurrent validity of the FSIQ with other common measures of fatigue has not been established in either subtype.

Objective: To examine relationships of fatigue to other symptoms in persons with PMS compared to RRMS, and determine the concurrent validity and MDC of the FSIQ in persons with PMS compared to RRMS.

Method: In a single online survey, 806 individuals with MS (637 RRMS, 169 PMS) completed 16 measures of fatigue and self-reported functioning. Mann-Whitney U tests were used to examine differences in fatigue among subtypes, and Spearman correlations were used to examine concurrent validity.

Results: Persons with PMS demonstrated significantly greater fatigue ($p<0.001$) than RRMS. All subsections of the FSIQ (physical, cognitive emotional, coping impacts, daily) demonstrated moderate to excellent concurrent validity with four common measures of MS fatigue in both RRMS and PMS subtypes ($p\leq0.001$). Greater fatigue was associated with poorer health-related quality of life in both RRMS ($r=-0.837$; $p<0.001$) and PMS ($r=-0.682$; $p<0.001$). MDC values for FSIQ in PMS were established for the physical (5.406), cognitive emotional (4.483), coping impacts (5.278), and daily score (3.313) domains.

Conclusion: The FSIQ is a simple clinical measure that can be used for patients with both RRMS and PMS. The FSIQ should be considered in evaluating persons with MS to examine fatigue. Valid measures of fatigue for all MS subtypes are critically needed to monitor change over time and with intervention.

Christopher Gill
Assistant Clinical Professor of Nurse Anesthesia

Effect of Peer-Mentorship on Perceived Stress Levels Among Student Registered Nurse Anesthetists

Authors: Christopher Gill, Ph.D., MBA, CRNA, James Dunn, DNAP, CRNA, Brian Panfalone, DNAP, CRNA, Thomas Shadhaya, DNAP, CRNA, Stephanie Sturtz, DNAP, CRNA, Dominic Tironi, DNAP, CRNA,

Abstract

Student registered nurse anesthetists (SRNAs) can experience high levels of stress during clinical training. Stress during clinical training programs can come from a variety of sources like the rigorous academic curriculums and clinical commitments. Ineffectively managed stress can have negative implications on academic success, mental health, and overall wellness. The purpose of this study was to identify the impact, if any, that peer mentorship programs have on decreasing the level of perceived stress of SRNAs.

Keywords: stress, student registered nurse anesthetists, coping mechanisms, peer mentorship

Alexa Hongisto

Is Grad School Life Ruff? Considerations for a Successful Therapy Dog Program

Authors: Alexa Hongisto, B.S.Kin, OTS; Evangeline McKenzie, B.S.Ed, OTS; Rachel Eckhout, BHSc, OTS; Gracie Cabana, B.S.HES, OTS

Faculty mentor: Christine Kivlen, PhD, OTRL

Abstract

Introduction: Graduate students experience mental health challenges, including high levels of stress and anxiety related to balancing academic responsibilities along with various life occupations. Previous studies suggest that therapy dog programming produces positive mental health benefits among college students. Researchers have yet to investigate specific factors needed to create a successful therapy dog program for graduate students. Investigators conducted focus groups to explore graduate students' perspectives of current therapy dog programs in order to gain an understanding of the factors required for successful program development.

Objective: To evaluate the overall perceptions of programming and what factors need to be considered to create a successful therapy dog program.

Methods: A total of 25 graduate students attended one 45-60 minute focus-group where they were questioned about their past experiences with animals and potential involvement with previous AAI programs. Data was analyzed using a 6-step thematic analysis outline by Virginia Braun and Victoria Clarke (2006).

Results: Three primary themes were uncovered during thematic analysis, including (1) the overall effects of therapy dog programs on students, with subthemes being a happy environment, increased mood, and reduced stress; (2) lessons learned from past therapy dog programs; and (3) therapy dog wish-list for developing future programs. The subthemes that accompanied the lessons learned and therapy dog wish-list included, ratios, time, location, scheduling, activities allowed during the sessions, and diversification of size and breed of the dogs.

Conclusions: Researchers confirmed perceived mental health benefits from graduate student involvement with animals and therapy dog programming. Findings also suggest areas of improvement to therapy dog program implementation, thus giving rise to the most beneficial program outline to incorporate into different universities' graduate programs.

Jessica Ling

The step test evaluation of performance on stairs (steps): Validation and reliability in chronic stroke

Authors: Paige Dobbs, SPT; Haley Jurczyszyn, SPT; Jessica Ling, SPT

Faculty mentors: Nora Fritz, Andrew Moul, Victoria Pardo

Abstract

INTRODUCTION: Falls during stair ascent or descent are common across neurological conditions; unfortunately, there is a profound lack of outcome measures to assess the quality of stair climbing. The Step Test Evaluation of Performance on Stairs (STEPS) was designed to assess stair performance in persons with Huntington's disease, but may be applied to other neurological conditions. The purpose of this study is to determine the interrater and intrarater reliability of the STEPS tool in persons with chronic stroke, and to determine the concurrent validity of the STEPS tool to other balance and mobility outcome measures.

METHODS: Thirteen participants (mean age 59.23 ± 10.96) with chronic stroke (mean time since stroke 8.77 ± 5.28 yrs) took part in this observational study. In a single visit, participants completed the STEPS tool, as well as measures of balance and mobility (Tinetti-POMA, Fugl Meyer LE Motor and Sensory, Four Square Step Test, 5 Times Sit to Stand, Lower Extremity Functional Scale, Stair Self-Efficacy Questionnaire, Timed Single Leg Stance, GAITRite in forward, fast, and backward conditions). The Montreal Cognitive Assessment (MOCA-B) was used to examine cognition. During the STEPS, participants were guarded by a physical therapist, observed by two student physical therapists, and video recorded. Interrater reliability among the three in-person raters and intrarater reliability among the four video raters across two viewings, one week apart, was determined with two-way, random effects intraclass correlation coefficient (ICC) class 2 models. To determine concurrent validity, Spearman's rank correlation coefficient and 95% confidence intervals were determined among the STEPS total score and other balance and mobility outcome measures. To determine the relation of cognitive function (MOCA-B) to STEPS total score, while controlling for age, lower extremity disability level, and balance performance, linear regression was performed. Alpha level for this study was set at 0.05.

RESULTS: The STEPS tool demonstrated excellent interrater 0.979 (95% CI: 0.946-0.993) and intrarater reliability 0.967 (95%CI: 0.940-0.984) . The STEPS total score demonstrated good to excellent concurrent validity with the Four Square Step Test ($r= -0.827$, $p<0.001$) and the Tinetti-POMA ($r= 0.772$, $p= 0.002$), moderate to good validity with the Fugl Meyer LE Motor ($r= 0.723$, $p= 0.005$), and Timed Single Leg Stance on the impaired side ($r= 0.651$, $p= 0.016$). Spatiotemporal parameters of gait and coefficients of variability on non-hemiparetic leg exhibited moderate to excellent (≥0.50) correlation with STEPS performance in comfortable and fast walking; however only double support time during comfortable walking ($r= -0.699$, $p= 0.008$) and double support time ($r= -0.757$, $p= 0.003$) and single step length CV ($r= 0.624$, $p=0.023$) during fast walking were significantly correlated with STEPS performance on the hemiparetic leg. For backwards walking, step length ($r= 0.730$, $p= 0.005$), double support time ($r= -0.660$, $p= 0.014$), and step length CV ($r= 0.721$, $p= 0.005$) were significantly correlated with STEPS performance on non-hemiparetic leg, while nearly all spatiotemporal parameters of walking were significantly related to STEPS performance on the hemiparetic leg. After controlling for age, disability and balance performance, MOCA performance explained 82.8% of the variance in STEPS total score.

DISCUSSION: The STEPS tool demonstrates excellent interrater and intrarater reliability in persons with chronic stroke. The STEPS tool demonstrates good to excellent concurrent validity with the Four Step Square Test and Tinetti-POMA, and moderate to good concurrent validity with Fugl Meyer LE Motor, and Timed Single Leg Stance on the impaired side. Based on correlation with the STEPS tool and various spatiotemporal parameters of gait, walking bilaterally (both hemiparetic and non-hemiparetic legs) is the best indicator of STEPS performance, as well as backwards walking being strongly related to fall in neurologic populations. Our results also suggest that cognitive function may be an important contributor to stair-climbing performance.

CONCLUSIONS: The STEPS tool is reliable and valid and should be used by clinicians to evaluate stair climbing performance in persons with chronic stroke.

Rami Maasri

Cold therapy does not alter neuromuscular fatigue for consecutive exercise workbouts

Authors: Rami E. Maasri, SPT, Jonathan R. Jarvie SPT, Jacob S. Karski SPT, Logan J. Smith SPT, and Moh H. Malek, PhD

Faculty mentor: Moh H. Malek, PhD

Abstract

Modalities using cold-water immersion or whole-body cryotherapy target muscles and joints so that there is an accelerated return of physiological parameters to basal levels from acute inflammation or local swelling. Studies determining the efficacy of cooling the body on human performance have primarily used cold-water immersion or cold packs. Furthermore, the effect of cold therapy on delaying neuromuscular fatigue has become an area of interest in recent years. To date, however, no studies have examined the effect of cold therapy on the physical working capacity at the fatigue threshold (PWCFT) which is a proxy for neuromuscular fatigue. The purpose of this study, therefore, was to determine whether cold therapy after the first exercise test influences the PWCFT during the second exercise test. We hypothesized that cold therapy would delay the onset of PWCFT for the second exercise test relative to the control condition (i.e., no cold therapy). Eight healthy college-aged men [mean ± SEM: age, 24.3 ± 0.4 y; weight, 88.1 ± 4.3 kg; and height, 1.83 ± 0.04 m] ranging from 23 to 26 years-old volunteered for the present study. The subjects visited the laboratory on two occasions separated by 7 days. For each visit, subjects performed incremental single-leg knee-extensor ergometer followed by either resting for 30 mins (control condition) or having a cold pack applied for 15 mins and then resting for 15 mins (experimental condition). Thereafter, subjects repeated the incremental single-leg knee- extensor ergometer a second time. The order of visits (control vs. experimental) was randomized for each subject. The exercise indices and PWCFT was determined for each of the four visits and statistically analyzed using two way repeated measures analysis of variance. The results indicate no significant ($p > 0.05$) mean differences for maximal power output, heart rate at end-exercise, and PWCFT between the control and cold therapy conditions. Moreover, there was no significant ($p > 0.05$) mean differences between the first and second exercise workbout within each condition. The findings of this study suggest that cold therapy did not influence neuromuscular fatigue.

Jacqueline Magusin

A review on the effects of resistance training on articular cartilage health

Authors: Jacob Burcicki, Jacqueline Magusin, Lindsay Yankasky

Faculty mentor: Dr. Joseph Roche

Abstract

INTRODUCTION: The purpose of this study is to examine the available research on the effects of resistance training on articular cartilage health to gain a better understanding of the impact the type of training has on the health and structure of the articular cartilage in people with osteoarthritis.

METHODS: A narrative review of the existing literature on resistance training on articular cartilage health in individuals with osteoarthritis was completed using four databases. Studies were selected from in accordance with previously determined inclusion and exclusion criteria. The results of the studies were examined by students focusing on the impact resistance training had on cartilage health biomarkers and cartilage thickness.

RESULTS: Six articles were identified that met all of the criteria for the review. Several studies reported significant improvements in WOMAC, VAS, and KOOS scores. Most studies showed no significant increase in cartilage volume. One study showed increase in cartilage volume following a resistance training program. Studies showed improvements significant biomarkers of osteoarthritis- such as interleukins, tumor necrosis factor, and aggrecans- and in collagen alignment and integrity.

DISCUSSION: There is conflicting evidence on the effects that different resistance training programs have on cartilage health. Overall, resistance training has a beneficial effect on osteoarthritis as it improves quality of life, function, and pain levels. It also may contribute to improved health of the cartilage.

CONCLUSIONS: Resistance training has many beneficial effects for individuals with osteoarthritis including improved pain, quality of life, function and presence of osteoarthritis biomarkers. Clinicians should include resistance training in programs for patients with osteoarthritis.

Conor McKelvey

Caregiver Lived Experiences: "This Was My Life, My New Life"

Authors: Conor McKelvey, Dennis Bevza, Hala Saif, Hannah Suciu, Mary Ellen East, MS, COTA, Fredrick Pociask, PT, PhD, Rosanne Dizazzo-Miller, PhD, OTRL

Faculty mentor: Rosanne Dizazzo-Miller

Abstract

INTRODUCTION: Caregivers of people who are aging comprise the largest group of caregivers and tend to maintain their role for the longest amount of time, second only to parent caregivers of children. It is recognized that caring for a person who is aging can give rise to stress, depression and anxiety for the caregiver. The role of caregiving is widely stigmatized as burdensome and undesirable, with variance across this perspective having been examined only through the lens of differing cultural expectations. Twenty percent of individuals spend an average of 40 hours per week caregiving for an aging person once assuming the role. Limited research suggests that potential and actual caregivers assumed there were benefits to providing care; however people who were undecided or unwilling to become caregivers perceived fewer gains and more losses in the role.

OBJECTIVE: The purpose of this phenomenological study is to identify common themes based on the perceived “burden” on caregiving for individuals who are aging.

METHOD: Qualitative interviews based on phenomenological principles attempted to capture feelings and experiences associated with caregiving for the aging.

RESULTS: Three main themes emerged including life changing in terms of perspective and diagnosis; role strain in terms of time, depression, fear and anxiety and resources and support; and role reversal in terms of life coming full circle, loss and preconceived notions.

CONCLUSION: Contrary to the perceived “burden” of caregiving, many caregivers felt joy from coming full circle and being able to care for their parent. Findings imply that professionals do not have enough resources to support caregivers of the aging. Future research should focus on further exploring how positive experiences can help aide in the stress management of caregivers as well as investigate how to make resources more readily available to these caregivers.

Olivia Mears

Health is Wealth: Increasing Knowledge of General Health Concepts in the School-Aged Population Through Health Fair Interventions

Authors: Olivia Mears, PA-S (co-author); Carley Huelskamp, PA-S (co-author); Corinne Gratson, MS, PA-C; Bindiya Nandwana, MS, PA-C, MPH

Faculty mentors: Bindiya Nandwana and Corinne Gratson

Abstract

INTRODUCTION: Health awareness is of increasing need in the United States, evidenced through rising rates of obesity and physical inactivity within the school-aged population. Nearly 80% of all cases of heart disease, stroke, and Type 2 Diabetes are preventable with health education (Pulimeno, 2020), thus the importance of starting education at a young age.

OBJECTIVE: To increase the knowledge of general health concepts in the school-aged population through health fair interventions.

METHODS: Wayne State University Physician Assistant Studies students and faculty developed and administered a 9-question multiple choice questionnaire to students from Charles R. Drew Transition Center (Detroit Public Schools) and Crissman Elementary School (Utica Community Schools). The questions assessed general health knowledge in the areas of nutrition, physical activity, and mental health. Students then attended a health fair conducted by WSU PAS students and faculty at their associated schools. Answers to each of the survey questions were taught in 12 different presentations. Post-tests were completed within 24-hours of health fair attendance. A pre-/post-test study design was used to assess the effectiveness of the intervention. Data was reported as means with an associated 95% confidence interval and a paired t-test was used to evaluate the statistical significance between the pre-/post-test results.

RESULTS: Of 104 participants, 78 completed the pre-/post-test (n=78). Pre-test mean was 66.81 [95% CI: 62.86-75.84]. Post-test mean was 82.47 [95% CI 80.04,84.20], $P<0.001$. There was a mean difference of 15.67 with a moderate effect size (d=0.749).

CONCLUSION: Our data demonstrated improvement in general health knowledge following participation in the health fairs. Study limitations include pilot study challenges, sample size, pre/post-test administration difficulties, accessibility due to COVID-19 restrictions, and students' access to resources. Future research is aimed at including a broader patient population, increased guardian education/involvement, socioeconomic evaluation, and examining the potential for longitudinal studies.

Grace Michalski

Fire-Related Deaths: A Case Report

Author: Grace Michalski, Master of Sciences in Pathologists' Assistant

Abstract

Determining the cause and manner of death in fire-related cases can be very challenging for forensic pathologists. Differentiating whether death occurred from the fire or other means is critical for establishing a cause of death. Decedents of fire-related cases can present with a wide range of injuries. A decedent may have soot in the mouth, nares, upper and lower airways, but no burn injuries. Burn injuries themselves may range from superficial burns to extensive charring. Decedents could also have signs of foul play, such as a gunshot wound, masked by extensive burn injuries. This case report analyzes a decedent found after a house fire whom, at autopsy, presented with soot in the nares, on the tongue, and in both the larynx and trachea. There were no burn injuries outwardly identified. This case will be compared to ten other fire-related cases. The literature review will demonstrate the differences and similarities fire victims can present with and illustrate the importance of forensic pathologists to analyze every aspect of the case before determining the cause and manner of death in fire-related cases.

Abdallah Mrech

A Novel Therapy to Enhance Aging-Induced Mitochondrial Dysfunction in Skeletal Muscle

Authors: Abdallah Mrech SPT, Mohamed Ghamloush, SPT, Belal Bazzi, SPT, Gerry Hish, DVM, Maik Huttemann, PhD, and Moh H. Malek, PhD

Faculty mentor: Moh H. Malek, PhD

Abstract

As initially published by Harman in the 1950s, age-related decreases in mitochondrial function have been shown to play a major role in loss of skeletal muscle. Studies show that skeletal muscle of elderly subjects have increased nonfunctional mitochondria, an increase in mutated and deleted mitochondrial DNA, and reduced mitochondrial density. Recently, mitochondrial transplantation has been used to replace native damaged mitochondria with viable, structurally intact, respiration competent mitochondria isolated from healthy tissue. Therefore, the purpose of this study is to use a unique strain of rats that exhibit generational skeletal muscle dysfunction and determine the effect of mitochondrial transplantation. We hypothesized that mitochondrial transplantation, will reverse the mitochondrial dysfunction in the hindlimb muscles of rats compared to placebo. Twelve 18 months old male rats (equivalent to 70-year-old human) from generation 40 that were selectively bred for low capacity running (LCR) were randomized into either the mitochondrial transplantation (LCR-M) or placebo (LCR-P) group. One LCR rat was used as the donor animal to harvest skeletal muscle to isolate mitochondria for the transplantation. Rats received an intramuscular injection of the placebo (i.e., vehicle) or isolated mitochondria in each of the following muscles per hindlimb: quadriceps femoris (150 µL), tibialis anterior (75 µL), and gastrocnemius complex (100 µL). Four weeks after mitochondrial transplantation animals were euthanized and hindlimb muscles harvested for molecular and cellular analyses. Aging significantly ($p< 0.02$) reduced running capacity by 70%. Mitochondrial injection increase cytochrome c oxidative activity by 250% in the LCR-M group, whereas ATP concentration was increased by 50% relative to the LCR-P group. The results of this study indicated that mitochondrial transplantation could recuse the muscle from aging-induced mitochondrial dysfunction.

Jessica Phillips
Assistant Clinical Professor of Nurse Anesthesia

Gabapentin applications in anesthesia – A literature review

Authors: Mary Walczyk, DNP, CRNA; Haider Abdulzahra, DNAP, CRNA; Meghan Zorza, DNAP, CRNA; Emily Bleech, DNAP, CRNA; Lam Truong, DNAP, CRNA; Daniel Tanner, DNAP, CRNA

Abstract

Gabapentin's clinical use began in the 1990s, with practitioners benefiting from its relative safety and ability to produce analgesia alternatively to opioid analgesics. Gabapentin's relative safety profile and non-opioid analgesic properties, in the setting of an opioid epidemic, has seen its off-label use greatly surpass its Food and Drug Administration (FDA) approved indications. With 64 million prescriptions written in 2016, gabapentin became the 10th most commonly prescribed drug in the US. Although gabapentin's off-label use has increased over the years, evidence of clinical effectiveness is conflicting and limited to a few low-quality studies. Research has revealed gabapentin's use in anesthesia practice for reducing preoperative anxiety, reducing postoperative nausea and vomiting as well as decreasing postoperative myalgia. Other reports also emphasize its role in opioid sparing techniques perioperatively, ultimately decreasing anesthetic requirements. This review aimed to identify the most common uses of gabapentin in anesthesia, evaluate the evidence of gabapentin's efficacy for anesthetic applications and explore recommendations for future practice. This was achieved by searching over 7 scientific databases for articles utilizing key terms such as gabapentin, opioid sparing, fasciculations, then evaluating the articles utilizing the CONSORT checklist. Guidelines were then developed for the anesthesia professional on correct dosage and administration of gabapentin in treatment of preoperative anxiety, analgesia and utilization in opioid sparing techniques, prevention of postoperative nausea and vomiting, and myalgia prophylaxis.

Veronica Prieur

Contributors to Turnout in College Dancers

Authors: Veronica Prieur, SPT; Aaron Huizenga, SPT; Nick Krotchen, SPT; Blake Siersema, SPT

Faculty mentor: Dr. Marie Eve Pepin

Abstract

INTRODUCTION: Turnout is a common technical skill in dance and is described as an external rotation (ER) of the leg that comes primarily from the hip and allows the feet to face outward. Compensations during turnout have been correlated to increased injury risks in dancers. Limited research has explored the relationship between objective measures of mobility, strength and movement competency to the ability to perform turnouts. The purpose of this study was to investigate the relationship between hip and ankle passive range of motion (PROM), hip strength and movement competency screen (MCS) and various measures of turnout.

METHODS: Cross-sectional retrospective study. Twenty-one full-time undergraduate ballet/ modern collegiate dancers (19 females) from Wayne State University dance programs participated in this study. Hip and ankle PROM, hip strength, movement competency screen and various turnout measures were obtained in a single session. Primary analysis was performed using Pearson's r correlation (α=0.05).

RESULTS: Compensated turnout in 1st position showed moderate to high correlation with hip ER PROM and MCS scores and fair correlation to hip ER strength. Compensated turnout in 5th position was highly correlated with hip ER PROM only. Turnout measured in dynamic situations (landing position after a jump) demonstrated fair to no correlation to the included measures.

DISCUSSION: This study's findings showed a relationship between compensations found during common dance positions and a dancer's movement competency, as well as hip ER range of motion and strength.

CONCLUSION: Physical therapists may benefit from screening hip PROM, strength and movement competency as those seem to affect a dancer's ability to perform turnout measures, particularly in static positions. Considering the relationship between compensations in turnout and injury risks, addressing the deficits contributing to turnout compensation has the potential to reduce injury risks. The contributors to turnout in dynamic conditions need further investigation.

Joseph Roche
Associate Professor of Physical Therapy

A systematic review on the cognitive and neuropsychiatric sequelae of long-COVID and its occupational therapy implications

Authors: Joseph A. Roche, BPT PhD; Alexander Kokesh, BS; Alexandra Eibler, BS; and Renuka Roche, PhD OTR/L

Abstract

INTRODUCTION. Post-acute effects of COVID-19, known as "Long COVID" or Post COVID-19 condition, have been reported. Cognitive and neuropsychiatric symptoms, which affect occupational participation and performance, have been reported in Post COVID-19 condition.

OBJECTIVE. We reviewed the literature to identify the most common cognitive and neuropsychiatric symptoms of Post COVID-19 condition, elucidate the risk factors associated with these symptoms, and investigate the assessment tools that are used in the context of Post COVID-19 Condition.

METHODS. We used the PRISMA 2020 statement to perform and report this systematic review. We searched for articles with the terms "Post COVID-19 Condition", "long COVID", "Post-Acute Sequelae of COVID-19 (PASC)", "cognitive symptoms", "neuropsychiatric symptoms", and variations of these terms. Our initial search returned 1,400 articles. After stringently applying our inclusion criteria, and reviewing 226 articles, we identified 154 articles that met all our inclusion criteria.

RESULTS. ~40% of the studies reported sex differences, of which, ~95% of the studies reported a higher incidence of post-COVID-19 condition in the female sex. ~50% studies mentioned risk factors, and hypertension and diabetes were identified as the most common risk factors. Fatigue (~97% studies) and dyspnea (~94% studies) were the most common physical symptoms. In terms of cognitive dysfunction, "brain fog" was the most common symptom (~90% studies). Depression and anxiety were the most common neuropsychiatric symptoms (~92% studies). Quality of life measures were reported in ~30% of the studies, of which ~95% of the studies reported a decrease in quality of life measures.

CONCLUSION. Post COVID-19 condition is associated with symptoms that affect the quality of life. Our ongoing work stresses the importance of clinics to identify and treat Post COVID-19 condition (i.e. Long COVID), and the specific need for occupational therapists to be involved in these clinics due to their expertise in both physical and mental health.

Joseph Roche
Associate Professor of Physical Therapy

The effects of yoga on Duchenne muscular dystrophy – A critical appraisal of the literature with the Physiotherapy Evidence Database's PEDro scale

Authors: Joseph A. Roche, BPT, PhD; Mohan Ganesan, PT, PhD; Matthew Chase, MASP, MLIS

Abstract

INTRODUCTION. Duchenne muscular dystrophy (DMD) causes progressive degeneration of both skeletal and cardiac muscle, and leads to early death. Standard care has a minimal effect on disease progression. Surveys indicate that ~80% of caregivers seek alternative therapies, such as yoga, for persons with DMD.

OBJECTIVE. We critically appraised the published literature using the PEDro scale, to examine the evidence on the effects of yoga on DMD.

METHODS. We developed search strategies for health and medicine databases, with the terms "DMD" and "yoga." Our stringent search returned just three randomized controlled trials (RCTs). We assessed the methodological quality of the RCTs with the PEDro scale, which has 11 items pertinent to internal validity and statistical reporting, and yields scores that can range from zero (lowest quality) to 10 (highest quality). Based on the range of total scores, the RCTs we found were categorized as "poor" (score 0-3), "fair" (score 4-5), "good" (score 6-8), and "excellent" (score 9-10) in quality.

RESULTS. All three studies received a score of 5/11 (fair), implemented yoga as an adjunct to standard care, and used a combination of yoga techniques, which focused on breathing, relaxation, body postures, and meditation. Each study focused on different primary outcome measures, namely, pulmonary function tests, sympathetic and parasympathetic control of heart rate, and pediatric quality of life status. All three studies reported improvement in outcomes with yoga. Due to divergent outcome measures, we could not perform a meta-analysis.

CONCLUSION. Our examination of the literature indicates that yoga as an adjunct to standard care might have the potential to improve outcomes in individuals with DMD. However, there is, a lack of high-quality evidence on the effect of yoga as an intervention on the symptomatology of DMD, thus emphasizing the need for additional well designed research studies.

Joanne Rush
Assistant Clinical Professor of Nurse Anesthesia

Nurse anesthesia student's perception of virtual/e-learning: A survey of Doctorate of Nurse Anesthesia Practice Students

Authors: Ian Kain, Nathaniel Johnston, Shannon Inman, Andrew Mathews, Curtis Loehr

Abstract

From the onset of the pandemic until September 2021, the Wayne State Nurse Anesthesia program converted to a virtual/e-learning environment (VEL). The purpose of this study was to assess perception of VEL as a primary method of learning compared to face-to-face learning. A survey was sent to nurse anesthesia students utilizing Qualtrics and analyzed with routine software. The top 3 advantages of VEL were being at home (87%), home as a learning environment (66%), and access to online materials (64%). The top 3 disadvantages of VEL were class interaction/cohesiveness (83%), socialization (72%), and interaction with instructors (55%). Regarding concepts applied in the clinical setting, 56% (n=30) strongly agreed/agreed that VEL was effective, while 89% (n=47) strongly agreed/agreed that face-to-face was effective, this being statistically significant. 77% (n=41) strongly agreed/agreed that VEL is effective as a primary means of learning core concepts/principle courses, while 74% (n=39) strongly agreed/agreed that face-to-face learning is effective. This study demonstrated an acceptance of VEL for nurse anesthesia students when used with core/principle concepts. As the trend continues towards VEL, emphasis should be placed on improving the teaching of clinical skills and clinical-based scenarios, as well as improving socialization within the VEL environment.

Keywords: e-learning, face-to-face learning, student registered nurse anesthetists, virtual

Alyssa Swanson

A Review of Blunt Force Injury in Relationship to Subcutaneous Emphysema and Impact on Forensic Autopsies

Author: Alyssa Swanson

Abstract

Introduction: Forensic pathology is critical in determining the cause of death. An abnormal collection of air under the skin called subcutaneous emphysema, can be seen on both CT and X-rays. This finding can result when a person experiences blunt force to the chest or neck. This case report describes findings from an autopsy of a 26-year-old male who died after being struck by a vehicle while riding a motorcycle. He presented with multiple injuries however this case report will focus on the uncommon finding of subcutaneous emphysema.

Objective: The literature review will present an analysis of different case scenarios in which subcutaneous emphysema occurred after blunt force injury or motor vehicle accidents. Also, the clinical presentation of subcutaneous emphysema is evaluated so it can be identified in forensics.

Method: The following databases were used: PubMed and Science Direct in July 2022. The articles must have been published from 2016-2022. The case reports were included if they met the following criteria: blunt force injury to the neck or chest, presence of subcutaneous emphysema, and damage to the trachea or larynx.

Results: Whenever an abnormal opening of the larynx or trachea is created by injury, a subject is at risk of developing subcutaneous emphysema. During the autopsy, the most discernible characteristic of subcutaneous emphysema is swelling, erythema, and crepitus. The identification of crepitus may indicate an internal injury causing the presence of air pockets. In a case where the patient survives the blunt force injury, they can present with tenderness around the cervical area and present with dyspnea for similar reasons.

Conclusion: Although not all traumatic injuries to the chest and neck present with subcutaneous emphysema, it is important to palpate each region because it is indicative of internal injury which may warrant further investigation.

Taylor Takla

Cortical Brain Activation During Backward Walking and its Relation to Cognitive Performance

Authors: Taylor Takla, B.S.; Dmitry Belous, MD; Nora Fritz, PhD, PT, DPT, NCS

Faculty mentor: Nora Fritz

Abstract

Intro: Backward walking (BW) is a non-automatic motor skill that has been linked to falls in the elderly and persons with neurodegenerative diseases. Previous studies have found BW speed is related to fall risk and cognitive performance. However, cortical brain activation during BW and its relation to cognitive function are poorly understood.

Objective: Therefore, the goals of this study were to determine differences in cortical activation between forward walking (FW) and BW and to determine the relationship of cognitive performance to both activation during BW and to BW speed. We hypothesized that BW would show greater levels of cortical activation than FW, and that slower BW velocity and greater levels of cortical activity would be related to poorer cognitive performance.

Method: In a single session, participants completed the Brief Visuospatial Memory Test (BVMT) and walked forward and backward on a treadmill while wearing a functional near-infrared spectroscopy (fNIRS) cap to measure cortical activity. fNIRS is a non-invasive neuroimaging device that uses light to measure changes in hemoglobin concentration to infer underlying cortical activation.

Results: 22 healthy individuals (mean age: 30.5, SD:13.1, 8M:14F) participated in our study. Two channels, recording activity from the premotor and primary motor cortices, showed significantly greater cortical activation during BW compared to FW ($p < 0.05$). No relationship was found between BW speed and BVMT performance. Interestingly, four channels from prefrontal and premotor regions were positively correlated with BVMT learning scores ($p< 0.05$), indicating that greater levels of cortical activity during BW was related to better cognitive performance.

Conclusion: This study provides evidence that BW is associated with increased cortical activity in the premotor and motor cortices in healthy adults. Future studies should examine the relationships among BW cortical activity with BW speed and BVMT performance in clinical populations.

Alexandra Wilbanks

Impact of COVID-19 on Doctor of Physical Therapy Students Stress Levels

Authors: Brianna Lareau, SPT; Alexandra Wilbanks, SPT; Bailey Zmuda, SPT; Sara Maher, PT, PhD; Jennifer Dickson, PT, DPT, OMPT

Faculty mentors: Dr. Jennifer Dickson and Dr. Sara Maher

Abstract

INTRODUCTION: Physical, emotional, and mental health is a growing concern for college students, as effects of poorly managed stress may lead to health disorders. The COVID-19 pandemic and subsequent quick transition to remote learning added additional stressors for graduate students, including students in Doctor of Physical Therapy (DPT) programs.

OBJECTIVE: The purpose of this study was to examine stress levels before and amid COVID-19 for DPT students at a small midwestern university.

METHODS: A cross-sectional repeated measures design with convenience sampling was used. Participants included full-time DPT students in the first (PY1), second (PY2), and third (PY3) professional years. Data were collected using a Qualtrics survey, administered on three separate occasions, two prior to and one during, the COVID-19 pandemic. Survey questions included demographic information and the Modified Stress Questionnaire (MSQ), a validated survey to collect perceived level of stress on eight constructs. Demographic data were analyzed using frequency and descriptive statistics and tests of normality were conducted for all variables. A one-way ANOVA was conducted for between group comparisons to examine differences among three cohorts.

RESULTS: Stress among DPT students was evident during all data collections. Prior to COVID-19, PY3 participants had significantly lower stress than their peers and PY2 participants had highest levels of stress. Amid COVID-19 and the transition to remote learning, stress between participants equalized, with no significant differences observed between cohorts.

CONCLUSION: Higher stress in PY2 students may be due to increased lab time, required application of knowledge and critical thinking, and more practical examinations. With the transition to remote instruction, stress levels equalized between DPT cohorts possibly due to decreased lab and commute time. Understanding common stressors for graduate students and timing of heightened stress levels may assist faculty and programs in curriculum and course design and student utilization of mental health resources.

Hayah Abbasi

Wanna Meet on Zoom? The Value of a Virtual Interprofessional Team Visit

Authors: Hayah Abbasi, BHS, Pharm.D Candidate, Esraa Nigma, BHS, Pharm.D Candidate, Aline Saad, Pharm.D, Christine Kivlen, Ph.D, OTR/L, Martha Schiller PT, DPT, Brittany Stewart, RD, Pharm.D

Faculty mentor: Dr. Brittany Stewart

Abstract

INTRODUCTION: Wayne State University's healthcare students participated in a virtual interprofessional team visit (vIPTV) with participants 50 years and older to discuss health concerns. Prior to fall 2021, the team visit was conducted in-person and was successful. During fall 2021, the team visit transitioned to virtual platforms to safely incorporate all parties during the Covid-19 pandemic. Following the vIPTV, participants completed a survey to identify benefits and challenges with the transition to a virtual visit and to report interest in participating in focus groups to gain perspectives about the vIPTV and make assessment-driven decisions to determine the value of the program and future direction for vIPTV.

OBJECTIVE: To evaluate focus group participants' perspectives about the transition from an in-person team visit to vIPTV.

METHODS; The survey identified 54 participants interested in engaging in focus groups. A total of 43 (80%) participated in seven structured focus groups with an average of six participants per group. Program faculty facilitated the focus groups on December 21, 2021 and January 19, 2022. Four primary questions were asked to receive feedback on participants' experiences with the vIPTV program. An inductive thematic analysis was used to evaluate responses.

RESULTS: Three primary themes emerged including the value of the IPTV program, program model enhancements and the importance of human interaction. Some subthemes included mutually beneficial experiences for students and participants, educating students, the flexibility of a potential hybrid model, and the importance of an in-person human connection.

CONCLUSION: The study highlights potential enhancements to the future delivery of the vIPTV and the value of community partnerships in education. Overall, the successful implementation of vIPTV supports continued improvement in healthcare education training through community participant feedback.

Lana Alkahwaji

Analogs of Thymulin Peptide and their Activity with Zinc Metal Binding

Authors: Lana Alkahwaji, PharmD Candiate 2023, Dr. Steven Firestine, PhD, Dr. Shiv Sharma, PhD

Faculty mentor: Dr. Steven Firestine

Abstract

Introduction: Thymulin is a zinc containing thymic nonapeptide with the sequence PyGlu1-Ala2-Lys3-Ser4-Gln5-Gly6-Gly7-Ser8-Asn9. Thymulin has been shown to be involved in several diseases including cancer, sickle-cell anemia, pain and aging. Unfortunately, the clinical utility of thymulin is limited by its poor pharmacokinetic properties (t½ ~10 min) which we hypothesize is due to the weak binding of zinc to the peptide. Therefore, thymulin analogs with enhanced zinc binding could be be more potent and bioavailable peptides.

Objective: The aim of this study is to evaluate zinc binding to a variety of thymulin analogs. The analogs were designed based upon previous NMR structural studies of the peptide bound to zinc. An alanine scan was done to examine critical residues and the putative zinc binding residues were replaced with amino acids that are found in traditional zinc binding sites.

Methods: Peptides were synthesized via an in-house synthesizer. Analogs are evaluated for zinc binding via a competitive zinc absorbance assay to determine Kd and zinc stoichiometry. For the determination of affinity of a peptide for zinc, change in absorbance will be monitored. Protein samples were prepared in 10 mM HEPES, pH 7.2, containing 100 mM KCL. The sample was excited at 325nm and 366nm, and the emission scans were taken from 250nm to 500nm. After each subsequent metal titration, the sample was mixed, and a scan of the sample was recorded. The results were analyzed using DynaFit software to get the fit and determine the metal binding affinity.

Results: Preliminary results pending poster presentation.

Conclusions: Complete results are pending due to preliminary data that was analyzed. Additional studies are needed to elucidate the complete mechanism and understanding of metal binding in this process. Identification of thymulin analogs with improved stability and potency is the ultimate goal.

Andrew Berti
Assistant Professor of Pharmacy Practice

Antimicrobial efficacy Against Antibiotic-Tolerant Staphylococcus aureus Depends on the Mechanism of Antibiotic Tolerance

Authors: Emily M. Meredith; Lauren T. Harven; Andrew D. Berti, Pharm.D. Ph.D.

Abstract

Introduction: Bacteria can adopt an alternate metabolic state favoring small molecule synthesis over growth. In Staphylococcus aureus this is induced by factors present during infection including nutritional limitation, host responses and competition with other bacteria. Isogenic “tolerant" populations have variable responses to antibiotics and can remain viable. Survivors resume growth upon cessation of antibiotics and cause relapse or recurrent infection. In this study we compare the capability of antibiotics to reduce viability of S aureus made tolerant by different mechanisms.

Methods: Overnight S aureus SH 1000 cultures were diluted to 10^7 cfu/mL Tolerance was induced with mupirocin (nutritional), HQNO (competitive), peroxynitrite (oxidative) or serum (humoral). Tolerant cultures were exposed to ceftaroline, daptomycin, gentamicin, levofloxacin, oritavancin or vancomycin at physiological concentrations and viability assessed by dilution plating. Minimum duration for 3 log viability reduction (“bactericidal activity”, MDK 99.9 and 24 h viability reduction were calculated independently for each of three biological replicates Significance (P<0 05) was determined using Student’s t test.

Results: Each antibiotic is ineffective against at least one type of induced tolerant staphylococci. Only daptomycin remains effective against humoral tolerant staphylococci Oritavancin remains effective against all forms of induced tolerance except for humoral tolerance.

Conclusions: Antibiotic potency against tolerant staphylococci depends on the mechanism of tolerance. Each tolerance mechanism renders at least one antibiotic ineffective and each antibiotic is rendered ineffective by at least one mechanism of tolerance. Further studies to evaluate additional antibiotics, combination therapy and different tolerance inducers are warranted.

Natasha Bhutani

Evaluation of Bacteriophage-Antibiotic Combination Therapy for Biofilm-Embedded Multidrug-Resistant Pseudomonas aeruginosa

Authors: Natasha Bhutani, BS, MS, PharmD Candidate 2023; Dana Holger, PharmD, MPH; Amer El-Ghali, PharmD, MPH Candidate 2023; Ashlan Kunz-Coyne, PharmD, MPH Candidate 2023; Michael J. Rybak, PharmD, MPH, PhD

Faculty mentor: Michael J. Rybak

Abstract

Introduction: Multidrug resistant (MDR) P. aeruginosa is an emerging pathogen of concern responsible for 2,700 deaths in the United States in 2017. There are few treatment options available for these MDR bacteria, particularly targeting their biofilm-forming properties. Lytic (bacterio)phages can target and lyse specific bacterial species and they have demonstrated anti-biofilm properties.

Objective: To examine two biofilm-producing clinical P. aeruginosa strains, MDR R9010 and Difficult-to-Treat Resistant (DTR) R10266 and their responses against phages with host susceptibility at baseline, 14207 and EM, respectively.

Methods: Antibiotic and phage susceptibility of selected MDR strains was confirmed using minimum inhibitory concentration (MIC) assays. An initial screen was performed with modified checkerboard MIC assays for antibiotic-phage synergy. Following the initial screen, phage-antibiotic combinations were used in 24-h time-kill analyses (TKAs) against biofilm-embedded R9010 and R10266. Cultures were then isolated and underwent repeat phage and antibiotic susceptibility testing.

Results: Synergy was demonstrated in the initial screen with gentamicin (GEN)-phage and ciprofloxacin (CIP)- phage combinations, but not with azithromycin (AZM)-phage combinations. Similarly, in biofilm TKAs, GEN-phage, CIP-phage, and GEN-CIP-phage all demonstrated bactericidal and synergistic activity against both strains of P. aeruginosa. However, the addition of AZM to these effective regimens resulted in the loss of synergy. Against both organisms, the greatest bactericidal and synergistic effects were seen with the GEN-CIP-phage combination. In addition, CIP-phage combinations prevented the emergence of CIP resistance or phage resistance in R9010. CIP-phage combinations resulted in the lowering of the CIP MIC by 2 dilutions against both clinical isolates. Restoration of GEN susceptibility was not seen with any combination.

Conclusion: Phage-antibiotic synergy is a potential new therapeutic modality for MDR and DTR P. aeruginosa infections. The addition of AZM results in the loss of synergy against effective phage-antibiotic combinations such as GEN-phage, CIP-phage, and GEN-CIP-phage.

Mirna Eshaya

Phage-Antibiotic Combinations Against Multidrug-resistant S. aureus and E. faecium: Protein Synthesis Inhibitors Antagonize Phage Activity

Faculty mentor: Dr. Michael J. Rybak

Authors: Mirna Eshaya, BHS, PharmD candidate; Ashlan J. Kunz Coyne, PharmD; Kyle Stamper, BS; Amer El Ghali, PharmD; Biswajit Biswas, MS, PhD; Melanie Wilson; Michael V. Deschenes; Susan Lehman, PhD; Cesar Arias, MD, PhD, MS; Michael J. Rybak, PharmD, MPH, PhD

Abstract

Introduction: Bacteriophage (phage) may augment antibiotic efficacy and is a possible therapeutic option to increasing antimicrobial resistance. Limited studies have assessed phage-antibiotic combinations (PAC) and associated synergy (PAS); however, the impact of antibiotic mechanism of action on PAC efficacy is lacking.

Objective: To evaluate PAS and antagonism (PAA) among PAC with protein synthesis inhibitors (PSI) and cell wall active agents (CWA) against clinical strains of multidrug-resistant (MDR) S. aureus and E. faecium.

Methods: Three strains of MDR S. aureus (D712, N315, 684) and E. faecium (R497, HOU503, SF12047) were each evaluated against two phages (S. aureus: Sb1 and Intesti13, E. faecium: NV-497 and NV-503-01) in PAC with PSI (linezolid, minocycline, rifampin) or CWA (daptomycin, ceftaroline). PAS and PAA were evaluated using modified checkerboard (CB) minimum inhibitory concentration (MIC) testing followed by 24h time-kill analyses (TKA). Synergy and antagonism were defined as a fractional inhibitory concentration (FIC) of ≤0.5 and >4 in CB and a ≥2 colony forming units (CFU)/mL reduction from baseline or a PAC with CFU/mL higher than the most effective single treatment in TKA, respectively. Phage infection efficiency was evaluated in TKA using efficiency of plating (EOP). Data were compared by one-way ANOVA and Tukey (HSD) test ($p<0.05$).

Results: PAC with PSI against S. aureus and E. faecium strains demonstrated PAA, while CWA in PAC demonstrated PAS in both CB and TKA (ANOVA range of mean differences 0.52-2.59 log 10 CFU/mL; $p<0.001$). Phage EOP decreased in the presence of PSI but not CWA compared to untreated controls (0.07±0.02 vs. 0.87±0.06 plaque forming units, respectively; $p<0.001$).

Conclusion: These data highlight significant PAA and decreased phage EOP demonstrated by PAC with PSI and PAS with CWA. Studies assessing the impact of phage activity, location of ribosomal protein synthesis inhibition, and bactericidal vs. bacteriostatic antibiotic activity are warranted.

Jackie Fleury

Building Confidence and Knowledge Through Peer-to-Peer Education at an Interprofessional Prescription Writing Workshop

Authors: Fleury, Jackie; Khalifa, Ziad; Saad, Aline, PharmD; Guyer Christopher, MD; Stewart, Brittany, RD, PharmD

Faculty mentor: Brittany Stewart

Abstract

Introduction: Second year medical students (M2s) at Wayne State University (WSU) participated in an interprofessional prescription writing workshop developed by faculty and facilitated by WSU fourth year student pharmacists to increase student knowledge and confidence in prescription writing skills. M2 students completed pre- and post-workshop surveys to assess their confidence in prescription writing and perceptions of the workshop.

Objective: To assess M2 students' confidence and knowledge of writing error-free prescriptions in accordance with legal requirements and evaluate their perceptions of the prescription writing workshop.

Methods: Medical and pharmacy school faculty developed an 11-item survey administered through Qualtrics both before and after the workshop. Respondents indicated their level of agreement to statements related to prescription writing confidence and workshop experiences using a 5-point Likert-scale (1=strongly disagree, 5=strongly agree). Descriptive statistics and paired t-tests were used for data analysis.

Results: Of the 298 students who participated in the workshop, a total of 271 participants completed both the pre- and post-workshop survey, which represents a 91% response rate. On the 11-item confidence survey, all items showed a significant increase in pre- and post-survey comparisons with a cumulative average for all 11 items of 1.85 pre-workshop to 4.17 post workshop, ($p < .001$). 90% (243/271) of post-survey respondents somewhat or strongly agreed that the workshop added to their knowledge and skills in prescription writing. 86% (232/271) of respondents somewhat or strongly agreed that the workshop met their expectations.

Conclusion: M2 students' confidence in their ability to write error-free prescriptions increased significantly after participating in an interprofessional prescription writing workshop facilitated by student pharmacists. This study highlights that peer-to-peer education positively impacts student perceived knowledge and confidence. Future studies could evaluate students' perceptions about the value of peer-to-peer education and outcomes related to workshop participation.

Roukia Hamoud

Impact of Ambulatory Care Pharmacist-Led Diabetes Mellitus Management on Hemoglobin A1c Values Among Patients with Diabetes in a Primary Care Clinic Over Two Years

Authors: Roukia Hamoud, Pharm D Candidate '23; Alyssa Poyer, PharmD; Insaf Mohammad, PharmD, BCACP

Faculty mentor: Insaf Mohammad

Abstract

Introduction: Type 2 diabetes is a major health crisis that affects approximately 460 million people worldwide. Patients with diabetes often present with preventable microvascular and macrovascular complications that account for an estimated 5 million deaths every year. Literature has shown the positive impact of ambulatory care pharmacists on diabetes management, although additional studies are needed to evaluate novel collaborative models. .

Objective: To evaluate the impact of an ambulatory care pharmacist embedded in an adult internal medicine clinic on glycemic control among patients with uncontrolled diabetes compared with usual care over a 2-year period.

Methods: Using a retrospective matched cohort study, patients managed by the ambulatory care pharmacist will be matched via a propensity score to patients who received usual care with their primary care physician. Electronic medical record reports will identify patients with hemoglobin A1c (HbgA1c) >8% who had a least two encounters with the ambulatory pharmacy team between August 2017 through August 2019. The primary outcome is to evaluate the mean change in HgbA1c among patients managed by the ambulatory care pharmacist- compared with usual care over two years. The secondary outcome is to evaluate the difference in adherence to guideline directed management by the ambulatory care pharmacist compared with usual care. The primary outcome will be analyzed with an analysis of variance if normally distributed. A sample size of ~128 patients is expected based on the population available. This results in study power ranging from 59% to 88%, depending on the estimate of the standard deviation of the primary outcome (ranging from 3.0 to 2.0).

Results: TBD

Conclusion: TBD; We anticipate that this study will contributing to the literature by demonstrating that patients with type 2 diabetes managed by the ambulatory care pharmacist will have significantly improved HgbA1c by at least 1% compared to patients managed by usual care.

Paige Hanke

Evaluation of the Safety and Benefits of Peripherally Administered Anti-thymocyte Globulin in Kidney Transplant Recipients

Authors: Paige Hanke, BS, 2023 PharmD candidate; Franceska Spaillari, BS, 2023 PharmD candidate; Adina Poparad-Stezar, PharmD; Bryant Summers, PharmD, BCPS; Mary Grace Fitzmaurice, PharmD; Arin S. Jantz, PharmD

Abstract

Purpose: Rabbit anti-thymocyte globulin (rATG) is the most widely used kidney transplant induction immunotherapy in the United States. Administration of rATG through central intravenous line has been the standard of care for many years. The maintenance of central-line access may delay or prevent the administration of rATG and place patients at increased risk of morbidity. Health systems have begun to explore the use of peripheral administration as a standard of care. To better understand the use of peripheral administrated rATG, this study evaluates the safety, tolerability and benefits in kidney transplant recipients. The primary end point is to quantify the incidence and type of adverse events in patients receiving peripheral rATG and discover the potential benefits such as cost saving and decreased length of hospital stay.

Methods: This is a retrospective, single-centered, descriptive cohort in the process of IRB approval. Evaluating the use of peripheral administered rATG in kidney transplant recipients 18 and older receiving rATG induction therapy at Henry Ford Hospital. Pregnant women were excluded. Data was obtained from Henry Ford Hospital's electronic medical record system Epic between August 1st,2021 – August 31st 2022. Kidney Transplant recipients who qualify for rATG therapy receive three doses. One dose during the transplant and the others on the two proceeding days. Patients were screened for individual adverse events that occurred during each of the peripheral infusions to assess safety. To assess benefits of peripheral rATG, we evaluated the time in operating room, types of intravenous lines used, cost of medication, and length of hospital stay. The primary outcome will be described using simple frequencies, and descriptive statistics for numerical data. Nominal data will be analyzed using measures of central tendency.

Results: Forty-Seven kidney transplant recipients met inclusion criteria. No differences were detected in baseline characteristics. Demographically the median age was 59 years old and 51% were female. We anticipate seeing little to no adverse events occur with the peripherally administered rATG due to pre-medications (acetaminophen, hydrocortisone and diphenhydramine) one hour before rATG infusions, diluted drug concentrations and slower infusion time. We also expect to see benefits of peripheral administration such as a decreased time in operation room, reduced costs due to shortened hospital length of stay and ease of line access.

Conclusion: As literature purposes, peripheral administered rATG may demonstrate low adverse events and high benefit in kidney transplant recipients. These findings support the need for randomized controlled trials evaluating peripheral administered rATG to standardize it's use in healthcare.

Ian Hay

Development of Novel Inhibitors Targeting KRAS-SOS1 Interactions

Authors: Ian Hay, Tom Lucaj, Evan Malin, Jeremy M. Kelm, and Navnath S. Gavande

Faculty mentor: Dr. Gavande

Abstract

With the development of novel cancer agents, targeting mutated RAS proteins like KRAS widens the scope of available therapies for cancers with little treatment options. KRAS proteins are present in pancreatic, colorectal, and lung cancer, and are directly associated with increased mortality rates. There is great interest in targeting KRAS as it is prevalent in 1 out of 5 cancers. Functionally, KRAS is responsible for transducing extracellular stimuli from surface receptors by cascading intracellular receptors governing survival and proliferation. KRAS operates in a normal physiological state by partially binding to GTP, whereas mutated KRAS exhibits resistance to factors that enhance GTP hydrolysis. SOS1 interacts with KRAS by loading GTP, promoting downstream signaling of cellular proliferation. This interaction between proteins creates a complex called KRAS-SOS1. The role of SOS1 in cellular proliferation allows for new targeted therapies to be developed to disrupt this interaction. We have developed several inhibitors targeting KRAS-SOS1 interactions which aims to reduce mortality.

Sameera Javed

Pharmacist Perceptions of Delivering Patient Care through Telehealth

Authors: Sameera Javed, PharmD Candidate; Ayah Habhab, PharmD Candidate; Reem Hammoud, PharmD Candidate; Melissa Lipari, PharmD, BCACP; Alison Lobkovich, PharmD

Faculty mentors: Melissa Lipari, Alison Lobkovich

Abstract

Introduction: During the COVID-19 pandemic, telehealth has allowed providers to provide care to patients from any location and has shown to be useful in eliminating barriers. With its use increasing, many studies have surveyed an array of healthcare team members regarding their stance related to telehealth communications. However, there is a lack of data assessing pharmacists' perceptions.

Objective: To evaluate pharmacists' perceptions of benefits and barriers to telehealth as experienced in their telehealth visits.

Methods: This qualitative study used virtual focus groups and a validated questionnaire (Health Optimum Telemedicine Acceptance [HOTA]) to assess facilitators and barriers of telehealth. Participants were included if they were licensed pharmacists utilizing telehealth in the outpatient setting. Pharmacist focus group responses were transcribed and analyzed using Miles & Huberman's qualitative data analysis model.

Results: Six pharmacists participated in this study. Their responses were placed into two categories: clinical effectiveness and patient experience. All participants performed at least 20 virtual visits, and all agreed that telemedicine improved patient health status. Respondents agreed that telehealth is clinically effective due to having more frequent interactions and being able to provide multiple types of care for patients virtually. However, technological difficulties and the inability to provide physical examinations and obtain lab work were identified limitations. The main benefit that patients gained from telehealth was the elimination of transportation concerns, allowing increased access to care. However, pharmacists voiced their concern for patient privacy and barriers to educate on medical devices.

Conclusion: Pharmacists felt that telehealth was useful in several clinical scenarios. However, they also identified opportunities to improve its development in clinical practice. Further investigation must be done to better grasp impediments in telehealth care in order to provide the most effective patient care.

Kelly Kepley

Evaluation of Venous Thromboembolism Prophylaxis Dosing in the Low Body Weight Population

Authors: Kelly Kepley, Dalia Kassabieh, Souheila Hachem, PharmD, Zachary Smith, PharmD, Mathew Jones, PharmD, Urszula Grabowski, BSPharm, David Gutenschwager, PharmD

Abstract

Introduction: Weight-based dose adjustments for medications are not commonly provided for patients with low body weight due to under representation of this population in clinical trials. Anticoagulants, such as enoxaparin and unfractionated heparin (UFH), are examples of High-alert medications that may require dose adjustments in the low body weight population.

Objective: To describe the dosing practices, safety, and efficacy of venous thromboembolism (VTE) prophylaxis in low body weight populations.

Methods: This was a retrospective cohort study assessing dosing of enoxaparin and UFH for VTE prophylaxis in low body weight populations. Patients weighing less than 45 kg were included if they were admitted to Henry Ford Health (HFH) between 7/1/2019 and 6/30/2022 and received enoxaparin or UFH for VTE prophylaxis for a minimum of three consecutive days. Patients were excluded if they were pregnant, incarcerated, had history of amputations, cognitively impaired, had a 20% weight increase from baseline, active bleed or acute VTE diagnosed within 48 hours of admission, baseline INR greater than 2, platelets less than 50 K/uL. The primary outcome was incidence of receiving Food and Drug Administration (FDA) labeled doses of enoxaparin or UFH for VTE prophylaxis compared to alternative dosing regimens. Secondary outcomes included adverse bleeding or VTE, and the frequency of dose adjustments. Bleeding was defined by the International Society on Thrombosis and Haemostasis criteria. VTE were defined as deep vein thrombosis or pulmonary embolism occurring during admission while on VTE prophylaxis, confirmed by radiologist documentation on ultrasound, V/Q scan, CT scan with contrast. All data collected was analyzed using descriptive statistics. A convenience sample of 100 patients were included with a 1:1 ratio of enoxaparin and UFH patients.

Results: In progress

Conclusion: In progress

Heidi Klotz

Medication Use Evaluation of Antibiotic Selection and Duration in Patients with Non-Severe Uncomplicated Community Acquired Pneumonia

Authors: Heidi Klotz, PharmD Candidate 2023; Ryan Herc, PharmD Candidate 2023; Emily Reich, PharmD; Sandra Hartnagle, PharmD, BCPS, BCIDP; Jennifer Pilotto, PharmD, BCPS

Abstract

INTRODUCTION: Community-acquired pneumonia (CAP) is a common infection of the lungs that often requires treatment with antibiotic therapy, either inpatient or outpatient. It has been demonstrated through recent performance measure reports from the Michigan Hospital Medical Safety Consortium (HMS) that there are opportunities to improve the treatment of CAP in many institutions. These reports are based on local guidelines for treatment of CAP and include measures such as overall antibiotic duration and appropriate use of broad-spectrum antibiotics in the course of therapy.

OBJECTIVES: The primary endpoint of this study is to evaluate the overall duration of antibiotic therapy prescribed to patients who are being treated for non-severe uncomplicated CAP at Beaumont Hospital, Troy. The secondary endpoint is to evaluate the prescribing patterns of broad-spectrum antibiotics in the above mentioned patient population to assess appropriateness based on indication.

METHODS: This study is a retrospective chart review that was approved by Beaumont's institutional review board. Inclusion criteria for the study includes patients ages 18 and older who were admitted to Beaumont Hospital, Troy between May 1st, 2021 and April 30th, 2022. Patients must have had a diagnosis of non-severe uncomplicated CAP based on ICD-10 codes to be included. Patients excluded from the study include severe or complicated CAP as defined by local guidelines, positive COVID-19 test during admission or in the 30 days prior to admission, concomitant infection, lung cancer, comorbid lung infection, were transitioned into hospice, or died during the admission. Information was gathered via the hospital electronic medical record. Overall duration of antibiotics will include inpatient treatment along with any antibiotics prescribed outpatient. Evaluation for appropriateness of broad-spectrum antibiotic use will be completed through comparison to local guidelines to determine the percentage of patients who received broad-spectrum antibiotics without an appropriate indication.

RESULTS: Research in progress.

CONCLUSION: Research in progress.

Bhargav Kovuru

Retrospective analysis of Sugammadex use in the operation room

Authors: Dr. Safana Atwan, Pharm D. and Bhargav Kovuru, Pharm D. Candidate Class of 2023

Faculty mentor: Dr. Safana Atwan

Abstract

Introduction: Neuromuscular Blockade Agents (NMBAs) are utilized in operating rooms to optimize surgical conditions and/or for rapid sequence intubation. NMBA's are divided into depolarizing agents and non-depolarizing agents due to their differing mechanisms of action at nicotinic receptor sites. Succinylcholine is the only existing depolarizing agent while rocuronium and vecuronium are two widely used non-depolarizing agents, all a mainstay in paralytic requiring processes. Although NMBAs provide value in operating rooms, their residual effects can increase the risk of pulmonary complications including pneumonia and respiratory failure. Reversal of their residual effects is key to avoiding these negative outcomes. Sugammadex is a unique cyclodextrin agent used in the reversal of non-depolarizing agents by chelation and elimination, thereby reversing neuromuscular blockade and decreasing the risk of pulmonary complications. Sugammadex has been found to have faster reversal times, better outcomes, and a smaller side-effect profile compared to the alternative reversal agent, neostigmine. To minimize risks and maximize benefits, Beaumont Health System outlined a comprehensive guideline to streamline appropriate use of sugammadex. The use of sugammadex is limited to patients at high risk of postoperative respiratory complications, rescue from residual NMBA following reversal from non-depolarizing agents requiring postoperative ventilatory support when succinylcholine is contraindicated, and in "cannot ventilate, cannot intubate" scenarios.

Objective: To evaluate the utilization patterns and compliance rate of intraoperative Sugammadex usage based on the Beaumont Health guidelines.

Methods: This is a retrospective study including all adult patients (≥18 years of age) who underwent a surgical procedure requiring rocuronium or vecuronium, reversed with Sugammadex, at Beaumont Hospital Dearborn between January 2021 to January 2022. Data collection from medical records includes baseline demographics, type of surgery, duration of surgery, dose of Sugammadex, co-administration of neostigmine, and train of four. All data to be reported with descriptive statistics.

Results & Conclusion: In progress

Lauren Danelle Lim

Equitable Distribution of Monoclonal Antibodies for the Treatment of COVID-19

Authors: Lauren Danelle Lim PharmD Candidate, Nataliya Sorochak PharmD Candidate, Christopher A. Giuliano, PharmD, MPH, Pramodini B. Kale-Pradhan, PharmD, FCCP, Michelle Dehoorne PharmD

Faculty mentor: Pramodini B. Kale-Pradhan

Abstract

Introduction: Monoclonal antibody (mAb) therapy is an effective COVID-19 treatment for non-hospitalized patients with mild to moderate disease. However, early studies suggested differential receipt or refusal of therapy depending on certain socioeconomic characteristics.

Objective: The purpose of this study is to examine the receipt of mAb therapies in relation to socioeconomic factors.

Methods: We conducted a cross-sectional evaluation that included patients of Ascension Michigan and socioeconomic characteristics in the American Community Survey (ACS). Adult patients 18 years and older were included if they had an indication for monoclonal antibody therapy for COVD-19. All data requested was aggregated at the zip code level within 2021. The primary outcome was to evaluate the association between socioeconomic characteristics and receipt of mAb therapies. Secondary outcomes included the evaluation of associations between demographics of a zip code and demographics of patients that received mAb therapy and the association between socioeconomic characteristics and refusal of mAb therapies.

Results: A total of 3000 patients from Ascension Michigan and ACS were merged into 240 zip codes. No association was observed between receipt of mAb therapy and socioeconomic characteristics. There was a weak association observed in patients that reported having primary care providers (PCP) with receipt of mAb therapy ($r=0.111$, $p<0.084$). Demographics of patients that received mAb therapy correlated highly with the demographics of the population. There was a high correlation between the percent of African Americans in a zip code on the ACS and percent of African American that received mAb therapy ($r=0.757$, $p<0.001$). A similar observation was seen for Caucasian patients ($r=0.613$, $p<0.001$).

Conclusion: Socioeconomic factors did not significantly affect the receipt of mAB therapy and demographics of patients that received mAb were similar to their respective zip code.

Jovan Lozo

Prevalence and Risk Factors for Paclitaxel Hypersensitivity Reactions

Authors: Jovan Lozo, PharmD candidate 2023; Brittany Lines, PharmD, BCOP; Sarah Alsomairy, PharmD, M.S.

Abstract

Background: Paclitaxel is a chemotherapy medication , used in various cancer treatments that range from but not limited to gynecological, breast to lung cancer. Recently, there has been a noted increase in paclitaxel hypersensitivity infusion reactions, such as flushing, shortness of breath, anaphylaxis, hives, hypertension, hypotension, bradycardia or tachycardia, and pain. In order to prevent or reduce the risk of these reactions, pre-medications, such as dexamethasone, diphenhydramine and famotidine are administered first.. However, these hypersensitivity reactions may still occur as soon as the first few minutes of the first or second cycle of treatment. The primary objective of this study is to determine if there has been an increase in paclitaxel infusion reactions within the past year at the Cancer Treatment Center (CTC) Beaumont Dearborn, MI. Secondary objective is to assess the risk factors that may have contributed to the increase of developing a hypersensitivity reaction to paclitaxel.

Methods: This is a single-centered, retrospective cohort of patients with cancer who were treated at Beaumont Dearborn CTC between July 2021 – July 2022. Inclusion criteria are patients 18 years or older, who received paclitaxel at Beaumont CTC between July 2021- July 2022. Patients who are younger <18 years old and protected patient populations (children, pregnant women, etc.) will be excluded. Baseline characteristics will be collected, along with cancer type, date of treatment, chemotherapy received, rate of infusion of paclitaxel, and any noted reactions to infusion. Data will be analyzed using descriptive statistics and the results will be used to analyze the risk factors related to the increased reaction to paclitaxel infusion.

Results: pending

Conclusion: pending

Kristen Lucas

Evaluation of Eravacycline in Patients with a History of C. Difficile-Associated Disease

Authors: Kristen Lucas, MPH; Sara Alosaimy, Bsc Pharm, PharmD, BCPS, AAHIVP; Ashlan Kunz Coyne, PharmD; Michael Pierce, PharmD; Mark Biagi, PharmD; Kyle Molina, PharmD; Kimberly Claeys, PharmD, BCPS; Leonor Rojas, PharmD, BCPS, BCIDP; Lena Kang-Birken, PharmD, FCCP, AAHIVP; Madeline King, PharmD, BCIDP; Benjamin Pullinger, PharmD; Reese Cosimi, PharmD, BCPS, PharmD, BCPS, BCIDP; Serina Tart, PharmD; Michael Veve, PharmD, MPH; Susan Davis, PharmD; Michael Rybak, PharmD, MPH, PhD

Faculty mentor: Dr. Michael Rybak

Abstract

Background: Clostridioides difficile infection (CDI) is classified as an urgent threat by the CDC. Tetracyclines, including eravacycline (ERV), have not demonstrated an association with CDI compared to carbapenems, fluoroquinolones, cephalosporins, and clindamycin. We evaluated clinical outcomes with ERV use in patients with a history of CDI in the real-world setting.

Methods: Multicenter, retrospective, observational cohort study conducted at 9 geographically distinct U.S. medical centers from May 2019 to August 2021. Adults who received ERV for ≥72 hours and had a history of/current CDI were included. Clinical success was a composite defined as the absence of the following from ERV initiation: 30-day mortality, 30-day CDI recurrence, and no signs/symptoms of persistent infection.

Results: A total of 25 unique patients were included. Median (IQR) age was 60 (32-79), 56% were female, and 52% were Caucasian. 17% had a recent hospital admission, 20% were admitted from a nursing home, 32% had chronic kidney disease and 64% received antimicrobials for ≥24 hours with 90 days of index culture collection, including cefepime (28%) and piperacillin-tazobactam (20%). Median APACHE II and SOFA scores were 19 (11-31) and 4 (0-12), respectively. Common infection sources included intra-abdominal (44%) and respiratory tract (20%). Pathogens for which ERV was most often used to treat were Escherichia coli (20%) and Klebsiella oxytoca (12%). ERV was used for a median of 5 (2-38) days and was combined with another agent in 40% of cases, primarily meropenem (12%). ERV was selected primarily for a history of CDI (44%) or to consolidate the regimen (28%). Clinical success occurred in 80% (92% 30-day survival, 100% absence of 30-day CDI and 88% did not experience persistent signs/symptoms of infection).

Conclusions: ERV use in patients with a history of CDI is associated with positive clinical outcomes including the lack of 30-day CDI recurrence.

Mary Marogi

Optimization of Methods For Our Studies on IL-1β-Induced Oxidative Stress in β cells

Authors: Mary Marogi,* PharmD; Selena Hailo,* PharmD; Noah Gleason, MS; Anjaneyulu Kowluru, PhD. **MM and SH are Research Scholars in the PharmD Program. They both contributed equally to this work.*

Faculty mentor: Dr. Anjaneyulu Kowluru

Abstract

Introduction: Exposure of insulin secreting clonal β cells, rodent islets, and human islets to proinflammatory cytokines, including IL-1β, TNFα and IFNγ leads to their metabolic dysregulation and demise. Published evidence suggests that exposure of these cells to IL-1β results in increased expression of inducible nitric oxide synthase (iNOS) and subsequent generation of nitric oxide (NO), which has been implicated in the onset of cell dysfunction.

Objective: The objective of this study is to establish experimental conditions to assess the effects of IL-1β, a pro-inflammatory cytokine, on iNOS expression and NO release in insulin-secreting pancreatic β cells. Our long-term goal is to determine potential effects of IL-1β on phagocyte-like NADPH oxidase (Nox2) in the generation of intracellular oxidative stress in various subcellular locations, including the nuclear compartment.

Methods: INS-1 832/13 cells were incubated with IL-1β (5 ng/ml; 24 hours). Western blotting was used to measure iNOS expression. The quantification of NO was achieved through a Griess Reagent assay kit (Promega).

Results and Conclusions: Exposure of INS-1 832/13 cells to IL-1β resulted in expression of iNOS, in conjunction, a marked increase in NO release (1.8 ± 0.18 μM) was also observed under these conditions. Together, we were able to establish optimal conditions under which we plan to quantify IL-1β-induced Nox2-derived reactive oxygen species (ROS) generation and potential association of Nox2 with the nuclear fraction. We will quantify ROS generation using a commercially available kit (Abcam) and determine association of Nox2 subunits (gp91phox) with the nuclear fraction (isolated using NE-PER kit; Thermo Scientific) by western blotting.

Esraa Nigma

Tried and Tested: Discovering Benefits and Challenges with a Virtual Interprofessional Team Visit

Authors: Esraa Nigma, BHS, Pharm.D Candidate; Hayah Abbasi, BHS, Pharm.D. Candidate; Brittany Stewart, RD, Pharm.D; Aline Saad, Pharm.D; Christine Kivlen Ph.D, OTR/L; Martha Schiller PT, DPT

Faculty mentor: Dr. Martha Schiller

Abstract

INTRODUCTION: Wayne State University's healthcare students participated in interprofessional team visits (IPTV) with teams of 3-4 students from 9 different healthcare disciplines. During the visits, students performed discipline-specific assessments to address health concerns with community participants 50 years and older. The COVID-19 pandemic caused a shift in healthcare education training requiring the IPTV program to transition to a virtual platform for its delivery. Following the virtual visit, participants were asked to fill out a survey to assess the benefits and challenges of the program.

OBJECTIVE: To evaluate participants' perspectives regarding the benefits and challenges of the virtual shift of the IPTV program.

METHODS: Team visits were conducted via virtual platforms in Fall 2021. Following the visit, a survey was sent to all IPTV participants (n=202). The survey was developed by IPTV faculty and distributed through Qualtrics. The survey included participant demographics and open-ended questions related to the benefits and challenges of the virtual delivery of the program. An inductive thematic analysis was used to analyze the qualitative data.

RESULTS: Eighty-two participants submitted the survey (41% response rate). The average age of the participants was 73; 77% were female and the majority were Caucasian. Participants identified the following benefits: telehealth convenience, social interactions, partnering in students' education, and health-related resources provided. Forty-nine participants reported no challenges, seven participants reported a lack of in-person interaction and four participants reported challenges in technology. Fifty-four participants (66%) were interested in providing further insight through focus groups.

CONCLUSION: This study highlights the benefits and challenges related to virtual delivery of the IPTV program. Overall, community participants felt the virtual visit is convenient and beneficial. Data gathered from this study led to an additional study with focus groups to discuss the value of the IPTV program.

Rana Noori

Prescribing Patterns for Skin and Soft Tissue Infections in Hospitalized Patients

Authors: Anna Hejnar- PharmD student; Rana Noori- PharmD student; Shaina Kwiatkowski- antimicrobial stewardship specialist- PharmD; Vince Procopio- critical care specialist, PharmD; Amy Beaulac- antimicrobial stewardship specialist, PharmD

Abstract

Introduction: Skin and soft tissue infections (SSTIs) are one of the most common infections encountered in the hospital, and studies have identified variability in empiric antibiotics ordered and duration of therapy. Optimizing antibiotic use is critical to effectively treat SSTIs while balancing antimicrobial stewardship.

Objective: To describe the duration of antibiotic therapy and outcomes for patients with SSTI.

Methods: Retrospective observational cohort study of hospitalized patients who received antimicrobial therapy for SSTIs within 48 hours of admission and for a duration of least 72 hours. This study was conducted at five Henry Ford Health Hospitals between 1/1/2022-6/30/2022 and included 100 patients. The primary outcome was to evaluate if duration were compliant with guidelines.

Results: Of the 100 patients reviewed, the mean treatment duration was 11.25 days (SD=6.31). The mean inpatient duration was 6.32 days (SD=2.48) and the mean outpatient duration was 4.92 days (SD=5.91). Infectious diseases were consulted for 62% of patients. 7% were admitted to the ICU. Mean length of stay was 6.98 days (SD=5.25). 37% of patients re-presented to the emergency department within 30 days with 23% patients being readmitted.

Conclusion: The average duration of therapy was longer than the recommended duration of 5 days based on the national and local guidelines. Further evaluation will be conducted to assess the appropriateness of the antibiotic selection.

Klea Noskey

Assessment of Comprehensive Medication Management Incorporating a Patient Self-completed Medical/Medication Form

Authors: Klea Noskey, Brooke Penny, Kelly Kepley, Sara Barakat, Hanadi Thomas RPh., Francine Salinitri, Pharm.D., Richard Lucarotti, Pharm.D., Melissa Lipari Pharm.D., BCACP

Faculty mentors: Francine Salinitri and Melissa Lipari

Abstract

Introduction: Pharmacists require necessary medical information about the patient's current medications and disease states to prevent drug related problems (DRPs) from occurring. Currently there is no standard process for obtaining this information. However, one process in community practice for collecting this information is to interview the patients upon their first visit to the pharmacy. This study evaluated the benefit of incorporating a standard medical and medication history patient information (MnM) form into the community pharmacy practice.

Objective: To evaluate the impact of a self-completed MnM form in community practice.

Methods: This was a retrospective chart review and a prospective survey study conducted on participants 18 years and older who self-completed an electronic MnM form during a visit at Merriman Drugs Pharmacy. Participants who completed the MnM were provided the standard of care from a student pharmacist and pharmacist who reviewed their medical and medication history to optimize their medication therapy. Data was retrospectively collected on information provided on the MnM form as well as any medication recommendations. A follow-up visit was conducted with participants to assess their attitudes regarding providing this information in the community setting with a 10-question survey. This survey also evaluated the participants' perceptions of the overall interactions with the pharmacy student investigators.

Results: Preliminary data of 16 participants shows that 11 DRPs were identified by the student pharmacist with adherence accounting for the greatest amount of the DRPs. The most common intervention conducted by the pharmacy student investigator to resolve the DRPs for 9 participants was patient education. Twelve participants completed the survey with 100% either strongly agreeing or agreeing to understanding why a pharmacist needs this information to optimize care.

Conclusion: Utilizing a self-completed MnM form within community practice is an effective process to collect necessary information needed to identify and resolve DRPs.

Klea Noskey

Evaluation of Antimicrobial Prophylaxis in Spine Surgery within Enhanced Recovery Program at a Large Community Teaching Hospital

Authors: Klea Noskey; Richard Zoltowski; Sabrina DiPietro, PharmD; Tania Saeed, PharmD, BCCCP; Sapna Shah, PharmD, BCPS

Abstract

Introduction: The risk of surgical site infections post spine surgery is 0-18%. The American Society of Health System Pharmacists (ASHP) and the Enhance Recovery After Surgery (ERAS) Society have guidelines that recommend administration of antimicrobial 30 minutes prior to incision. Antimicrobial agents of choice recommended in the guidelines is cefazolin 2 grams (3 grams if patient weight over 120 kilograms). In the setting of a severe cephalosporin allergy, clindamycin 900 milligrams (mg) or vancomycin 15 mg/kg are alternative antimicrobial agents recommended.

Objective: To determine the number of patients who received the appropriate antimicrobial prophylaxis recommended by the ASHP/ERAS Society guidelines.

Methods: The Institutional Review Board (IRB) approved this single-center; retrospective chart review performed at a community-teaching hospital. Patients who underwent spine fusion surgery through the enhanced recovery program at Beaumont Hospital, Troy between January 1, 2022 through June 30, 2022 were included via electronic medical record (EMR). Four hundred and two patients were identified meeting the inclusion criteria. The primary outcome was to determine the number of patients who received appropriate antibiotic prophylaxis recommended by the ASHP/ERAS Society guidelines. Secondary outcomes included the incidence of patients with surgical site infections within 30 days of surgery, number of patients with reported allergies/intolerance to either penicillin or cephalosporin, characterization of alternative pre-operative antibiotics selection, and time to discharge from post-op floor. Descriptive analysis will be utilized for data analysis.

Results: Research in progress

Conclusion: N/A

Sandi Nuzha

Sequential Dosing of Phage-Antibiotic Combinations in MDR Pseudomonas aeruginosa

Authors: Sandi Nuzha, BHS, PharmD candidate, Amer EL Ghali, PharmD, Kyle Stamper, BS, Dana Hogler, PharmD, Ashlan J. Kunz Coyne, PharmD, Jose Alexander, MD, FCCM, BCMAS, Susan M. Lehman, PhD, Michael J Rybak, PharmD, MPH, PhD

Faculty mentor: Michael Rybak

Abstract

Introduction: Multi-drug resistant (MDR) Pseudomonas aeruginosa (PSAR) causes significant morbidity and mortality. Bacteriophages (Phages) are promising alternatives against MDR PSAR through phage-antibiotic combination (PAC) therapy. Therapeutic outcomes of PAC administration on PSAR may be influenced by the sequence in which PAC are administered and the nature of their interactions.

Objective: To compare the effects of staggering Phage-Ciprofloxacin(CIP) dosing on different MDR P.aeruginosa isolates.

Methods: The time between staggered doses was determined via one-step growth (OSGC) curves for three specific PSAR phages, LL-5504721-AH (LL), E2005-C (EC), and 109. We screened the phages against well-characterized clinical strains (R9010, R9316) of MDR PSAR using plaque assay methodology. Phage-CIP (CIP 0.25 x MIC) activity was analyzed via 24h time-kill assays (TKA) in duplicate using differing phage multiplicities of infection (MOI) 0.1-1. We compared adding phage prior to CIP administration vs. adding CIP prior to phage hourly for 5h over the 24h TKA based on OSGCs. We compared CFU/ml across different time points of CIP-Phage using ANOVA with Bonferonni analysis.

Results: Overall, adding phage before CIP showed increased bacterial killing compared to adding CIP before phage or simultaneously. CIP-LL-EC-109 (MOI 0.1) vs R9316 showed 1.22 ($P<0.05$) log10 reduction in CFU/mL when adding CIP after 1 hour. CIP-LL-EC-109 (MOI 1) vs R9010 showed a 1.24 log10 reduction in CFU/mL ($P<0.05$) when adding CIP after 3h vs. 0h. Conversely, adding CIP before phage showed reduced killing in R9316 and R9010 with an average increase of 1.5 ±0.5 ($P<0.05$) and 0.3 ±0.2 log10 CFU/mL among all time points, respectively.

Conclusion: Our results demonstrate that adding phage prior to antibiotics may result in better killing than giving antibiotics before or simultaneously. It also shows that specific organism characteristics and varying phage MOI may influence these interactions. Further studies using in-vitro/in-vivo models, different antibiotic combinations, bacteria and phages are warranted.

Obioma Opara

Student pharmacist perceptions of community overdose response training

Authors: Obioma Opara, BHS, M.Sc, Parker Tomkinson, B.S., Lauren Meloche, MS, Victoria Tutag Lehr, PharmD

Faculty mentor: Dr. Victoria Tutag Lehr

Abstract

Introduction: Pharmacists provide naloxone to reverse opioid overdose, yet persons at high overdose risk may not frequent a pharmacy. Our university is located in Wayne county, with the highest rate of fatal opioid overdoses in Michigan. Students must be prepared to respond to an opioid overdose. We partnered with AmeriCorps Community Training for Overdose Rescue (ACT) program to pilot naloxone training for pharmacy students. A post-training survey evaluated student perceptions of preparedness to identify an opioid overdose and administer naloxone.

Study Design: Survey

Methods: The WSU-IRB determined the study as exempt. First through third-year pharmacy students were encouraged to attend a one-hour virtual training presented by ACT members in January - February 2022. Content included identifying opioid overdose, calling 911, hands-only CPR, administering naloxone nasal spray in a pre-hospital setting, monitoring, survivor referral, and COVID-19 precautions. Upon completion, students received a naloxone nasal spray kit at no charge and a certificate of completion. In addition, they were invited to complete a voluntary 15-item electronic de-identified survey regarding their perceptions of preparedness to respond to an opioid overdose and experiences with opioid overdose.

Results: Of 112 students trained, 99 completed the survey (88.4%). The majority (83%; 82/99) perceived being fully prepared to recognize signs of opioid overdose, with 86% (86/99) fully prepared to administer nasal naloxone spray. Ten percent (9/99) reported having a previous encounter with an individual experiencing an opioid overdose; 17% encountered individuals regularly using opioids. Student responses by program year did not differ ($p>0.05$).

Conclusion: Community overdose response training prepares pharmacy students to identify an opioid overdose and administer naloxone. Students may encounter overdoses in the community, and Naloxone training should be a new requirement for first-year pharmacy students. Limitations include one university, responder bias, self-assessed competency, and small sample size.

Carolina Orzol

Novel Beta-Lactam/Beta-Lactamase Inhibitor Combination Use in Morbidly Obese Patients with Pseudomonas aeruginosa Pneumonia: Multicenter Evaluation of Clinical and Safety Endpoints

Authors: Carolina Orzol, BS, PharmD candidate; Ashlan J. Kunz Coyne, PharmD; Kristen Lucas, MPH; Michael P. Veve, PharmD, MPH; Michael J. Rybak, PharmD

Faculty mentor: Dr. Michael J. Rybak, PharmD

Abstract

Introduction: P. aeruginosa (PA) is a leading cause of hospital-acquired and ventilator-associated bacterial pneumonia (HABP/VABP) with high mortality rates. Novel beta-lactam/beta-lactamase inhibitor combinations (BL/BLIs) are often used for these difficult-to-treat infections; however, obese patients may be at increased risk of treatment failure due to their altered pharmacokinetics.

Objective: To evaluate whether obese patients (body mass index (BMI) ≥35 kg/m2) receiving BL/BLI (ceftolozane/tazobactam, ceftazidime/avibactam, meropenem/vaborbactam) for PA HABP/VABP had worse clinical and safety outcomes compared to non-obese patients (BMI <35 kg/m2).

Methods: Multicenter, retrospective study of patients hospitalized at two urban medical centers in Detroit from May 2010-February 2021. Included patients had: (1) PA respiratory isolate, (2) diagnosed lower respiratory tract infection, (3) receipt of ≥48h of BL/BLI within 72h of culture collection. Patients were excluded if they died prior to culture result, transferred into the hospital with known PA culture, or had cystic fibrosis. Primary outcome was a composite of treatment failure defined as all-cause in-hospital mortality or failure to improve clinically on BL/BLI. To mimic a randomized treatment situation, inverse probability of treatment weighting (IPTW) was applied to balance potential covariate bias.

Results: In total, 285 patients were included (obese n=95; non-obese n=190). Mean age was 62 years and 84.2% were admitted to the ICU. In both unweighted and IPTW-adjusted analysis, obese patients demonstrated significantly higher treatment failure compared to non-obese patients (58.9% vs. 37.9%; OR 1.545, 95% CI (1.326, 1.913) and aOR 1.675, 95% CI (1.465, 1.979)), respectively. Obese patients also had significantly higher risk of BL/BLI-induced nephrotoxicity compared to non-obese patients (aOR 1.363, 95% CI (1.147, 1.894).

Conclusion: Obese patients with PA HABP/VABP receiving BL/BLI were at a significantly higher risk of treatment failure compared to non-obese patients. Further studies are warranted to assess BL/BLI labeled dosing and therapeutic drug monitoring for obese patients with PA HABP/VABP.

Brooke Penny

Zooming into student success: Student Pharmacists Learning Community (SPLC) 2019-2022

Authors: Brooke Penny, PharmD Candidate; Sarah Kosel Agnihotri, MA TESOL; Victoria Tutag Lehr BSPharm, PharmD
Authors program, if different than mine:

Abstract

Introduction: The Student Pharmacists Learning Community (SPLC) has three third-year student peer mentors who assist in optimizing student success during the challenging first two (P1, P2) years. Mentors create opportunities for peer connection and learning. During the Covid pandemic, the mentors adapted SPLC sessions for program continuation. During 2019-2020, sessions were in-person, and then converted to virtual in 2020-2021. Combined virtual and in-person (hybrid) formats were implemented for 2021-2022.

Objective: To evaluate student perceptions of the SPLC during the Covid-19 pandemic period 2019-2022 using a survey.

Method: WSU-IRB deemed project as exempt. During winter semesters, P1 and P2 students were invited to complete a voluntary de-identified, electronic 8-item survey regarding their perceptions of SPLC and academic success, professional development, social interaction and relationships with peer mentors using a 9-point Likert scale format (1-strongly disagree-9 strongly agree). Students were asked about their utilization of the SPLC with opportunity for comment about the program.

Results: Overall, 126/562 (22%) of enrolled P1 and P2 students completed the survey. Attendance at one or more SPLC sessions increased from 26% of P1/P2 students in 2019 to 56% and 53% over next two academic years. Students agreed the SPLC is beneficial in improving academic success: 6.91 ± 1.62 (2019-2020), 7.70 ± 1.57 (2020-2021), and 7.61 ± 1.63 (p=0.14). Comments were overall positive; “peer mentors were accessible, shared wisdom, experiences and adapted format/timing of sessions”. Reasons for not using SPLC included “can study on own, don’t need help, no time to attend, and unaware of SPLC”.

Conclusion: Student perception of SPLC during 2019-2022 was overall positive and did not change significantly with implementation of virtual programming. Attendance increased during virtual and hybrid formats. The hybrid format was adopted for 2022-23 with increased messaging to students about the SPLC. Limitations include small, unbalanced sample sizes, and response bias.

Brooke Penny

Daphnid immobility as a measure of the toxicity of volatile organic compounds

Authors: Brooke Penny; Dima Awad; Zoha Siddiqua; Rucha Joshi; Shawn McElmurry, Ph.D.; Donna Kashian, Ph.D.; David K. Pitts, Ph.D.

Faculty mentor: David K. Pitts Ph.D.

Abstract

Introduction: Benzene (B), toluene (T) and ethylbenzene (E) are volatile organic compounds (VOC) commonly found as environmental contaminants which pose an exposure risk to humans. Previous work has established that exposure to B, T, and E can significantly affect the swimming behavior of Daphnia pulex. Determining the relative potency of individual VOCs to induce immobility is a first step in the design of studies to evaluate the toxicity of mixtures. Immobility (IM) was used to study potency rather than lethality. IM50 values were calculated as the concentration that produces immobility in 50% of the Daphnia. The over-arching hypothesis for the project is that a concentration-addition mathematical model can adequately explain the toxicity of VOC mixtures.

Objective: To calculate IM50 values from concentration-response curves for BTE over a 24-hour period.

Methods: VOC vials were utilized to hold solutions (0 to 243 PPM) of benzene, toluene, or ethylbenzene diluted in COMBO media. Mobility of each Daphnid was visually recorded at specified time points over 24 hrs. Each VOC was tested in two trials with 5 animals at each concentration (n=10 animals per concentration). Immobility was defined as D. pulex not moving for a minimum of 4 minutes. Microsoft Excel and Statistica were utilized to analyze the mobility data.

Results: At 60 minutes, benzene (243ppm), toluene (54ppm) and ethylbenzene (48.6ppm) reduced the daphnia mobility by 50% (IM50). When averaged across all time points, the IM50 of benzene, toluene and ethylbenzene was 243ppm, 27ppm and 81ppm respectively.

Conclusion: BTE exposure has been shown to produce concentration- and time-dependent immobility of Daphnia. The potency estimates will be used to design experiments with mixtures and test the utility of the concentration-addition model in predicting toxic interactions (e.g., additivity, synergism, antagonism).

Linh Pham

A Prescription for Success: Student pharmacists train medical students about best prescription writing practices through an Interprofessional Education Workshop

Authors: Linh Pham, PharmD. Candidate; Aline Saad, PharmD; Christopher Guyer, MD; Brittany Stewart, RD, PharmD

Faculty mentor: Dr. Brittany Stewart

Abstract

Introduction: Prescription writing is an essential skill to physician practice. Prescription errors negatively affect health outcomes and the healthcare infrastructure. Wayne State University (WSU) School of Medicine does not have prescription writing content in the current didactic curriculum. WSU pharmacy and medical school faculty collaborated to develop a prescription writing workshop for second-year medical students. Fourth year student pharmacists facilitated the workshops and educated the medical students about prescription writing best practices and legal requirements to reduce errors.

Objective: To evaluate knowledge increase related to prescription writing practices, including electronic prescribing, using a simulated electronic health record (EHR) platform among medical students.

Methods: Second-year medical students participated in a live prescription writing workshop facilitated by fourth year student pharmacists as an activity within their Clinical Skills course. Prior to the workshop, medical students completed a self-study module and a pre-quiz that included an electronic prescribing assessment question. Following the workshop, medical students completed the same assessments in order to evaluate the medical students' knowledge increase. A paired proportions test was used to evaluate the data.

Results: 298 second-year medical students participated in the workshop, 284 completed the pre-quiz, and 295 completed the post-quiz. There was a statistically significant improvement in students' performance on 80% of the quiz questions. On the pre-quiz, 7% of students (21/284) completed the electronic prescribing assessment correctly and 51% of students (149/295) completed it correctly on the post-quiz.

Conclusion: This study highlights the increase in knowledge related to prescription writing skills of second-year medical students after attending an interprofessional workshop led by fourth-year student pharmacists. These findings could lead to improved prescription writing practices and future studies could evaluate the benefit of interprofessional peer-to-peer education.

Rebecca Scribner

Antibiotic Appropriateness and Social Determinants of Health in Pelvic Inflammatory Disease

Authors: Rebecca Scribner, PharmD Candidate 2023, Dr. Michael Veve, PharmD, Dr. Susan Davis, PharmD

Faculty mentors: Dr. Susan Davis, Dr. Michael Veve

Abstract

Background: Pelvic Inflammatory Disease (PID) impacts approximately 2.5 million sexually active women of reproductive age. The receipt of guideline directed antibiotic therapy (GDT) has been shown to improve short and long-term patient outcomes, but the proportion of women receiving GDT is unknown. The study objective was to characterize antibiotic selection and duration in patients with PID and to evaluate potential health disparities.

Methods: An IRB approved, retrospective cohort study of women diagnosed with PID that received antibiotic therapy in inpatient and outpatient settings between 1/2010-12/2019 were included. The primary outcome was receipt of GDT, defined as antibiotic drug selection, dose, and duration in accordance with national guidelines. Descriptive statistics were used to describe patient, infection, and treatment characteristics. Social determinants of health evaluated included age, race, gender identity, insurance status, and income.

Results: A total of 401 patients were included: 93 (23%) received GDT, 308 (77%) did not receive GDT. The median (IQR) age was 27 (22-33) years and 262 (65%) were black or African American. 345 patients were treated as outpatients with oral antibiotics, while 56 were hospitalized and treated with IV antibiotics. Of the 345 outpatient treatments, 44/345 (13%) were prescribed GDT. In patients who received initial IV therapy, 49/56 (88%) were GDT; of patients transitioned to oral-stepdown therapy, 29/53 (55%) were GDT. Patients who did not receive GDT more commonly required retreatment or unplanned hospitalization compared to who received GDT (48% vs. 21%, P<0.001).

Conclusions: An overwhelming majority of outpatients with PID received discordant antibiotic therapy. Patients that did not receive GDT more commonly developed adverse outcomes after 12 months than those receiving GDT. These results suggest antimicrobial stewardship strategies are necessary to improve the care of patients with PID, especially those receiving care in outpatient settings.

Victoria Tutag Lehr
Clinical Professor of Pharmacy Practice

Commercial and Medicaid opioid analgesic policies and the revised CDC Treatment of Chronic Pain Guidelines

Authors: Victoria Tutag Lehr, BS Pharm, PharmD; Cynthia Arfken, PhD.

Abstract

Background: Prescribing policies after 2016 CDC Treatment of Chronic Pain Guidelines often restricted access to opioid analgesics, particularly for patients with intractable pain receiving long-term opioids ≥90 MME/day. In 2019, CDC advised against hard opioid daily limits and abrupt tapering. The CDC guidelines underwent revision; draft released for public comment February 2022 no longer recommends specific opioid dose limitations or treatment duration. Previously we showed opioid daily limits of 90 MME implemented by commercial insurance and Medicaid policies increased in Michigan after 2016 guidelines publication. The impact of the revision is unknown. We hypothesized an increase in prescribing policies allowing opioid dosage limits above 90 MME/day and longer duration.

Methods: Using same Michigan payer entities as our prior analysis, we examined number and timing of commercial and Medicaid payer opioid policies implemented from 2019-2022 (following publication of their warning and during CDC Clinical Practice Guideline for Prescribing Opioids revision). Policies from seven large commercial payers in Michigan and Medicaid fee-for-service were categorized 2019-second quarter 2022 into one or more 10 discrete strategies.

Results: The seven payers implemented 207 new strategies across 36 months, averaging 10.3 strategies per year, fewest during 2020 (n=25) and 2021 (n=51). The number of strategies implemented following announcement of guidelines revision 2019 and during public comment year 2022 was similar (65 versus 66). Most common strategy was limiting number of days for initial prescriptions (n=40) and least common was prior authorization for refills (n=1). Payers differed in opioid prescribing daily limit. However, by 2022-second quarter, all payers had prior authorization and/or step edit policies for prescribing opioids > 90 MME/day for 6 month-1-year accommodating high dose therapy.

Conclusion: Commercial and public payers policies on opioid analgesic prescriptions continue to be complex and rapidly changing, complicating clinical decisions. However, policies regarding opioid dosage limits and duration may be responding to CDC revisions, allowing flexibility to accommodate clinical need. Policy implementation increased during 2019 and 2022 guideline revision and public comment; activity slowed by Covid pandemic in 2020-21. The impact of these policies requires ongoing examination.

Halah Yaldo

Disproving the Dogma: Does Duration of Magnesium Infusion Rate Matter?

Authors: Halah Yaldo, PharmD Candidate; Christopher Giuliano, PharmD, MPH; Carrie Hartner PharmD; Renee Paxton PharmD

Faculty mentor: Dr. Christopher Giuliano

Abstract

Introduction: Prolonging the infusion rate of intravenous magnesium has been hypothesized to increase the retention of magnesium because of decreased renal wasting of magnesium; however, there is limited evidence to support prolonging the rate of the infusion.

Objective: To compare the absolute change in serum magnesium levels (mg/dL) from baseline to 24 hours after the end of the infusion.

Methods: This was a single-center, retrospective, observational study of intravenous magnesium therapy comparing standard infusion rate (0.5 g/h) versus prolonged infusion rate group (0.167 g/h). The primary aim was to compare the change in serum magnesium levels from baseline to 24 hours after the end of the infusion between the two groups. Secondary outcomes included obtainment of goal magnesium level, the time magnesium level was within goal range 48 and 72 hours after the end of the infusion, and both number and type of intravenous lines. The goal magnesium level was defined as 2 mg/dL to 2.6 mg/dL. For safety analysis we included the documentation of arrhythmia or seizures within 72 hours of discharge and bacteremia within hospital stay. Chi-square test was used for nominal data and Student's t-test for continuous data.

Results: There were 138 patients included in each group for a total of 276 patients. No differences existed between the groups for any demographic variables (all P> .05). The absolute change in serum magnesium level was 0.341 versus 0.255 (P= .001) in the standard and the prolonged infusion groups, respectively. No differences existed between groups for secondary outcomes or safety analysis data (all P> .05).

Conclusion: Standard infusion rates were associated with slightly improved magnesium retention in the body compared to the prolonged infusion rates with no significant differences in safety outcomes.

Ryan Verstraete

Stratifying Risk for Severe AKI in Patients Undergoing Open Heart Surgery

Authors: Ryan Verstraete, PharmD Candidate; Benjamin Fine, PharmD; Lama Hsaiky, PharmD, BCPS; Farzad Daneshvar, PharmD, BCCP; Safana Atwan, PharmD, BCCCP

Abstract

Background: The incidence of hospital-acquired acute kidney injury (AKI) in the United States is 0.8%, but it can be significantly higher in more vulnerable populations, such as in ICU. There are many populations in the hospital who are particularly vulnerable to AKI, with surgery patients, particularly cardiac surgery patients, experiencing a higher-than-normal incidence rate. Severe AKI can increase the odds ratio of mortality by 3-8 times for patients experiencing cardiac surgery. To date, studies looking specifically at independent risk factors for severe AKI in patients undergoing open heart surgery are limited. Here at Beaumont in Dearborn our incidence of severe AKI following open heart surgery is 3.6%. This study will look at the population of Beaumont health system as a whole and determine which risk factors identified in the literature are independently associated with severe AKI in our patients undergoing open heart surgery.

Purpose:
Primary objective: To determine which risk factors are independently associated with higher incidence of severe AKI in patients undergoing open-heart surgery within the Beaumont Health System.
Secondary objectives: To determine to what effect severe AKI was associated with increased mortality or length of stay in patients undergoing open-heart surgery within the Beaumont Health System.

Study Design: Retrospective case-controlled study

Methodology: This will be a retrospective case-controlled study with a case number of 50 matched against 100 controls, sufficient to give a power of 0.12 to detect a relative risk of 1.3 given an exposure of 0.25, and alpha of 0.05. Patients will belong to two groups, those who experienced severe AKI (As defined by AKIN) within 72 hours following open heart surgery, and those who had open heart surgery during the same time period but did NOT experience any AKI within 72 hours. The list of patients will be provided by external quality. Controls will be selected via simple random sampling of assigned values and a random number generator.
This study will be a retrospective review of patients undergoing open-heart surgery within the Beaumont Health System from March 2019 to January 2022. After being identified for the study, data collection will consist of going into the patient's chart to obtain information pre-surgery related to the prespecified risk factors identified (age over 65, female gender, BMI over 30, elevated WBC above 12,000/mm^3, prior CABG, heart failure, peripheral vascular disease (PVD), diabetes, diagnosed hypertension, COPD, Hgb <12.5, baseline serum creatinine, use of nephrotoxic agents within 48 hours of surgery start [NSAIDs, ACEi/ARBs, allopurinol, aminoglycosides, chemotherapy agents, loop diuretics, thiazide diuretics, vancomycin], iodinated contrast use within 48 hours, ejection fraction, and whether the procedure was emergent), as well as, some post/in-surgery factors (post-operative hypotension under 100/60 mmHg, cardiopulmonary bypass time >140 min, sodium fluid usage during the procedure, vasopressor usage during or after surgery, blood loss, mortality, length of stay). Analysis will then be done to determine if these factors were significantly associated with AKI.

Results: Results are still in progress. We expect to see increased incidence of severe AKI following patients undergoing open-heart surgery with the following risk factors: age over 65, female gender, BMI over 30, elevated WBC above 12,000/mm^3, prior CABG, heart failure, peripheral vascular disease (PVD), diabetes, diagnosed hypertension, COPD, Hgb less than 12.5, baseline serum creatinine, use of nephrotoxic agents within 48 hours of surgery [NSAIDs, ACEi/ARBs, allopurinol, aminoglycosides, chemotherapy agents, loop diuretics, thiazide diuretics, vancomycin], iodinated contrast use within 48 hours, ejection fraction, and whether the procedure was emergent, post-operative hypotension under 100/60 mmHg, cardiopulmonary bypass time >140 min, sodium fluid usage during the procedure, vasopressor usage during or after surgery, blood loss, mortality, and length of stay, which will lead increase length of stay in the hospital and increased mortality and morbidity.

Conclusion: This study will show which risk factors predispose patients to severe AKI following open-heart surgery. This data can be used in the future to identify high-risk patients and prevent severe AKI in patients following open-heart surgery, which will shorten length of stay and lower incidence of mortality and morbidity.

Salma Althobaiti

Reprogramming Tumor Microenvironment in Pancreatic Cancer by TME-targeted CD40 Nanoliposome

Authors: Salma Al-Thobaiti, (MS Candidate); Duy Luong (PhD Candidate); Prahlad Parajuli (PhD); Samaresh Sau (PhD); Navnath S. Gavande (PhD); and Arun K. Iyer (PhD)

Abstract

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is the most common primary malignant neoplasm of the pancreas as it accounts for more than 90% of all pancreatic cancer types. The PDAC microenvironment is made up of malignant cells that are surrounded by desmoplastic stroma, which hinders tumor infiltration by immune cells, thus making PDAC immunologically inert (cold) tumor, which is unresponsive to immunotherapy. Treatment with CD40 agonists and Metformin have been shown to break the desmoplastic ECM to a great extent. However, use of soluble CD40 ligand has been shown to cause tremendous systemic toxicity due to non-specific activation of peripheral immune cells.

Objectives: Our objective is to develop 'pHe-triggered, tumor/stromal cell -adhesive nanoliposomes (pHTANL)' loaded with CD40 agonist antibody that could be directly cytotoxic to tumor cells and alter the desmoplastic stroma, while also enhancing tumor immune infiltration and activation in PDAC with minimal systemic toxicity.

Methods: To obtain a potent pHTANL-CD40a, we rationally designed and screened a library of various NL formulations that comprised of innovative D+/A+ lipids and cholesterol (Chol) for stabilizing the NL. Use of diverse D+ lipids containing variable fatty acid chain (64% or 84.9 mole%), Chol (31 or 8.4 mole%), and A+ lipids (5 or 6.7 mole%) provided the optimum NL composition of A+ and D+ that were required for pHe-triggered tumor adhesion and delivery of CD40a. Dynamic light scattering (DLS) and Transmission electron microscopy (TEM) were used to characterization of NLs size and morphology. Subsequently, a fluorescence imaging study using NLs was performed by loading the NLs with FITC dye to confirm the adhesion of to CD40 receptor on the surface of macrophage cells. Efficacy and safety studies of pHTANL-CD40a were performed in vitro/vivo.

Results: The TEM/DLS analysis showed well-defined spherical vesicles (pHTANL-CD40a) with a small size of ~100-180 nm that allows tumor targeting by the EPR effect. Furthermore, the choice of lipids in the formulation revealed better NLs adhesion to tumor cells at acidic pH (~5.5-6.5) in comparison to physiological pH (~7.4). The zeta potential determination estimated the surface charges to be -14.7 mV and 37.17 mV at pH 7.4 and pH 6.5, respectively, indicating that the NL preparations were physically stable at physiologic pH. pHTANL-CD40a have achieved sustained release of CD40a in acidic condition (pH 5.5-6.5), similar to that in the tumor ECM. pHTANL-CD40a was more effective than free CD40a in activating macrophages in vitro, as determined by the expression of antigen-presentation and co-stimulatory/activation markers MHC class II, CD86 and CD11c. Treatment of Panc02 transplanted C57Bl6 mice with free CD40a significantly reduced the growth of tumor, but the tumors grew rapidly after the treatment was stopped and there was no survival benefit compared to the control groups. Whereas treatment with pHTANL-CD40a further inhibited the tumor growth with a treatment efficacy of 61.5% with survival up to 29 days, compared to 20 and 22 days in the control and free CD40a, respectively.

Conclusion: Our approach of pHTANL-CD40a delivery can an open new avenue for selectively activating tumor-killing immune cells with minimum systematic side effects. Our NLs platform can also be used for delivery of other toxic antibodies selectivity to the PDAC TME.

Chris Armstrong

Development of small molecules synergistically targeting Aβ and Tau as potential disease modifying treatment of Alzheimer's Disease

Authors: Christopher Armstrong, Aloke Dutta PhD

Faculty mentor: Dr. Aloke Dutta

Abstract

Introduction: Alzheimer's disease (AD) is the leading form of dementia in the United States and world. The pathophysiology of AD is complex and multifaceted in nature. Accumulation of senile plaques, neurofibrillary tangles (NFT's) are hallmarks of AD. The aggregation of amyloid beta (senile plaques) and tau tangles (NFT's) results in the death of neurons in the cortex and hippocampus, which manifests itself in cognitive decline and memory loss. Current therapies rely on conventional approaches that have only treated underlying symptoms without disease modification. Data from clinical studies point to a complex role of Aβ in a way that enhances the Tau phenotype throughout the disease process. To address co-pathogenic role of Aβ and tau, we undertook development of multi-target drugs aiming at both tau and amyloid beta to slow or stop disease progression and provide neuroprotection.

Results: Our work has led to the development of initial molecules D-688, D-687 and D-692 which demonstrate efficacy in inhibiting Aβ aggregation and tau fibrilization. Specifically, D-688 and D-687 are able to completely inhibit aggregation of Aβ1-42 and Ac-PHF6, a hexapeptide important for tau fibrilization, in a dose-dependent manner. These compounds also demonstrate efficacy in disaggregating aggregates in a dose dependent manner. The compounds are efficacious even at much lower doses. Lastly, D-688 provided significant neuroprotection against Aβ induced toxicity in an SH-SY5Y cell model.

Conclusion: Our experimental data have demonstrated that Aβï€ and tau can be targeted synergistically by small molecules which could potentially lead to development of disease modifying treatment agent for AD.

Dima Awad

Mixture Toxicology: Measuring the effects of BTEX on Daphnia pulex

Authors: Dima Awad, Brooke Penny, Zoha Siddiqua, Rucha Joshi, Shawn McElmurry Ph.D., Donna Kashian Ph.D., David K. Pitts Ph.D.

Faculty mentor: David K. Pitts

Abstract

Introduction: BTEX stands for Benzene, Toluene, Ethylbenzene and Xylenes which are all volatile organic compounds (VOCs) associated with petroleum products. BTEX often occurs as complex mixtures which contaminate the environment. Contaminated ground water can bring vapor into homes and buildings (i.e., vapor intrusion). Evaluating the toxicity due to exposure is a challenge because of BTEX volatility and potential chemical interactions affecting biological response (synergistic, additive, or antagonistic). A specialized VOC chamber was designed to evaluate the effects of BTEX mixtures on D. pulex. This initial study focuses on a binary mixture of Toluene and Ethylbenzene.

Objective: Measure behavior in a swimming assay during exposure to a binary mixture of Toluene and Ethylbenzene at concentrations estimated to cause immobility of 10% of Daphnids (IM10s).

Methods: D. pulex swimming behavior was digitally recorded within the VOC chamber for 4 hours during exposure to a binary mixture of toluene and ethylbenzene at IM10 concentrations in COMBO media. COMBO media alone served as control. The effect of exposure to the mixture on swimming behavior was measured as angular change (turning behavior, degrees) and distance traveled (mm) and evaluated using ANOVA with repeated measures over time.

Results: There was a significant ($P<0.001$) decrease in the distance travelled, and a significant increase in the mean angle ($P<0.001$) for Daphnids exposed to the binary mixture over a 4-hour period.

Conclusion: The results demonstrate that the binary mixture of toluene and ethylbenzene elicits significant behavioral toxicity with a relatively large decrease in swimming distance and large increase in turning behavior. Additional experiments examining the individual constituents at the IM10 concentrations and more complex mixtures will be conducted to determine if there are additive or synergistic toxic effects using the concentration-addition model.

Courtney Campbell

Elucidating the Metal Binding Properties of the Bacterial Protein, YlaN, and its Potential Role in the Sulfur Mobilization Pathway

Authors: Courtney J. Campbell, B.S.; Karla Esquilin-Lebron, Ph.D.; Kylie Ryan Kaler, Ph.D.; Jeffrey M. Boyd, Ph.D.; Timothy L. Stemmler, Ph.D.

Faculty mentor: Dr. Timothy Stemmler

Abstract

Iron-Sulfur (Fe-S) cluster-containing proteins are utilized in every biological pathway in most organism. In bacteria, Fe-S clusters are synthesized primarily in two independent pathways which include the sulfur mobilization (SUF) pathway and the iron sulfur cluster assembly (ISC) pathway; these exhibit redundancy, but the SUF pathway is predominant under oxidative stress or Fe-limiting conditions, while the ISC pathway dominates at a basal level. This pathway is comprised of 6 proteins: cysteine desulfurase (SufS), its accessory protein (SufE), a scaffold protein (SufB) and its partner (SufD), an ATPase (SufC), and a delivery protein (SufA). While many steps in the SUF pathway are generally understood, the identity and role of an iron chaperone that delivers to the complex for cluster assembly remains unknown. Previous studies showed depletion of the protein YlaN leads to phenotypes resembling depletion of the SUF complex, indicating that YlaN functions in the assembly of Fe-S clusters. My work focuses on YlaN as a potential Fe chaperone for the SUF pathway, biophysically characterizing how the protein binds to divalent metals including Fe(II).

We used a variety of spectroscopic and calorimetric methods to study metal binding characteristics of YlaN. We determined YlaN binds divalent metals at physiologically relevant levels, Fe(II) binding does not change secondary structure of YlaN, and Fe(II) binding thermodynamically stabilizes YlaN. X-ray Absorption Spectroscopy (XAS) studies indicated an Fe(II) binding environment constructed using only O/N ligands as a six coordinate high-spin ferrous complex. We conclude that Fe(II) binds YlaN at a physiologically relevant affinity consistent to what is seen in the published crystal structure of the protein. Combined, these findings lead us to believe that YlaN is a good candidate for the Fe chaperone within the SUF pathway. If accurate, YlaN would be the first identified Fe chaperone utilized in an Fe-S cluster assembly pathway.

Noah Gleason

Novel Regulatory Roles of smgGDS in Insulin Secretion in Pancreatic β-cells

Authors: Noah Gleason, MS; Anjaneyulu Kowluru, PhD

Abstract

Introduction: Small G protein Guanine Dissociation Stimulator (smgGDS) has been shown to play vital roles in regulation of newly synthesized small G proteins within their early prenylation signaling events. smgGDS has two splice variants, namely smgGDS-607 and smgGDS-558. smgGDS-607 binds to pre-prenylated small G proteins while smgGDS-558, which lacks one of the 13 armadillo (ARM) domains, binds to prenylated small G proteins. Previous studies from our laboratory have implicated G protein prenylation in physiological insulin secretion. However, putative regulatory roles of smgGDS in insulin secretion remain unexplored.

Objectives: The overall objective of the current study is to determine the expression and regulatory roles of smgGDS in insulin secretion elicited by a variety of insulin secretagogues in pancreatic β-cells.

Methods: Abundance of smgGDS in cell lysates was determined by western blotting. Insulin secretion in control or smgGDS-depleted INS-1 832/13 cells was quantified by ELISA (Cytoskeleton) following incubation with basal glucose (2.5 mM), high glucose (20 mM), KCl (50 mM), or forskolin (2.5 μm).

Results and Conclusions: Western blotting data indicated that smgGDS is expressed in INS-1 832/13 cells, rat islets and human islets. siRNA-mediated knockdown of smgGDS resulted in a significant inhibition of insulin secretion by induced by glucose (- 60%), KCl (- 49%) and forskolin (- 27%). Together, our findings provide the first evidence for the expression and novel regulation of physiological (glucose-induced), calcium-dependent (KCl) and cAMP-mediated insulin secretion by smgGDS in pancreatic β-cells.

Mirabela Hali
Research Assistant

Alpha4, a non-canonical subunit of protein phosphatase 2A, mediates islet beta cell dysfunction under glucotoxic conditions

Authors: Mirabela Hali, MSC; Brian Wadzinski, PhD; Anjaneyulu Kowluru, PhD.

Faculty mentor: Anjaneyulu Kowluru

Abstract

Introduction: The α4 protein (also known as IgBP1), is associated with a variety of protein phosphatases (e.g., PP2A) and regulates cell spreading, migration, apoptosis, and cell survival. Deletion of α4 protein has been shown to induce progressive loss in cell viability. Using quantitative proteomic approaches, we previously identified α4 as an interacting partner of the catalytic subunit of PP2A in pancreatic β-cells. We also reported a marked increase in PP2A activity in human islets, rat islet and INS-1 832/13 beta cells glucotoxic conditions.
Objective: To determine roles of α4 in islet β-cell function under normal (insulin secretion) and metabolic stress (cell demise) conditions.

Methods: Pancreatic islets were isolated from rats by collagenase digestion. Human islets were from Prodo Labs. INS-1 832/13 cells were cultured under basal (2.5 mM glucose) or glucotoxic (20 mM glucose) conditions for 24 hrs. GSIS and KSIS in control and siRNA-α4 transfected cells were quantified by ELISA. Subcellular fractions were isolated using commercially available kits. Phosphorylation status of various stress kinases was quantified by western blotting and densitometry. Degree of cell death was quantified using Cell Death Detection ELISA kit.

Results and conclusions: α4 is expressed in human islets, rat islets and clonal insulin-secreting INS-1 832/13 cells. siRNA-mediated depletion of α4 exerted no significant regulatory effects in GSIS and KSIS. Chronic exposure of INS-1 832/13 cells and rat islets to a variety of diabetogenic stimuli significantly increased the expression of α4. Deletion of alpha4 markedly increased p38MAPK and JNK1/2 phosphorylation under LG conditions, comparable to the degree seen under HG conditions. HG-induced CHOP expression (ER stress marker) and Caspase-3 activation were significantly attenuated in cells following alpha4 knockdown. Alpha4 knockdown significantly reduced HG-induced beta cell death. We conclude that alpha4 contributes to HG-induced metabolic dysfunction of the islet beta cell.

Tiara Hinton

Drosophila melanogaster Frataxin: Protein Crystal and Predicted Solution Structure with Identification of the Fe-Binding Regions

Authors: Tiara V. Hinton, BS; Andria V. Rodrigues, PhD; Sharon Batelu, PhD; John Rotondo, MD; Lindsey Thompson, BS; Joseph S. Brunzelle, PhD; Timothy L. Stemmler, PhD

Faculty mentor: Timothy Stemmler

Abstract

Friedreich's ataxia (FRDA) is a hereditary cardio- and neurodegenerative disease affecting 1 in 50,000 Americans. FRDA arises from a cellular inability to either produce sufficient quantities or production of a non-functional form of the protein frataxin, a key molecule associated with mitochondrial iron-sulfur cluster biosynthesis. Within the mitochondrial iron-sulfur cluster (ISC) assembly pathway, frataxin serves as an allosteric regulator for cysteine desulfurase, the enzyme that provides sulfur for [2Fe-2S] cluster assembly. Frataxin is a known iron binding protein and is also linked to the delivery of ferrous ions to the scaffold protein, the ISC molecule responsible for the direct assembly of [2Fe-2S] clusters. The goal of this report is to provide structural details for the Drosophila melanogaster frataxin ortholog (Dfh), using both X-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy, to provide foundational insight needed to understand the structure/function correlation of the protein. Additionally, we used NMR Fe(II) titrations to provide metal contacts on the protein to better understand how it binds iron and aids in its delivery to the ISC scaffold protein. Here, we also outline the structural and functional similarities of Dfh to orthologs. Structural data show bacterial, yeast, human and Drosophila frataxins are structurally similar, apart from a structured C-terminus in Dfh that likely aids in protein stability. The Dfh iron-binding location on helix-1 and strand-1 is also conserved across orthologs.

Ruchi Jaiswal

Phospholipase C-γ 1 interactome in human skeletal muscle tissue

Authors: Ruchi Jaiswal, M.Pharm; Xiangmin Zhang, Ph.D.; Arifur Rahman, M.Pharm; Berhane Seyoum, M.D., M.P.H.; Zaher Msallaty, M.D.; Abdullah Malisho, M.D.; Zhengping Yi, Ph.D.

Faculty mentor: Dr. Zhengping Yi

Abstract

Introduction: Skeletal muscle insulin resistance is a major defect preceding the development of type 2 diabetes. Phospholipase C-gamma 1 (PLCG1), a signal transducer protein, has been reported to play a role in insulin-stimulated glucose transport. However, whether there are novel PLCG1 interaction partners in skeletal muscle tissue from human participants is currently unknown.

Objective: To identify new PLCG1 interaction partners in human skeletal muscle tissue

Method: Vastus lateralis (thigh muscle) tissue from 4 lean healthy participants were collected using Bergstrom needle, cleaned, and frozen in liquid nitrogen. Biopsies were homogenized, resultant protein lysates were cleared with NIgG (control), followed by PLCG1 immunoprecipitation. The coimmunoprecipitates (IPs) were resolved on 1D-SDS PAGE gel, followed by in-gel trypsin digestion, peptide purification, and label-free HPLC-ESI-MS/MS analysis using a tribrid mass spectrometer-Orbitrap Fusion Lumos with high mass resolution and high mass accuracy. Peptides/proteins were identified using Maxquant. Pathway analysis was performed using DAVID (Database for Annotation, Visualization and Integrated Discovery)

Results: 18 proteins were detected in all PLCG1 IPs but not in NIgG IPs, suggesting that they are PLCG1 interaction partners. None of these interactions have been reported in any type of tissue or in any species so far, in 3 large interaction databases (BIOGRID, STRING or INTACT). Pathway analysis indicated multiple enriched pathways such as glycolysis, glucose metabolism, glucagon signaling pathway, regulation of actin cytoskeleton, signaling by receptor tyrosine kinases, RAF-MAP kinase cascade, and metabolic pathways.

Conclusion: Our work is the first to identify PLCG1 protein-protein interactions in human skeletal muscle tissue from well-characterized human participants. We identified 18 PLCG1 interaction partners which have not been previously reported and thus appear to be novel. These findings will help future studies in finding new molecular targets to treat/manage metabolic diseases.

Keywords: PLCG1, skeletal muscle, interaction partners, human, proteomics

Jeremy Kelm

Discovery of Replication Protein A Targeted PROTACs for the Treatment of Lung and Ovarian Cancers

Authors: Jeremy M. Kelm, PharmD, Jitender Dev Gaddameedi, PhD, Amirreza Samarbakhsh, MS, Hussein W. Kansou, BSc, Pamela S. VanderVere-Carozza, MS, Sara Serafimovski, PharmD Candidate, John J. Turchi, PhD, and Navnath S. Gavande, PhD

Faculty mentor: Navnath S. Gavande

Abstract

Despite remarkable advances within the field of molecular cancer therapeutics, DNA-damaging agents retain a central role in the treatment of cancer. The clinical response to DNA-damaging therapies is varied within and across cancer subtypes where a robust DNA damage response (DDR) predicts recalcitrance. Replication protein A (RPA) is the predominant human single-stranded DNA (ssDNA)-binding protein, playing essential roles in the DDR, DNA replication, recombination, and mitigation of replication stress. RPA overexpression is observed in a broad array of cancers and correlates with poor responses to DNA-damaging drugs. Inhibition of the RPA–DNA interaction is an approach to cancer drug discovery that holds potential to provide single-agent activity and/or synergy with existing therapeutics. However, cell permeable, potent inhibitors of protein-DNA interactions are difficult to design and do not address the important protein scaffolding roles of RPA within the DDR. Targeted protein degradation is an evolving trend within drug discovery that is particularly applied where target affinity, scaffolding roles, overexpression, and selectivity pose challenges. Herein, we describe the biological evaluation of an RPA targeted proteolysis targeting chimera (PROTAC) library conceived by conjugation of a diarylpyrazole RPA inhibitor with an E3-ligase ligand via various linkers. Linkers were carefully designed to minimize cell permeability liabilities imposed by the inherently high molecular weights of PROTACs. Cellular uptake across the compound library was broadly improved relative to the parent RPA inhibitor. Similarly, RPA engagement by the PROTAC series was widely unhindered by linker-IMiD derivatization. A subset of the compound library displays cellular IC50 values (viability) in the mid nanomolar – low micromolar range across H460, A549, H358, and A2780 cell lines. Several compounds appear to induce modest RPA70 ubiquitylation and degradation at 1 μM with longer linkers outperforming their shorter congeners.

Aaron Lotvola

C-Myc is downregulated by ABHD5 in Prostate Cancer Cells

Authors: Aaron Lotvola, Guohua Chen,PhD; Jian Wang, PhD

Faculty mentor: Dr. Jian Wang

Abstract

ABHD5 (ab hydrolase domain containing 5) is an essential coactivator of ATGL (adipose triglyceride lipase), the rate-limiting lipase that hydrolyzes and mobilizes the intracellular triglyceride (TG) store through lipolysis in many cell types. Importantly, ABHD5 functions as a tumor suppressor. However, the mechanism of ABHD5-dependent tumor suppression is not well understood.

Our earlier results demonstrated that ABHD5-mediated lipolysis acts as a functional barrier suppressing the anabolic signaling of cancer cells. Mechanistically, ABHD5 triggers futile cycling of TG hydrolysis and re-synthesis, resulting in AMP accumulation, AMPK activation, and mTORC1 inactivation. Our metabolomics profiling further revealed that overexpression of ABHD5 significantly decreases the metabolite abundance of serine metabolic pathways, including PHGDH-mediated serine synthesis, serine-mediated one-carbon metabolism, nucleotide synthesis, transsulfuration, and glutathione synthesis, suggesting a unique role of ABHD5 in suppressing serine-mediated anabolism in cancer cells.

Interestingly, our RNAseq transcriptomics and gene set enrichment analysis (GSEA) revealed that overexpression of ABHD5 significantly represses the gene targets of c-Myc, a proto-oncogene and a master transcriptional driver for anabolic gene expression. Furthermore, we showed that ABHD5 strongly downregulates c-Myc protein expression in a manner requiring proteasomal activity, which is accompanied by the downregulation of PHGDH and SHMT2, the critical serine biosynthesis and utilization enzyme, respectively. Thus, our studies identified c-Myc as a critical molecular mediator potentially important to connect ABHD5 metabolic signaling with cancer cell anabolic downregulation in tumor suppression.

Therefore, we propose the following aims to accomplish our objective in understanding ABHD5-dependent tumor suppression: 1) Determine the molecular mechanisms by which ABHD5 inactivates c-MYC signaling and 2) Determine the molecular underpinning and functional significance of the ABHD5/MYC/PHGDH/SHMT2 axis in the anti-tumor functions of prostate cell proliferation. Successful completion of this study may serve as a novel platform to discover new therapeutic targets for cancer intervention in prostate cancer and MYC-driven cancers.

Duy Luong

Tumor Stroma Targeting Smart Nanoparticles for Reversal of Drug Resistance and Immune Modulation in Kidney Cancer

Authors: Ayatakshi Barari, MS; Duy Luong, MS; Somrita Dey, Ph.D.; Samaresh Sau, Ph.D.; Prahlad Parajuli, Ph.D.; Navnath Gavande, Ph.D. and Arun K. Iyer, Ph.D.

Faculty mentor: Dr. Arun Iyer

Abstract

Renal cell carcinoma (RCC) is the major (>90%) and the most lethal form of kidney cancer. RCC has high therapy resistance and metastatic index with a 5-year disease-free progression at less than 10%. Thus, developing efficacious combination treatment remains an urgent and unmet need for therapy-resistant RCCs. For overcoming the critical challenges of poor delivery efficiency of currently approved drug therapies for RCC, we developed a tumor penetrating and tumor multicomponent targeting library of nano-sized oligomers (OMs) encapsulated with experimental drugs such as CFM4.16, Belzutifan (Bel), and CB. A drug synergism study showed a superior cell killing with the combination of Bel and CFM 4.16 or with CB. Flow cytometry analysis showed that Bel and CB or Bel and CFM 4.16 combination showed a significant increase in the M1 phenotype of macrophages and a strong decrease in the M2 phenotype of macrophages in their treatment in bone marrow-derived macrophages (BMDM). Based on the current data, OMs encapsulated Bel and CB are anticipated to have a strong potential of killing the RCC cells and modulate the immune system to enhance the anti-tumor efficacy.

Duy Luong

Folate receptor targeted therapy of MRSA using antibiotics loaded Nanoparticles

Authors: Kushal Vanamala, MS; Ketki Bhise, Ph.D.; Hiram Sanchez, Ph.D.; Razieh Kebriaei, Ph.D.; Duy Luong, MS; Samaresh Sau, Ph.D.; Hosam Abdelhady, Ph.D.; Michael J. Rybak, Ph.D.; David Andes, Ph.D.; Navnath Gavande, Ph.D. and Arun K. Iyer, Ph.D.

Faculty mentor: Dr. Arun Iyer

Abstract

Methicillin-resistant Staphylococcus aureus (MRSA), commonly called a superbug, is a highly alarming antibiotic-resistant population of Staphylococcus aureus (S. aureus) bacteria. Vancomycin (VAN) was first approved by the FDA in 1988, and it is still regarded as the treatment of choice for MRSA. The efficacy of VAN treatment has become less effective due to the development of VAN resistance in MRSA and the potential for nephrotoxicity. This study aims to improve the efficacy of VAN treatment by identifying the folate receptor for MRSA-infected tissues and developing folate-decorated lipid nanoparticles containing VAN (LVAN). In comparison to conventional VAN, LVAN showed a higher bactericidal effect and a superior ability to inhibit biofilm in MRSA with an enhanced accumulation in MRSA-infected thigh tissues and a reduced accumulation in kidneys. The results suggested that LVAN is a promising candidate to overcome the current limitations of bacterial resistance and adverse side effects in kidneys found in VAN.

Morgan Minjares

The Role of G-Protein-Coupled Receptor 35 in the Regulation of Endothelial Health Under Mitochondrial Oxidative Stress

Authors: Morgan Minjares, PhD

Faculty mentor: Dr. Jiemei Wang

Abstract

Studies have pointed to endothelial dysfunction as one of the major pathological changes between exposure to cardiovascular risk factors and the actual development of cardiovascular diseases. A critical factor in maintaining endothelial cell health is the regulation of superoxide production as an overabundance can lead to mitochondrial damage. GPR35, a G-protein-coupled-receptor, has become a potential therapeutic target in the treatment of cardiovascular diseases and previous studies have shown that inhibiting this GPCR aids in maintaining cellular health.

In the inhibition of GPR35 in human dermal microvascular endothelial cells (HDMVECs), fluorescent staining with MitoSox revealed a decreased superoxide formation within the mitochondria under high glucose conditions but not in the normal glucose control. GPR35 was then overexpressed in HDMVECs and stained with MitoTracker. Images taken with a fluorescent microscope showed an overlay between GPR35 and the mitochondria in high glucose conditions but not in the normal glucose control.

In determining the effects of GPR35 on mitochondrial health, we found that the inhibition of this GPCR within a high glucose environment protects the mitochondria from oxidative stress, thereby reducing the risk of endothelial dysfunction. Furthermore, fluorescent imaging suggests that GPR35 is transported into the mitochondria under high glucose conditions but remains in the cytosol in normal glucose, proposing that the protein does not externally influence the production of mitochondrial superoxide but becomes damaging to the cell after being brought into the mitochondria.

These findings are critical in understanding the function of GPR35 and how its role is essential in the regulation of endothelial cell health under mitochondrial oxidative stress.

Ashley Pall

Understanding the Mechanism of Iron-Chelating Drugs through an Integrated Biophysical, Biochemical and Molecular Cell Approach: Targeting Friedreich's Ataxia

Authors: Ashley Pall BS, Danielle Bailey PhD, Daniel Kossman PhD, Timothy L. Stemmler PhD

Faculty mentor: Timothy Stemmler

Abstract

Cytotoxic accumulation of iron within the brain is a hallmark feature of several neurodegenerative disorders including Alzheimer's Disease, Parkinson's Disease, and Friedreich's Ataxia [1]. Iron chelation therapy has proven to be efficacious at treating systemic iron overload disorders and is an attractive approach for treating brain-iron accumulation [2]. Developing a chelator that can affectively cross the blood brain barrier and selectively target cellular iron without depleting the systemic circulation and disrupting cell function makes this approach challenging. The brain penetrating iron chelator, PBT434, has shown promising results in vitro as well as successful completion of phase 1 clinical studies. [1,3]. Nevertheless, the molecular reactivity of PBT434 is not well defined.

Our objective is to characterize the biochemical properties of PBT434 in order to rationalize the drug's therapeutic efficacy in early clinical trials and to support the continued development of the compound as a therapeutic agent. Using in vitro biochemical methods we assessed the iron binding properties of PBT434 including affinity, stoichiometry, and metal-ligand environment. Our results indicate that PBT434 weakly binds to ferrous iron (Kd = ~ 4.8 uM) in a 1:1 stoichiometric ratio using nitrogen/oxygen ligands. From these findings we conclude that PBT434 acts as a weak ferrous iron chelator, consistent with in vitro findings that suggest that PBT434 chelates free iron without disrupting normal cellular function.

Zheyun Peng

A siRNA-based targeted therapy for treating nonalcoholic fatty liver disease: A precision medicine approach

Author: Zheyun Peng

Faculty mentor: Wanqing Liu

Abstract

Non-alcoholic fatty liver disease (NAFLD) now has become one of the major health problems, which is estimated to affect 25% of the global population. Over time without treatment or intervention, NAFLD may be advanced to a stage called nonalcoholic steatoshepatitis (NASH), which is characterized by liver inflammation and the development of fibrosis. Eventually, it may further progress to cirrhosis and even hepatocellular carcinoma (HCC). Other than the risk of developing cancer, NASH can significantly promote cardiovascular disease which is the most significant risk factor accounting for NASH-related mortality. However, there is thus far no FDA approved drug that targets the causal factors of NAFLD or NASH, and patients in the late stage of NASH usually are left with no options but liver transplant. Novel treatment strategies against NAFLD are urgently needed.

The new drug development for NAFLD treatment could be complicated by the disease heterogeneity which is attributed to differentiated causal factors, especially genetic modifiers. A large body of previous studies have identified and confirmed the definite role of the PNPLA3 gene in the development of NAFLD and NASH. Hence it could be a potential target for NAFLD treatment. While the wild-type PNPLA3 is thought to possess triglyceride hydrolase activity, a single nucleotide polymorphism (SNP) rs738409 which causes an isoleucine (I) to methionine (M) change at the 148 amino acid position of PNPLA3 that leads to the loss-of-function of PNPLA3, is the direct cause of NAFLD. Previous studies in our lab have identified a small interference RNA (siRNA) complementary to the PNPLA3 148M mutant isoform, which showed a great potential in both gene knockdown efficiency and specificity for the mutant isoform, thus can be further developed into novel therapeutics for PNPLA3 I148M-specific NAFLD. My research aims to further modify this lead siRNA, with an ultimate goal to generate more stable, specific, potent and safer molecules capable of subsequent preclinical and clinical evaluations.

To this end, we further designed a series of siRNAs derived from the original siRNA with various chemical modifications. Stability assay and high throughput screening via HEK293 cells transfected with PNPLA3 I148I or PNPLA3 I148M showed prolonged half-life in serum and increased potency with 2-OMe and ASO modification. We then considered testing their efficacy in vivo. We have established two transgenic mice strain based on C57BL/6 that carried human PNPLA3 I148M or PNPLA3 I148I gene (hereafter referred to as Tg-mt and Tg-wt). Mice are fed with high sucrose diet for 9 weeks to induce hepatic steatosis, then assigned randomly to receive the above candidate therapeutic siRNA or its modified analogs. We conjugated our candidate siRNA with N-Acetylgalactosamine (GalNAc) as this is an FDA-approved hepatocyte-specific delivery strategy. Preliminary data demonstrated that while there is no weight loss after 6 weeks treatment, mice showed dramatically decreased hepatic fat accumulation examined by Oil Red O staining in the Tg-mt group. Evaluations on other outcomes including circulation AST, ALT and TG level, hepatic TG level, hepatic PNPLA3 expression level are ongoing. RNA-seq analysis will also be performed to examine the lipid metabolism-related gene change and the potential off-target effects. We will also evaluate the toxicity profile of these candidates. We anticipate that via such a comprehensive evaluation, novel therapeutics capable of a genotype-based targeting for PNPLA3 can be developed.

Amirreza Samarbakhsh

Design and Development of Potent SARS-CoV-2 PLpro Inhibitors for COVID-19 Antiviral Therapy

Authors: Amirreza Samarbakhsh, Hariprasad Aruri, Dineshsinha Chauhan, Abdullah Al-Homoudi, Alexander S. Jakubiec, Ladislau Kovari and Navnath S. Gavande1

Faculty mentor: Navnath Gavande

Abstract

The transmission of betacoronaviruses from animal hosts to humans has caused severe consequences formed as an outbreak and changed our lives as we know it especially during the last couple years. Severe acute respiratory syndrome (SARS-CoV-2) originates from a group of betacoronaviruses known as subgroup 2b. Therefore, in this study, we developed noncovalent drug-like scaffolds for future therapeutic development against subgroup 2b members. There are only two viral proteases in SARS-CoV-2, 3CLpro and papain-like protease (PLpro). So far, there is only a clinically available 3CLpro inhibitor (PAXLOVID® = nirmatrelvir/ritonavir combination) although there are no FDA approved PLpro inhibitors. The primary clinical challenges with nirmatrelvir/ritonavir are (i) drug interactions with medications metabolized by CYP3A4 which is mostly due to the requirement for boosting by ritonavir, (ii) viral illness rebound. Moreover, history demonstrates that proteases are quite susceptible to point-mutations that enable resistance so only having 3CLpro inhibitors available is a public health liability. In order to achieve this purpose, and after biochemical and structural evaluation of 2b members, it was revealed that their papain-like protease (PLpro) have narrow substrate specificity for K48 polyubiquitin and ISG15 originating from certain species, which its inhibition could stop the 2b members biological pathway. In order to design the candidate molecules to act as PLpro inhibitors, computational docking was used to get a better understanding of interaction between inhibitor binding pocket of PLpro with the hit molecules (GRL-0617 and GRL-0667), and our designed molecules. After the development and synthesis of the potential inhibitors, subgroup 2b PLpros were screened against this novel set of inhibitors along using FRET based assays with a ubiquitin-based substrate to help us identify the most active moieties for our further optimization.

Angel Schilke

Development of non-nucleotide analogs of NAIR as inhibitors of AIR carboxylase

Authors: Angel Schilke; Steven Firestine, PhD

Faculty mentor: Steven Firestine

Abstract

Cancer is the second leading cause of death in the United States with approximately 9.5 million deaths recorded in 2018. Although a wide variety of chemotherapeutic and immunotherapeutic treatments exist for various cancers, additional therapies focused on novel targets are needed to address resistant and refractory cancers. Our laboratory is interested in de novo purine biosynthesis since this pathway has been shown to be critical for rapidly replicating cancer cells. A key protein in this pathway is the bifunctional enzyme phosphoribosylaminoimidazole carboxylase succinocarboxamide synthetase (PAICS) which has been shown to be overexpressed in pancreatic, lung, prostate, bladder, and breast cancers. PAICS knockdown studies have shown decreased cell proliferation and cancer cell invasion, making PAICS an attractive anticancer target. One enzyme included in PAICS, phosphoribosylaminoimidazole carboxylase also called 5-aminoimidazole ribonucleotide (AIR) carboxylase, is strongly inhibited by the product analog 4-nitro-5-aminoimidazole ribonucleotide (NAIR). NAIR is a tight binding (Ki = 0.34 nM) inhibitor of the vertebrate enzyme but does not show anticancer activity. We have hypothesized that the presence of the phosphate group precludes transport into the cell and the nucleoside is 1,000-fold less potent than the nucleotide. To address this problem, we are investigating acyclovir-like NAIR phosphate bioisostere analogs such as phosphonate and squaric acid. Inhibition of human AIR carboxylase showed that NAIR had an IC50 of 75.7 nM. Both acyclovir-like phosphate and phoshonate analogs showed no inhibition against AIR carboxylase with a 3,300-fold decrease in binding. Additional analogs using the NAIR nucleoside will help to examine the effects of these phosphate bioisostere changes.

Marcella Sharma

Validation Studies of Novel Molecules Targeting Bacterial Aminodeoxychorismate Synthase

Authors: Marcella F. Sharma; Steven M. Firestine, PhD

Faculty mentor: Steven M. Firestine

Abstract

According to the CDC, antimicrobial resistance is responsible for more than 2.8 million infections each year in the United States, with at least 35,000 deaths attributed to resistant infections. To address this public health issue, the development of new antimicrobial agents targeting validated antibacterial pathways are needed. Recently, our lab became interested in folate biosynthesis. This pathway is a validated target where existing drugs such as sulfamethoxazole and trimethoprim target dihydropteroate synthase and dihydrofolate reductase, respectively. Part of the pathway that has received limited attention is the synthesis of the crucial folate precursor, para-aminobenzoic acid (PABA). PABA is produced from chorismate by the action of the glutamine-dependent aminodeoxychorismate synthase (ADCS) and aminodeoxychorismate lyase (ADCL). Previous work has shown that inhibition of ADCS is antibacterial, yet known inhibitors are riddled with issues such as the rapid development of resistance and mammalian cell cytotoxicity. It is notable that there have not been any high-throughput screening campaigns published that have targeted ADCS. To overcome this barrier, we are presenting the results of a high-throughput screening campaign conducted using a thermal binding assay. Twelve hits were identified after the primary screen and were subject to dose dependent studies in the thermal binding assay. A single site binding equation was used to calculate Kd values. Seven molecules were shown to be the most promising with Kd values under 20 μM. Future plans will be to validate hits in an enzyme activity assay that monitors change in absorbance.

Aishwarya Vasudevan

Ethanol Increases Crash Avoidance Reaction Time via Changes in Attention to the Task: Driving Simulator Studies

Authors: Aishwarya Vasudevan, Pharm D, MS(2nd year); Sami Ftouni, BS, Pharm D; Nicholas Ciaramitaro, BS, Pharm D(class of 2024); Chisom Ezeanya, BS(class of 2024); Ronith Murali, BS, Pharm D(class of 2025); Doreen Head, PhD; Randall Commissaris, PhD

Faculty mentor: Dr. Randall Commissaris

Abstract

Introduction:
(i) Alcohol-impaired driving continues to be a significant cause of car crash injuries and deaths. The blood alcohol concentration (BAC) cut-off level for drunk driving is 0.08% in Michigan, but it has been estimated that lowering the BAC cut-off to 0.05% would save 500–800 lives every year in the US alone.
(ii) Safe driving requires that a driver remain attentive and focused on the driving task. Alcohol impairs a person's ability to focus and 'pay attention' to a task, so it is possible that driving impairment from alcohol results from a loss of attention to the driving task.

Objectives:
i) Demonstrate the effects of alcohol (BAC 0.05-0.08%) on driving performance, specifically Crash Avoidance Reaction Time (CART).
ii) Test the hypothesis that these effects result from alcohol-induced changes in attention to the driving task.

Methods:
We used a portable virtual reality (VR)-based driving simulator and a crash avoidance reaction scenario. The primary driving performance measure was the time (in msec) required to initiate a steering avoidance response. On half of the crash avoidance trials, a Warning Bell was used to increase the drivers' attention to the driving task.

Results:
Treatment with 3, 4 and 5 drinks resulted in mean BACs (30-180 min) of 0.040, 0.058 and 0.073%, respectively; 4 and 5 drinks significantly increased CART compared to placebo controls. Presentation of the Warning Bell did not affect reaction time in placebo controls. In contrast, presentation of the Warning Bell significantly reduced the alcohol-induced increase in CART.

Conclusion:
These data (i) are consistent with the hypothesis that the BAC cut-off for drunk driving should be lowered to 0.05%. Moreover, (ii) these effects of alcohol result primarily from changes in attention to the driving task.

WSU IRB Approval (#066716B3E)

Hariprasad Aruri

Development of selective and potent drug-like USP10 inhibitors for the treatment of lung cancer

Authors: Hariprasad Aruri (PhD), Amirreza Samarbakhsh (MS), Mu Zhang (PhD), Komal (MS), Lisa Polin (PhD), Kay-Uwe Wagner (PhD), Gerold Bepler (MD PhD), Xiaohong Mary Zhang (PhD), and Navnath S. Gavande (PhD)

Faculty mentor: Dr. Navnatah Gavande

Abstract

Every day, many humans are fighting a constant battle with different types of cancers. Ubiquitin-specific peptidase 10 (USP10) plays an oncogenic role in breast cancer, glioblastoma, and prostate cancer, and serves as a tumor suppressor role in renal cell, gastric, and pancreatic cancers. Therefore, studying it and developing novel compounds to inhibit its pathway, is very important. Previous studies have shown that inhibition of USP10 dramatically reduces the growth of lung cancer xenografts lacking wild type p53 and sensitizes them to cisplatin. However, the exact role of USP10 in cancer remains unclear, due to the diversity of its associated proteins and substrates. These reasons encouraged us to study and develop novel drug-like USP10 inhibitors. So far, Wu-5 and a non-specific inhibitor, P22077, have been two of the best inhibitors developed. Therefore, we developed our inhibitors based on the molecular modeling that was performed using Schrodinger Suites to identify potential ligand binding pockets between USP10 and Wu-5. Moreover, 3D structures of USP10 protein using homology modeling were developed as there is no X-ray crystal structure of USP10 available to date. Based on the molecular modeling results, we synthesized more than 40 novel drug-like inhibitors and assessed USP10 activity in deubiquitinating enzyme (DUB) assay. Initial results showed that two of our inhibitors exhibited around 2 and 3-fold better USP10 activity than Wu-5 and P2207. Interestingly, our inhibitors also showed selective inhibition for USP10 over USP7, USP13 and USP47. At last, cellular viability of the selected inhibitors were assessed in H157 cells by MTT assay.

Dineshsinha Chauhan

Discovery and Development of Highly Potent and Selective Ku-targeted DNA-PK Inhibitors for Cancer Therapy

Authors: Dineshsinha Chauhan, PhD; Pamela VanderVere-Carozza, PhD; Tyler L. Vernon, PhD; Katherine Pawelczak, PhD; John J. Turchi, PhD; Navnath S. Gavande, PhD

Faculty mentor: Dr. Navnath Gavande

Abstract

DNA double strand breaks (DSBs) are the most cytotoxic of DNA lesions. DSB repair pathway deficiency, often observed in cancer cells, results in translocations and genetic mutations that contribute to genomic instability. The generation of DNA DSBs is the primary mechanism of numerous chem- and radio-therapeutic strategies used to treat various cancers. Modulating DSB repair pathways can have a profound impact on the clinical efficacy of DNA damaging therapies. NHEJ pathway is responsible for the repair of majority of ionizing radiation (IR) induced DNA DSB. The DNA dependent protein kinase (DNA-PK) is a validated target for cancer therapeutics and to date, development of inhibitors for DNA-PK has focused on targeting the active site with ATP mimetics. We have taken the unique and innovative approach to inhibiting DNA-PK via blocking the Ku70/80 heterodimer interaction with DNA, an essential step in DNA-PK activation and phosphorylation activity. Exploiting this unique mechanism of kinase activation, we have identified a series of highly potent and specific DNA-PK inhibitors that impart their inhibitory activity via disruption of Ku protein binding to DNA ends. Novel derivatives of our initial hit inhibit DNA-PK catalytic activity at nanomolar concentrations and potentiates cellular sensitivity to DSB-inducing agents like etoposide and bleomycin. Our data demonstrate that the cellular effects observed are a function of Ku inhibition and that this novel class of DNA-PK inhibitors can be further developed as anti-cancer therapeutics that can be used as an adjuvant to, or concomitant with radiotherapy and other cancer therapies that induce DNA damage.

Ashlan Kunz Coyne

Phage Cocktail Rescues Daptomycin and Phage Susceptibility Against Multidrug-resistant E. faecium in a Simulated Endocardial Vegetation Ex Vivo Model

Authors: Ashlan J. Kunz Coyne, PharmD; Amer El Ghali, PharmD; Kyle Stamper, BS; Razieh Kebriaei, PhD; Biswajit Biswas, MS, PhD; Melanie Wilson, Michael V. Deschenes, Gregory S. Canfield, MD, PhD; Breck A. Duerkop, PhD, Cesar A. Arias, MD, MSc, PhD; Michael J. Rybak, PharmD, MPH, PhD

Faculty mentor: Michael J. Rybak

Abstract

Introduction: Vancomycin-resistant E. faecium (VRE) is an intractable nosocomial pathogen with concerning antibiotic resistance. Daptomycin (DAP) is standard of care but failed to achieve adequate exposure against wild-type VRE strains, even at 12 mg/kg/day. Ceftaroline (CPT) increases DAP binding; however, in a simulated endocardial vegetation (SEV) pharmacokinetic/pharmacodynamic (PK/PD) model, DAP+CPT didn't achieve therapeutic efficacy against DAP non-susceptible (DNS) VRE isolates. Phage-antibiotic combinations (PAC) have been proposed for resistant high inoculum infections.

Objective: To identify PAC with maximum bactericidal activity and prevention/reversal of phage/antibiotic resistance in an SEV PK/PD model against VRE clinical blood isolate, DNS R497 (DAP MIC=16 mcg/mL).

Methods: Human-simulated doses of DAP (10 mg/kg every 24 hours) and CPT (600 mg every 8 hours), and phages NV-497 and NV-503-01 (each at a multiplicity of infection (MOI) of 10) were evaluated in a 96-hour SEV PK/PD model against R497. Synergistic and bactericidal activity were defined as a ≥2-log10-colony forming unit (CFU)/g kill compared to the most effective agent or combination therapy and a ≥3-log10-CFU/g reduction from baseline, respectively. Phage/Antibiotic resistance/resensitization were evaluated at each sampling time point with phage infection efficiency evaluated with efficiency of plating (EOP). Significant differences between regimens (reductions in log10CFU/g) were assessed by ANOVA with Tukey's post hoc test ($P<0.05$).

Results: Against R497, DAP+CPT combined with the phage cocktail NV-497+NV-503-01 demonstrated synergistic and bactericidal activity (2.09-6.98 log10 CFU/mL; $P<0.001$) and DAP resensitization (post-SEV DAP MIC = 4 mcg/mL). PAC containing DAP+CPT prevented phage resistance and maintained phage infectivity compared to untreated controls (0.92±0.03 vs. 0.21±0.11, respectively; $P<0.001$)

Conclusion: Our results provide novel data highlighting bactericidal and synergistic activity of PAC against DNS VRE isolate R497 in a high inoculum SEV PK/PD model with subsequent DAP resensitization and prevention of phage resistance. These data warrant further investigation of this PAC for endocarditis treatment in animal models.

Ashlan Kunz Coyne

Eravacycline in Immunocompromised Patients: Early Initiation Decreases Treatment Failure

Authors: Ashlan J. Kunz Coyne, PharmDl; Sara Alosaimy, PharmD;, Kristen Lucas, MPH;, Kyle Molina, PharmD; Lena Kang-Birken, PharmD; Abdalhamid M Lagnf, MD;, Kimberly Claeys, PharmD; Michael P Veve, PharmD, MPH; Madeline A King, PharmD; Benjamin M Pullinger, PharmD; Jeannette Bouchard, PharmD; Tristan Gore, PharmD; Leonor M Rojas, PharmD; Serina Tart, PharmD; Athena LV Hobbs, PharmD; Nicholson B Perkins III, PharmD; Mark Biagi, PharmD; Michael Pierce, PharmD; Reese Cosimi, PharmD; Bruce Jones, MD; James Truong, PharmD; Justin Andrade, PharmD; Glen Huang, MD; Taylor Morrisette, PharmD; Dana Holger, PharmD; Nicholas Rebold, PharmD; Amer El Ghali, PharmD; Susan L Davis, PharmD; Michael J Rybak, PharmD, MPH, PhD

Faculty mentor: Michael J. Rybak

Abstract

Background: Multidrug-resistant (MDR) infections in immunocompromised patients are independently associated with increased mortality rates. Early initiation of appropriate therapy improves patient survival. Eravacycline (ERV) has potent in-vitro activity against MDR bacteria, demonstrating non-inferiority to meropenem in the phage III IGNITE4 trial; however, the trial excluded immunocompromised patients.

Objective: To evaluate clinical endpoints of immunocompromised patients receiving early vs. late ERV as definitive antibiotic therapy.

Methods: Multicenter, retrospective observational study of patients at 17 U.S. medical centers from October 2018-September 2022. Patients meeting the following criteria were eligible for inclusion: Immunocompromised, ≥18 years old, receipt of ERV for ≥72h. Patients were excluded if they were pregnant, prisoners, or died within 72h of culture collection. The primary outcome was a composite of treatment failure including 30-day mortality, failure to improve on ERV, and 30-day microbial recurrence. Early and late ERV were defined as receipt of ERV within or after 72 hours of culture collection, respectively. To ensure groups were as similar as possible at the time of positive index culture collection and to allow unbiased comparisons between groups, analyses were adjusted for possible confounding with inverse probability of treatment weighting (IPTW) using baseline covariates with a P≤0.1.

Results: 82 patients were included (early ERV n=40, late ERV=42). Extended-spectrum β-lactamase producing E. coli and K. pneumoniae were the most common organisms isolated and treated with ERV (17% and 16%, respectively). In unadjusted and IPTW-adjusted analysis, early ERV therapy was associated with significantly lower odds of treatment failure (adjusted odds ratio (aOR) 0.675 (95% confidence interval (CI) 0.465, 0.979), which was consistent with Kaplan-Meier analysis (log rank p=0.034).

Conclusion: In hospitalized immunocompromised adult patients, early ERV was associated with significantly lower odds of treatment failure compared to late initiation. Further studies are warranted to assess time to ERV therapy in immunocompromised patients based on source- and organism-specific infections.

Amer El Ghali

Real-world Multicenter Assessment of Omadacycline Use in patients with Nontuberculous Mycobacterial Infections

Authors: Amer El Ghali, PharmD; Sara Alosaimy, PharmD, MPH; Taylor Morrisette, PharmD, MPH; Raaga Vemula, M.D; Julie Philley, M.D; Carlos Mejia-Chew, PharmD; Yasir Hamad, PharmD; Jeremy Frens, PharmD; Aaron Ong, PharmD; Ryan Stevens, PharmD; Catessa Howard, PharmD; Emily Kaip, PharmD; Brandon Bookstaver, PharmD, MPH; Jeannette Bouchard,PharmD; Saira Butt, PharmD; Christina Fiske, M.D, MPH; Anahit Simonyan, PharmD; Christo Cimino, PharmD; Tristan Gore, PharmD; Michael Veve, PharmD, MPH; Melissa Barger, PharmD; Gabriela Cabanilla, PharmD; Nicholas Rebold, PharmD; Dana Holger, PharmD; Ashlan Kunz Coyne, PharmD; Abdalhamid Lagnf, MPH; Kristen Lucas, MPH; Paige Witucki, BS; Michael Rybak, PharmD, MPH, PhD

Faculty mentor: Michael J. Rybak

Abstract

Background: Nontuberculous mycobacteria (NTM) is a ubiquitous pathogen with high levels of drug resistance. Omadacycline (OMC) is a novel aminomethylcycline antibiotic that has shown potent in vitro activity to NTM, receiving an FDA orphan drug designation for NTM including Mycobacterium abscessus complex (MABc) in August 2021.

Objective: Describe the clinical effectiveness, tolerability and safety of OMC for the treatment of NTM infections.

Methods: This was a multicenter, retrospective, observational study conducted from January 2020 to March 30, 2022. We included all patient ≥ 18 years of age that received OMC for any Mycobacterium spp indication ≥72 hours. The primary outcome was clinical failure , defined as all-cause mortality, persistence or re-emergence of infection during or after therapy, and escalation or alteration of OMC. Incidence of adverse effects while on OMC and reasons for OMC utilization were also analyzed.

Results: A total of 54 patients from 13 geographically distinct academic health systems were included in analysis. The median age was 57 (IQR, 44-66) years, 65% were female and 85% were Caucasian. Most patients had either respiratory (44%) or skin and skin structure infections (26%). The median duration of treatment was 4.1 (IQR, 3.0-8.7) months and 15% reported an MIC for OMC. Clinical success was observed in 88% of patients, with most receiving combination therapy with either clofazimine (44%), azithromycin (42%), imipenem (30%), or amikacin (30%). Adverse drug reactions were reported in 42% of patients with a majority being gastrointestinal related (28%). Reasons for prescribing OMC were primarily attributed to ease of administration (64%) and resistance to other agents (45%) with all patients having received OMC by mouth.

Conclusion: OMC demonstrated a high degree of clinical effectiveness and safety making it a potentially viable therapeutic option in the treatment of NTM infections. Larger, prospective, comparative studies are needed to confirm our findings.

Amer El Ghali

Phage-antibiotic Combinations Eradicate XDR Pseudomonas aeruginosa in biofilm and simulated endocardial vegetation models

Authors: Amer EL Ghali, PharmD; Dana Holger, PharmD, MPH; Kyle Stamper, BS; Susan M. Lehman, PhD; Jose Alexander, MD; Michael J. Rybak, PharmD, MPH, PhD

Faculty mentor: Michael J. Rybak

Abstract

Background: Phage-antibiotic combinations (PAC) have been previously shown to eradicate extensively drug-resistant (XDR) Pseudomonas aeruginosa (PSAR) in combination with antibiotics while also limiting the development of resistance and restoring antibiotic sensitivity to the target organism.

Objective: Evaluate the activity of phage cocktails in combination with ciprofloxacin (CIP) in 96-hour biofilm and simulated endocardial vegetation (SEV) models against a DTR PSAR isolate.

Methods: Two separate PACs containing 4 PSAR phages (EM-T3762627-2 (EM), LL-5504721-AH (LL), E2005-C (EC) and 109) at a multiplicity of infection (MOI) of 1 were tested against a well characterized clinical strain of XDR PSAR (R10266). The combination of LL-EC-109, EM-EC-109 and their components were tested with and without CIP in an SEV (starting inoculum of 8.5 log10 CFU/mL) and biofilm model (6.5 log10 CFU/mL), respectively. The reduction of CFU/ml across combinations was compared using ANOVA with Bonferonni posthoc analysis.

Results: CIP-LL-EC-109 finished at 2.85 log10 CFU/mL and CIP-EM-EC-109 went to detection limits (≤ 2 log10 CFU/mL) at 96 hours. CIP-LL-EC-109 and CIP-EM-EC-109 were significantly different compared to all other combinations ($P < 0.05$). CIP-LL-EC-109 resulted in a 7.4 and 3.9 log10 CFU/mL reduction at 96h ($P<0.05$) compared to growth control and the next best therapy (CIP-EC-109), respectively. While CIP-EM-EC-109 resulted in a 4.5 and 1.6 log10 CFU/mL reduction at 96h ($P<0.05$) compared to growth control and the next best therapy (EM-EC-109), respectively.

Conclusions: Both CIP-LL-EC-109 and CIP-EM-EC-109 demonstrated a significant reduction in bacterial burden in SEV and biofilm models, which represent two difficult-to-treat clinical situations. Further pharmacokinetic and pharmacodynamic studies are needed to properly assess the clinical utility of PAC's against MDR PSAR.

Prahlad Parajuli

Overcoming Drug Resistance in Pancreatic Ductal Adenocarcinoma using Novel Gemcitabine Analogs

Authors: Prahlad Prajuli, Ph.D.; Somrita Dey, Ph.D.; Samaresh Sau, Ph.D; Hariprasad Aruri, Ph.D.; Athira Rajan Pillai, M.S.; Arun K. Iyer, Ph.D.; Navnath S. Gavande, Ph.D.

Faculty mentor: Navnath Gavande

Abstract

Pancreatic cancer (PC) is the fourth leading cause of cancer-related death in the USA. To date, systemic chemotherapy combined with radiation therapy (chemoradiotherapy, CRT), represents the standard treatment for PC. However, many patients with pancreatic ductal adenocarcinoma (PDAC) are unable to benefit from the advances in chemotherapy, namely nab-paclitaxel (NP) and gemcitabine (GEM), due to the rapid development of drug resistance. Reduced sensitivity of PDAC to chemotherapy or acquired resistance to gemcitabine is attributed to multiple factors including nucleoside transporters, efflux proteins, inactivation of apoptosis pathways, and enzymatic deactivation of GEM by cytidine deaminase (CDA). In this study, we sought to develop novel gemcitabine analogs (GEM-As) with an aim to overcome the resistance mechanisms and enhance cytotoxic effect in pancreatic cancer cells. Based on preliminary in silico and in vitro data, we selected four chemically modified analogs of gemcitabine, termed as GL-302, GL-282, GL-349, and GL-351, and evaluated their cytotoxic activity against pancreatic cancer cell line AsPC-1 in vitro as well as in SCID mouse xenograft models. Our novel GEM-As, especially GL-302 and GL-282, showed higher tumor cytotoxic ability than gemcitabine in in-vitro, while GL-282 was able to significantly reduce the tumor growth, compared to gemcitabine, in mouse xenograft model of AsPC-1 cells. Higher tumor cytotoxic activity of selected GEM-As, especially GL-282, was associated with insensitivity to metabolic deactivation by CDA and higher accumulation in the tumor (lower efflux), compared to GEM, the parent molecule. Our results demonstrate that the GEM-As circumvent drug resistance mechanisms and have potential therapeutic utility in PDAC patients.

Maryam Abbawi

Backward Walking Training Induces Structural Changes in the Superior Cerebellar Peduncle: A Pilot Study

Authors: Maryam Abbawi; Jeffrey Stanley, PhD; Biaohua Yu, BS, BMS; Emily Myers, BS; Nora Fritz, PhD, PT, DPT, NCS

Faculty mentor: Nora Fritz

Abstract

Introduction: Multiple sclerosis (MS) is a complex neurodegenerative disease that is identifiable by the loss of myelin in the central nervous system (CNS), leading to motor decline. Our lab has shown that backward walking (BW) speed in addition to MRI measures may improve fall prediction for persons with MS (pwMS). Myelin Water Imaging (MWI), a novel technique for imaging myelin in vivo, has not been examined in relation to BW.

Objective: This study examines the impact of an 8-week BW training program on the superior cerebellar peduncle (SCP) utilizing MWI as well as relation of the change in the SCP to the change in function.

Method: Eight individuals with relapsing-remitting MS participated in this pilot study. Participants completed functional tests and a 3T MRI before and after the 8-week intervention, consisting of treadmill and overground BW 1x/week and home exercises 2x/week. Falls were monitored for 6 months after the intervention. T-tests were used to examine differences in SCP pre/post and Spearman correlations were used to examine relations among changes in SCP and changes in function. Due to the pilot nature of this study, effect sizes and rho values were prioritized.

Results: MWI variables of Myelin Water Fraction (MWF) and geomT2IEW of the SCP were extracted. The average MWF and geomT2IEW values increased after training, with effect sizes of -0.16 and -0.53, respectively. The change in geomT2IEW was strongly correlated with improvements in balance measured with wearable sensors (r=0.61), BW speed (r=0.79), forward walking speed (r=0.52) and prospective falls at 6 months (r=0.46).

Conclusion: Our pilot data suggests that BW training induces both structural (SCP) and functional (balance, gait, falls) changes over 8 weeks and shows potential for future larger-scale studies exploring efficacy.

Zade Abou-Rass

Impact of COVID-19 lockdown on Fatigue in Persons with Multiple Sclerosis.

Authors: Abou-Rass, Zade, Undergraduate; Feldpausch, Jennie, DPT student,; Plummer, Prue, PhD, PT, BPhysio(Hons); Fritz, Nora E, Ph.D., P.T., D.P.T., N.C.S.

Faculty mentor: Nora Fritz

Abstract

Introduction: Fatigue is a prevalent symptom of Multiple Sclerosis (MS) that adversely impacts quality of life. Although COVID-19 forced a massive lifestyle change for all persons, it may have had specific ramifications for individuals with MS-related fatigue, who are at risk for worsening symptoms and predisposed to inactivity and social isolation as a result of fatigue.

Objective(s): To examine the impact of the COVID-19 national quarantine and restrictions on mental, cognitive, and physical fatigue in persons with MS in the United States.

Methods: We conducted a nationwide survey using REDCap. The survey was open to all adults (>18 years) with MS. Participants were asked to provide demographic and disease-related information including age, sex, race, disease subtype, disease duration, and current level of function along with fatigue and activity levels prior to March 2020, March 2020-May 2021, and June 2021-January 2022. Fatigue subtypes of physical, mental, and cognitive fatigue were examined.

Results: Six hundred individuals with MS participated including 478 persons with relapsing-remitting MS and 122 persons with progressive MS (average(SD) age: 50.9(12.5) years; sex: 98M, 497F, 5 Non-Binary). Regardless of subtype, individuals reported greater fatigue (0-10 scale) during quarantine than before, and though the level of physical, mental, and cognitive fatigue declined following the lifting of quarantine restrictions, levels did not return to pre-quarantine levels, representing an overall decline of 0.6 points in physical fatigue, 1.0 points in mental fatigue, and 0.8 points in cognitive fatigue.

Conclusion: The COVID-19 quarantine resulted in an overall worsening of fatigue for persons with MS. It is critical that healthcare providers monitor physical, mental, and cognitive fatigue levels in persons with MS and facilitate appropriate referrals to physical, occupational, and psychological therapies to improve fatigue levels.

Norelhuda Almahadi

Interprofessional Education Between Clinical Laboratory Science and Physician Assistant Students: A Case Study Based Approach

Authors: Norelhuda Almahadi, Clinical Laboratory Sciences Student

Faculty mentor: Professor MaryAnne Stewart, EdD, MBA, MLS (CSMLS)

Abstract

Interprofessional education is a collaborative learning strategy for professionals and students that enables the expansion of their skills and identities in healthcare. The primary aim of interprofessional education is to meet the complex demands of patients while decreasing medical errors, essentially delivering better patient outcomes. As students continue to learn and grow in their respective programs, understanding the importance and work of other healthcare professionals eliminates communication gaps in healthcare. In collaboration with laboratory professionals, medical providers carry out an individualized plan of care to enhance a patient's health condition. Interprofessional education creates opportunities for growth and improvement in healthcare, maximizing the skills of all healthcare professionals while blending their complementary roles.

Purpose: The CLS/PA Interprofessional education session provided Wayne State University's Clinical Laboratory Science and Physician's Assistants students with the opportunity to collaborate on two patient case studies. The Clinical Laboratory Science students demonstrated and explained several diagnostic testing techniques while PA students observed and later participated in performing these tests. In turn, the PA students approached the cases from their direct patient care perspectives and explained their treatment plans. This collaborative experience provided the CLS and PA students with insight into these professions and an understanding of leveraging their expertise to maximize patient care. The overall positive feedback from this event was insightful and reflected the importance of interprofessional education in healthcare.

Trever Henderson

Smoking Methods & Relation to Cancer

Authors: Trever Henderson, BS, RTT (STUDENT); Nadine Elayan, BS, RTT (STUDENT); Maha Elgarmi, BS, RTT (STUDENT); Taylur Friend, BS, RTT (STUDENT); Jessica Giese, BS, RTT (STUDENT); Isabel Lee, BS, RTT (STUDENT); Melanie Mileski, BS, RTT (STUDENT); Khouloud Moussa, BS, RTT (STUDENT); Jenna Muflahi, BS, RTT (STUDENT); Madison Murray, BS, RTT (STUDENT); Monisha Sanders, BS, RTT (STUDENT); Julia Seng, BS, RTT (STUDENT)

Faculty mentor: Jeannetta Greer, Alisa Kagen, Kurt Frederick

Abstract

Introduction: Collectively as a class, this research will spotlight the various popular smoking modalities along with the effects of various chemical contributors to cancer.

Objectives: Punctiliously deliver research material covering the following key points. Address differing smoking modalities and identify key differences amongst them. Pin-pointing whether all modalities can be linked to cancer or if there are only certain modalities. If one style of smoking is recommended over the other to prevent cancer from forming and if there is any safe tobacco product. Address the 5-year survival rate of patients who have varying tobacco intake. Determine options available to those who desire to ascertain/consume nicotine instead of smoking and weigh advantages versus disadvantages. Discuss cancers associated with smoking and which types are more common with the respective style. Showcase facts on current smoking trends. Controversially, indicate the documented benefits of medical marijuana and its relationship with cancer.

Methods: Research was obtained by referencing professional scholarly research articles which have been published and reputable federal agency websites. The class divided the topic into subsections, researched with their partners, and collaborated their findings into one presentation.

Results: Identified popular/common smoking modalities and alternative options to acquire nicotine. Determined specific toxic chemicals in tobacco products that pose harm to health (i.e. hydrogen cyanide, formaldehyde, lead, arsenic, etc.). Cemented that there is no smoking method that is preferred to prevent cancer. Spotlight statistics support a lower life expectancy for smokers versus non-smokers. Holistic benefits of marijuana on the consumer.

Conclusion: There is no safe smoking modality and all have the potential of being the etiology of cancer. Identified that more research is necessary for electronic cigarettes to determine if they cause cancer. Marijuana yields nausea and pain relief and its effects are dependent on the strain.

Alyssa Kimbrough

Development of a novel peptide-based insulin sensitizer through disruption of Inositol polyphosphate 5-phosphatase K (SKIP) - p21-Activated Kinase 1 (Pak1) interactions

Authors: Alyssa Kimbrough; Jitender Dev Gaddameedi, PhD; Andrew Lipchik, PhD

Faculty mentor: Andrew Lipchik

Abstract

Introduction: Insulin-dependent glucose disposal varies several-fold across individuals. Approximately one in three individuals are sufficiently insulin resistant (IR) to be at risk for IR complications including type 2 diabetes (T2D). There are few therapeutic options for treatment of IR as thiazolidinediones are the only medications to improve insulin sensitivity. There is a need for the development of new therapeutics for the treatment of IR to prevent the onset of T2D. Inositol polyphosphate 5-phosphatase K (INPP5K/SKIP) is a potential target to treat IR. SKIP resides in the endoplasmic reticulum (ER) in resting cells, and translocates to the plasma membrane (PM) following growth factor stimulation. SKIP is recruited to the PM through binding to p21 activated kinase 1 (Pak1) and inhibits growth factor signaling through dephosphorylation of phosphoinositol-(3,4,5)-triphosphate. In obesity and IR, SKIP is overexpressed leading to PM localization and suppression of insulin signaling.

Objective: We aim to develop a novel insulin sensitizer using peptides derived from Pak1 to inhibit SKIP-Pak1 interactions and prevent PM localization.. We hypothesize that preventing SKIP localization to the PM will reconstitute insulin sensitivity through Akt activation.

Methods: Microwave-assisted solid phase peptide synthesis was used to synthesize a library of peptides corresponding to the F helix (residues 443-460) of Pak1. Biophysical properties of the peptides including helicity and binding were characterized using circular dichroism and cellular thermal stability shift assays (CETSA). Insulin sensitization was determined by measuring Akt activation via phosphorylation status in cellular models of IR in C2C12, 3T3-L1, and HepG2 cell lines.

Results: Pak1 derived peptides displayed alpha helical properties and thermostabilized SKIP. Additionally, treatment with the Pak1 peptides was sufficient to restore insulin sensitivity in vitro in skeletal muscle, adipose, and liver models of IR.

Conclusion: The Pak1 peptide-derived represent a novel insulin sensitizing therapeutic requiring further investigation.