



WAYNE STATE
Eugene Applebaum
College of Pharmacy
and Health Sciences

20TH ANNUAL COLLEGE RESEARCH DAY

October 11, 2023
Detroit, MI

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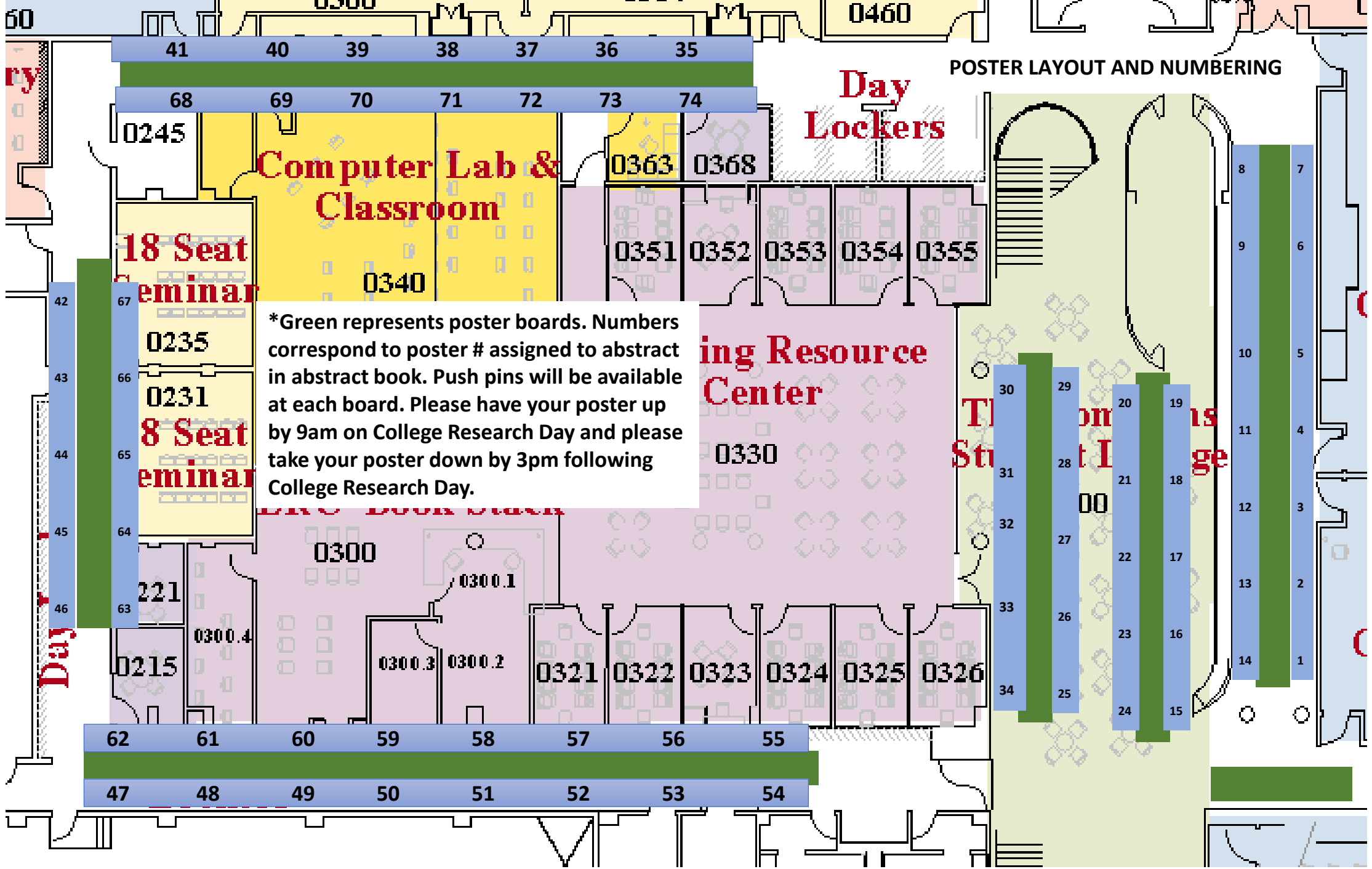
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AGENDA

- **8-9 a.m.** Poster setup
- **9-10:55 a.m.** Poster presentations
- **11 a.m.-noon** Keynote presentation by Dr. Patricia LoRusso of Yale University
- **12-3 p.m.** Continued poster viewing

KEYNOTE SPEAKER



[Patricia LoRusso](#), DO, Yale University professor of medicine (medical oncology); chief, experimental therapeutics; associate cancer center director, experimental therapeutics, brings more than 25 years of expertise in medical oncology, drug development, and early phase clinical trials. Prior to her Yale appointment, she served in numerous leadership roles at Wayne State University's Barbara Karmanos Cancer Institute, most recently as director of the Phase I Clinical Trials Program and of the Eisenberg Center for Experimental Therapeutics.

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

Kyle Burghardt, chair

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Sarah Agnihotri

Professional Development Programming for Student Pharmacist Peer Mentors: Exploring Deep Skillbuilding and Professional Identity Formation Opportunities for Learning Community Peer Mentors

Authors: Sarah Kosel Agnihotri, MA; Victoria Tutag Lehr, BSPHarm, PharmD

Abstract

Introduction: Peer mentoring/tutoring across disciplines including the health professions provides benefits to the peer mentors themselves as well as the students they support. In corporate Learning and Development, deep skill-building through peer-to-peer learning and curated cohort experiences is becoming a preferred method of talent development. These approaches provide tangible benefits to the peer mentors/employees while improving outcomes for the employer. Learning and development of peer mentors, along with its effect on professional identity formation, requires further exploration. The EACPHS Student Pharmacist Learning Community is piloting a professional development program for peer mentors.

Objective: 1) To develop peer mentor skills as future pharmacist educators and 2) expand peer mentor abilities in supporting P1 and P2 pharmacy students through learning community initiatives through a pilot professional development program.

Methods: This pilot longitudinal, cohort-based professional development program for student pharmacist peer mentors uses existing literature and best practices. Strategies incorporate deep skill-building, peer-to-peer learning, and a cohort experience to expand and enhance transferrable skills related to education, communication, and leadership. Peer mentors have designated one-hour pre-work assigned readings followed by one-hour in person training sessions with education specialist and faculty coordinators. Program outcomes are peer mentor reflections at monthly evaluations throughout academic year and survey responses of P1 and P2 learning community mentees (Fall and Winter semesters).

Results: Peer mentors for academic year 2023-2024 on-boarded and completed initial training and reflections. Survey of P1 and P2 students to be conducted at end of Fall semester.

Conclusions: Peer mentoring has potential tangible benefits for student pharmacists. Results of this pilot program will assist in determining if this level of peer mentor development is sustainable and beneficial. Identification of areas for program improvement are expected.

Mariam Aidibi

Validating a Risk Model for In-Hospital Hypoglycemia

Authors: Mariam Aidibi, BHS, Pharm.D. Candidate; David Wilpula, Pharm.D., BCPS; Farheya Robow, Pharm.D.

Abstract

Introduction: Predictive models have shown promise in identifying patients at-risk for in-hospital hypoglycemia. Previous models were often based on extensive regional or national datasets, and their outcomes do not consistently align on the specific risk factors. A hypoglycemia risk model from a retrospective cohort of hospitalized patients with diabetes at Corewell Health Dearborn Hospital (CHDH) was developed in 2020. Independent risk factors for in-hospital hypoglycemia were history of hypoglycemia, insulin dose > 0.3 units/kg/day, GFR < 30 mL/min, sulfonylurea use, and length of stay. The model was validated in a second data set from a retrospective cohort at the same site in 2021.

Objective: The primary objective is to externally validate the CHDH hypoglycemia risk model across various Corewell Health System locations. The secondary objective involves evaluating the model's generalizability for potential integration into the Electronic Medical Record (EMR) system.

Methods: A random sample of adult patients with type 1 or 2 diabetes will be enrolled in retrospective cohorts from 19 Corewell Health hospitals. Patients under 18 years of age will be excluded. In-hospital hypoglycemia (blood glucose < 70 mg/dL) will be predicted using the CHDH model. Model performance will be assessed by ROC curve and c-statistic. A sample size of 500 patients per hospital location is projected to exceed 10 events per variable. Results will be compiled for the overall validation cohort and subgroups by hospital locations exceeding 10 events per variable within the study period. Statistical analysis will be performed using Stata 18 and Microsoft Excel.

Results: Pending.

Conclusion: Pending.

Merin Babu

Clinical and Financial Outcomes of a Pharmacist-Managed Diabetes Clinic Compared to Usual Care

Authors: Merin Babu, PharmD Candidate; Endi Zaka, Pharm D Candidate; Sherlin Chacko, PharmD Candidate; Jasmine John, PharmD Candidate; Melissa Lipari, Pharm.D, BCACP

Faculty Mentor: Dr. Melissa Lipari

Abstract

Introduction: Patients with Type 2 Diabetes Mellitus (T2DM) managed by pharmacists have demonstrated improved glycemic control, increased diabetes-related interventions and cost-savings benefits in pharmacist managed pharmacotherapy clinics. However, pharmacists currently lack provider status, which limits the reimbursement they could receive for their services.

Objective: The purpose of this study is to assess the clinical and financial outcomes in T2DM patients managed by a pharmacist vs. a primary care physician (PCP).

Methods: This was a multi-center, retrospective cohort study. Patients were included if managed by a pharmacist or PCP for >12 months from January 1, 2018 - December 31, 2022. The primary outcome was mean change HbA1C from baseline to 12-months. Secondary outcomes included mean change in blood pressure, frequency of statin use, mean change in body weight, reimbursement, frequency of PCP visits, and other preventive measures.

Results: A total of 40 patients per group were included with 52.5% female and 47.5% male. Mean change in HbA1C for usual care at 12 months was 0.09% [range, -3.9 to 4.2] compared to 0.3% [range, -3.4 to 4.8] for the intervention group. In the intervention group, the average baseline A1C was 8.4% and the average 12-month A1C was 8.1%. In the control group, the average baseline A1C was 7.63% and the average 12-month A1C was 7.54%.

Conclusion: When patients with type 2 diabetes are subjected to usual care versus pharmacist pharmacotherapy management care, patients may experience a greater decrease in their A1C.

Nicholas Ciaramitaro

The effects of alcohol on crash avoidance reaction time in a driving simulator task in humans: The current drunk driving BAC cut-off (0.08%) is too high.

Authors: Nicholas Ciaramitaro, BS, Ronith Murali, BS, Aishwarya Vaseduvan, MS, Chisom Ezeanya, BS, Doreen Head, PhD and Randall L Commissaris, PhD.

Faculty Mentor: Randall L Commissaris, PhD.

Abstract

A major cause of alcohol-related motor vehicle crashes is an increase in the time required for a defensive driving maneuver in an emergency situation ("I didn't react quickly enough"). In the state of Michigan (and most states in the US), the 'cutoff' Blood Alcohol Concentration (BAC) for drunk driving is 0.08%. The present study used a portable driving simulator to test the hypothesis that a BAC of 0.08% reflects an effect-based threshold for alcohol-impaired driving performance. In a crossover design using male and female subjects, BAC, subject assessments of impairment ("Am I too drunk to drive") and actual driving performance (crash avoidance reaction time; CART) were assessed every 30 minutes (for up to six hours) following vehicle or alcohol treatment (4 [females] or 5 [males] "standard drinks"). The different alcohol dosing regimens for female and male subjects resulted in fairly comparable BAC versus time curves in the two groups, with peak concentrations slightly greater than 0.08% at 60-90 minutes, followed by a steady decline over time that was comparable in both groups; all subjects 'drove' the simulator with a range of BAC concentrations from 0.02 - 0.09%. Following vehicle treatment, CART was approximately 300-325 msec; alcohol treatment significantly increased CART to 350-400 msec. There was a significant correlation between BAC and the increase in CART values. The threshold BAC range to increase CART was 0.031-0.04%; in contrast, the threshold BAC range to affect subject-assessed impairment, 0.06-0.07%, was much higher. Both of these values are lower than the current 0.08% BAC cutoff for drunk driving. These results argue (1) subjects typically underestimate their perceived level of alcohol intoxication/impairment and (2) the 0.08% BAC cutoff for drunk driving in Michigan and many other states is too high.

Mirna Eshaya

Review of kidney transplant patients receiving Belatacept-based Maintenance Immunosuppression and the Incidence of CMV infection

Authors: Eshaya, Mirna, BHS; Mrowca, Morgan, BS; Fitzmaurice, Mary Grace, PharmD; Jakupovic, Lejla, PharmD; Janz, Arin, PharmD; Poparad-Steazar, Adina, PharmD

Abstract

Introduction: Cytomegalovirus (CMV) infection is a significant concern in kidney transplant recipients due to its potential to cause serious complications including graft dysfunction and increased morbidity and mortality. Among solid organ transplant recipients, CMV infection occurs primarily as a result of drug-induced immunosuppression post-transplant. Common immunosuppressive medications used post-transplant include calcineurin inhibitors, anti-metabolites, and corticosteroids. Belatacept is a novel alternative immunosuppressive agent utilized instead to minimize calcineurin inhibitor induced adverse effects. However, there is limited data on the incidence and management of CMV infection in kidney transplant recipients receiving belatacept-based maintenance immunosuppression.

Objective: To evaluate the incidence and management of CMV infection in kidney transplant patients receiving belatacept-based maintenance immunosuppression at an academic medical center. Secondary objectives include assessment of CMV infection severity, resistance patterns, and evaluating immunosuppression regimens during and after CMV infection.

Methods: This is a retrospective descriptive cohort reviewing kidney transplant patients on belatacept-based maintenance immunosuppression and the incidence of CMV infection. Inclusion criteria includes kidney transplant recipient patients 18 years of age or older receiving post-transplant care at Henry Ford Health, specifically receiving belatacept as maintenance immunosuppression. Exclusion criteria include non-kidney transplant patients and patients who received a simultaneous liver/kidney transplant. Data was obtained via Henry Ford Health's electronic medical record system between January 1, 2018 and August 1, 2023. Using retrospective chart review, patients will be screened using the hospital's secure electronic medical record (EMR), Epic;. Data will be collected with a standardized case report form involving patient demographics, lab values, transplant information, immunosuppression regimen and adjustments, CMV risk status and medications administered to treat CMV infection. Continuous variables and categorical variables will be expressed as median (IQR) and as proportions respectively.

Results: In progress.

Conclusions: In progress.

Brian Globerman

Trending: Continuous Glucose Monitoring in a Diabetes Elective Course

Authors: Brian Globerman, BS Psychology; Rena Dabish, Bachelors of Health Science; Alexandra Gavrilidis, BS Biology; Alison Lobkovich, PharmD; Helen Berlie, PharmD

Faculty Mentor: Dr. Helen Berlie and Dr. Alison Lobkovich

Abstract

Introduction: Continuous Glucose Monitoring (CGM) is quickly revolutionizing how diabetes is monitored and managed. However, no clear guidance exists on how to effectively incorporate CGM content into pharmacy curricula. Furthermore, empathy is a core value that should be included in pharmacy education. In turn, we developed a CGM user-experience for an advanced diabetes elective course.

Objective: To determine how to effectively implement CGM content into pharmacy curricula and assess if a user-experience builds empathy and increases knowledge.

Methods: We completed a quasi-experimental study where third-year pharmacy students in a diabetes elective course participated in a two-part education and user wear experience involving CGMs. Students completed a survey at three pre-specified time points to assess empathy and knowledge (foundational and counseling). Baseline characteristics were collected in the first survey. Additionally, student perspectives and experiences with CGM were collected across all surveys. Empathy was assessed using the Kiersma-Chen Empathy Scale (KCES-R). Knowledge was assessed using pre-defined multiple-choice questions. Statistical tests include repeated measures ANOVA and Bonferroni test for overall and subsections of the empathy and knowledge survey scores (SPSS Version 29).

Results: Thirteen out of the eighteen students enrolled in this course completed all three surveys. The user-experience demonstrated a significant increase in empathy ($p=0.009$). Compared to a traditional lecture, the user-experience did not provide added foundational knowledge ($p=1.0$), however, an increase in counseling knowledge was demonstrated ($p=.008$).

Conclusion: A CGM user-experience increased empathy and counseling knowledge. Foundational knowledge did not differ from a traditional lecture on CGM content. A CGM user-experience provides an advanced level of educational value and is an appropriate activity in a diabetes elective course. Future studies are needed to assess how to effectively incorporate CGM content into the core curriculum, balanced against the long-term feasibility/availability of CGM training devices.

Sabrina Gregor

Variability Upon Entry and Learning Similarities of Cultural and Social Determinants of Health (SDOH) Concepts Within Cohorts Across a Doctor of Pharmacy Curriculum

Authors: Sabrina Gregor, BS; Mary Beth O'Connell, PharmD

Faculty Mentor: Dr. O'Connell, PharmD

Abstract

Introduction: Understanding variability in cultural and SDOH knowledge and skills of students entering pharmacy school, and how these change over the program is important for developing effective educational strategies to prepare students to provide person-centered care.

Objective: Does variability exist in cultural and SDOH competency among students entering a culture-intensive first-year course? Is learning consistent as students' progress through the pharmacy curriculum?

Methods: Students anonymously completed the Self-Assessment of Perceived Level of Cultural Competence (SAPLCC) survey before and after a culture and SDOH-rich P1 course (required), after P3 capstone course (required) and after P4 APPEs (optional); four cohorts P1(pre/post 2021-2023), P3 (2021-2023) and P4 (2022-2023). SAPLCC consists of 75 items (4-point Likert scale) within six domains, and one global score (300 points). Descriptive statistics, Kruskal-Wallis and Mann-Whitney were used (SPSS v29; $p < 0.05$ significant).

Results: P1 students were 23.7 +/-3.9 years old, 68% female, 79% White, 40% Arab Americans 50% Christian, and 35% Muslim: not statistically different across cohorts.

Cohorts(no. students)	Statistical Differences (p-values) Within Cohort						
Domains	Knowledge	Skills	Attitudes	Encounters	Abilities	Awareness	Global
No. Items	16	11	15	11	13	9	75
P1 Pre (n=257)	0.008	0.043					
P1 Post (n=249)	0.004					0.026	0.010
P3 (n=239)			<0.001			0.030	
P4 (n=164)	0.003	0.033		0.037			0.033

(blank = not significant). Global scores were P1 pre 196.0+28.6, P1 post 246.3+32.1, P3 250.9+29.8, and P4 247.7+32.5: 66.0%, 83.0%, 84.3%, 83.4% of total score respectively.

Conclusion: Initially, students had significantly different knowledge and skills scores, but similar SAPLCC global scores. Learning was not consistent across the cohorts. After first and fourth year, students' global scores were statistically different. After P1, P3, and P4 years, 2-3 domains were statistically different between classmates. Additional knowledge, skills, and awareness training, including cultural encounters, are required for students to achieve similar cultural and SDOH competencies.

Shannon Habba

#ATimeToTalk: A strategy to destigmatize depression in a community pharmacy setting

Authors: Shannon Habba, PharmD Candidate; Lorden Kassab, PharmD Candidate; Kyle Burghardt, PharmD; Brittany Stewart, RD, PharmD

Faculty Mentor: Brittany Stewart, RD, PharmD

Abstract

Introduction: One in five adults in the United States (U.S.) have depression and are at risk for suicide, the twelfth leading cause of death in the U.S. It is critical to destigmatize mental health and community pharmacy settings are ideal for increasing access to mental health services.

Objective: To increase access to mental health services in a community pharmacy setting and assess patients' willingness to utilize these services.

Methods: Student pharmacists trained in Mental Health First Aid (MHFA) conducted 12 #ATimeToTalk screening events at Meijer Pharmacy. Participants 18-90 years old were recruited on site to take the Patient Health Questionnaire-9 (PHQ-9) and received counseling, education, and referral to mental health resources. A 2-week follow-up was completed via phone or email and participants reported on actions taken since the initial visit. Participant satisfaction data was collected at the initial screening and follow-up. Descriptive statistics, independent t-tests, and chi-square tests were used in data analysis.

Results: Seventy participants completed the depression screenings, the mean age was 52 years old and 75.7% were female. PHQ-9 scores ranged from 0-24 with an average of 3.96. Participants 55 years and older had lower PHQ-9 scores ($p=0.0246$) and those with a previous diagnosis of depression (25.7%) had higher PHQ-9 scores ($p=0.0006$). Most participants (92.9%) reported #ATimeToTalk screening events were helpful. Over 90% (65/70) of participants completed the 2-week follow-up and 92.3% reported they are comfortable seeking mental health services from a pharmacist. About half (53.8%) reported reading the educational materials provided and 24.6% helped a friend/family member. Some participants (16.9%) made a follow-up appointment for care after their initial visit, 38.9% of which had a history of depression ($p=0.0033$).

Conclusion: #ATimeToTalk screening events demonstrated increased access to mental health services. Participants found them helpful and are willing to utilize these services in a community pharmacy setting.

Fatima Hazimeh

Mental Health in Arab Americans: Insights from Community and Clinic Based Interventions

Authors: Fatima Hazimeh, BSPH, BHS, PharmD Candidate 2025, Paul E. Kilgore, MPH, MD, FACP

Faculty Mentor: Paul E. Kilgore, MPH, MD, FACP

Abstract

Introduction: Arab Americans represent diverse ethnic backgrounds but share a cultural heritage and experiences as immigrants from the Middle East and North Africa. Despite facing significant mental health needs, stigma deters many Arab Americans from seeking treatment. Culturally-appropriate interventions are needed.

Objective: This systematic review synthesized evidence on interventions for depression, anxiety, and psychological distress among the Arab population that can be applied to Arab Americans.

Methods: PubMed, PsycINFO, and Google Scholar were comprehensively searched for studies published 2000-2023. Eligible interventions were clinic-based or community-based. Randomized trials and pre-post studies were included. Two reviewers independently screened studies, extracted data, and assessed quality using the Mixed Methods Appraisal Tool. A narrative synthesis was performed.

Results: Across the 17 included studies, 15 evaluations of community-based interventions were identified, encompassing psychoeducation, support groups, multicomponent approaches, and internet based interventions. Only two of the included studies were carried out in clinic settings and included group psychotherapy and pharmacological treatment education. Nearly all interventions demonstrated feasibility, acceptability, and preliminary effectiveness for reducing symptoms and improving coping among Arab adults. Cultural tailoring and bilingual providers were frequently cited as key elements. Study quality ranged from 25-100% on the MMAT.

Conclusion: Preliminary evidence indicates mental health interventions can engage and benefit Arab American adults, countering cultural stigma through appropriate adaptations. Multimodal approaches addressing individual, social, cultural, and spiritual factors may be particularly impactful. However, significant research gaps remain regarding optimal intervention design, appropriate measures, cost-effectiveness, and longitudinal outcomes. There is a need for additional research studying the effectiveness and adherence of medication therapy in this population. High-quality randomized controlled trials comparing standardized interventions to usual care are critically needed to advance practice.

Stephen Hegenauer

Systemic corticosteroid exposure in patients admitted for COPD exacerbations

Authors: Stephen Hegenauer, PharmD Candidate; Dalia Al Najjar, PharmD Candidate; Pramodini Kale-Pradhan, PharmD, MPH; Christopher Giuliano, PharmD, FCCP; Melissa Lipari, PharmD, BCACP

Faculty Mentor: Melissa Lipari, PharmD,

Abstract

Introduction: Recent research on systemic corticosteroids (SCS) used to treat acute exacerbations of chronic obstructive pulmonary disease (AECOPD) has demonstrated similar efficacy and fewer adverse effects when a lower dose is used. A recent study demonstrated that 16/190 (8.4%) patients received the appropriate duration, and eight (4.2%) received the appropriate dose of SCS. Subsequently, St. John Hospital in Detroit, MI implemented an AECOPD order set which recommends the appropriate SCS exposure.

Objective: The purpose of this study is to compare the frequency of appropriate SCS exposure (defined as prednisone equivalent of 420 mg) use in patients admitted with AECOPD before and after order set changes were implemented.

Methods: This cohort study aimed to evaluate the effects of implementing an order set designed to provide guidance on prescribing SCS for the treatment of severe AECOPD. The study will include all patients admitted for severe AECOPD, as defined by ICD-9 or ICD-10 codes, both before and after the implementation of the order set.

The primary outcome of the study was to determine the frequency of appropriate corticosteroid exposure. Secondary outcomes included hyperglycemia, hypertension, appropriateness of corticosteroid dose and duration, and 30- and 90-day readmission rates.

Results: Research in progress

Conclusions: N/A

Linda Kobeissi

Stratifying Risk for Hypersensitivity Reactions in Patients Receiving Paclitaxel Infusions

Authors: Linda Kobeissi, PharmD. candidate 2024; Anna Hejnar, PharmD; Brittany Lines, PharmD., BCOP

Abstract

Introduction: Paclitaxel (Taxol), a widely utilized chemotherapeutic agent with potent antitumor effects, is associated with hypersensitivity reactions (HSRs) that can have severe and life-threatening consequences. Anecdotally, Corewell Health Dearborn Cancer treatment Center has seen an increase in reactions among our patient population over the past two years. Despite premedication efforts, reactions persist and can manifest differently including but not limited to shortness of breath, chest pain, and hypotension. This study aims to identify risk factors for paclitaxel induced HSRs to enhance patient safety during treatment.

Objectives: To determine which risk factors are independently associated with a higher rate of paclitaxel hypersensitivity reactions at Dearborn, Troy, and Royal Oak cancer treatment infusions center.

Methods: A retrospective case-controlled study will be conducted at three Corewell Health infusion cancer sites. These include the Dearborn, Royal Oak and Troy infusion sites. The study is projected to encompass 360 patients, comprising 30 matched cases experiencing hypersensitivity reactions and 90 controls without such reactions at each infusion site. The controls of the study will be selected through random sampling. The data collection will include information on age, infusion site, sex, pregnancy status, cancer type, cancer stage, documented infusion reaction, type of IV-line access, rate of infusion, Aprepitant therapy, concurrent platinum therapy and/or immune therapy, manufacturer of paclitaxel, concentration of paclitaxel, history of Covid, history of Covid vaccine and if applicable the number of doses, and history of tocilizumab therapy if indicated. The data analysis will include descriptive statistics and Chi-squared tests to analyze potential risk factors, while multivariate regression will assess their independence. Statistical analyses will be conducted using Excel or SPSS.

Results: n/a

Conclusion: n/a

Lauren Lim

Clinical and Drug Resistance Characteristics of *Providencia* spp. Infections

Authors: *Lauren Lim, PharmD. Candidate; Pramodini B. Kale-Pradhan, PharmD.; Heather Graskewicz, PharmD.; Meenal Malviya, MD; Meredith Coyle, MD; Christopher Giuliano, PharmD, MPH; and Leonard Johnson, MD

Faculty Mentor: Pramodini Kale-Pradhan, PharmD.

Abstract

Background: *Providencia* is a gram-negative bacillus that colonizes the urinary tract and is often resistant to many antimicrobials. This study aimed to evaluate resistance patterns of *Providencia* spp (*P. spp*) and clinical outcomes due to the paucity of topical data.

Methods: A multi-center, descriptive, retrospective chart review of adult patients with *P. spp.* infections was conducted from January 1, 2020 to May 31, 2022. The primary outcome was to describe the drug resistance patterns of *P. spp.* isolates. The study's secondary outcome was to evaluate the clinical outcomes of patients with *P. spp* infections.

Results: Of 312 patients screened, 243 were excluded primarily for polymicrobial infections. The mean age was 70 years and 39 (56.5%) were males. Of the 69 included cases, 46 (66.7%) were *P. stuartii*, 21 (30.4%) *P. rettgeri*, and 2 (2.9%) *P. alcalifaciens*. The most common infections were bacteremia 38 (55.1%), with urinary and wound being the most frequent bacteremia source; followed by 28 (40.6%) urinary tract and 3 (4.3%) wound infections. 45 patients (65.2%) had urinary catheters. Primary antibiotics used for treatment consisted of ceftriaxone, 25 (36.2%), cefepime, 20 (29%), and meropenem, 10 (14.5%). Five of 69 (7.2%) cases were multidrug resistant and required meropenem. Nineteen patients (27.1%) died during their admission but none related to *Providencia* infections. Ten of the 69 patients (14.5%) were readmitted within 30 days for reasons unrelated to progression or recurrence of *Providencia* infections.

Conclusion: *Providencia* bacteremia was the most common infection. Third generation cephalosporins remain an appropriate choice of antibiotics for *P. spp.* However, *P. stuartii* was the only species with multidrug resistance. Future studies should be carried out to confirm this observation.

Lauren Danelle Lim

Evaluation of an Interprofessional Practice-based Care Plan at a Student-run Free Clinic for People Experiencing Homelessness

Authors: Lauren Danelle Lim, PharmD Candidate; Cece Findlay, DPT Candidate; Iyanna Peppers, M.D. Candidate; Polina Chuikov, M.D. Candidate; Mina Juma M.D. Candidate; Judson Knott, PharmD Candidate; Manar HannaKachl, PharmD Candidate; Martha Schiller, PT, DPT, MSA,

Faculty Mentor: Aline Saad, Pharm.D.

Abstract

Introduction: In Detroit, an estimated 5,687 people experience homelessness with more than 50% of them managing one or more disabling conditions. The Community Homelessness Interprofessional Program (CHIP) is an interprofessional, student-run, faculty guided, free walk-in clinic that provides monthly services and resources to the underserved homeless population of Detroit. CHIP was developed in collaboration between pharmacy, medicine, social work, law, and physical therapy faculty and students within Wayne State University. A pilot interprofessional care plan (ICP) was implemented to optimize the experience of patients and students during CHIP clinics.

Objective: To evaluate the impact of the ICP on the experience of patients and students at the CHIP clinics

Method: Data was collected between November 2022 and July 2023 from two Qualtrics surveys distributed at the end of either the patients' or students' CHIP experience. A mixed methods analysis of data was completed. The primary outcome was to evaluate patients' satisfaction with the clinic experience. The secondary outcome assessed student feedback related to the usage of the ICP in service delivery. Responses were numerically coded and descriptive statistics were generated.

Results: 76 patients and 72 students completed the surveys. An average of 8 patients were seen per clinic. 94.4% of patients agreed that they received valuable assistance while being treated with courtesy and respect. Patients expressed gratitude for the care they received. Students cared for 2-3 patients per clinic. 85% of the students agreed that the ICP allowed for inclusion of various disciplines' input, a better understanding of team members' roles and responsibilities, and task delegation. 79% of students found the ICP to be useful in fostering team collaboration and including the patients in goal setting for care plans.

Conclusion: The implementation of an interprofessional care plan improved the interprofessional team dynamics and positively impacted patient experience at the CHIP clinics.

Brenda Manni

Evaluation of Student Pharmacists' Interventions during an Interprofessional Elective Dental Advanced Pharmacy Practice Experience

Authors: Brenda Manni, PharmD. Candidate; Samantha Jaboro, PharmD. Candidate; Francine Salinitri, PharmD; Brittany Stewart RD, PharmD; Melanie Mayberry D.D.S., M.S.-HCM; Aline Saad, PharmD

Faculty Mentor: Aline Saad, PharmD

Abstract

Introduction: Several publications described interprofessional educational activities where pharmacy and dental students learn together. However, most highlighted didactic opportunities for learners rather than interprofessional learning experiences. The Eugene Applebaum College of Pharmacy and Health Sciences collaborated with the University of Detroit Mercy School of Dentistry to develop an innovative elective Advanced Pharmacy Practice Experience (APPE) delivered in dental clinics. Dental and Pharmacy students collaborated to learn about, from, and with one another to appreciate their respective roles and responsibilities and optimize communication and teamwork in providing comprehensive care to dental patients.

Objective: To evaluate the impact of an interprofessional collaborative dental APPE on patient care by analyzing the student pharmacists' interventions and identified drug related problems (DRPs) in the dental clinics.

Methods: Eight fourth year (P4) student pharmacists completed this 6-week APPE between June 2021 and April 2023 along with more than 400 3rd and 4th year dental students. Students collaborated on their patient care plan development and delivery. Student pharmacists reviewed patient medical charts, identified DRPs, communicated pharmacy related interventions, and documented their findings. Pharmacy interventions and DRPs were analyzed and coded. DRPs were also shared with the patients' primary care providers (PCP) when appropriate.

Results: P4 student pharmacists delivered care to more than 300 dental patients. Student pharmacists documented 522 interventions related to taking medication history, chronic disease state management, medication reconciliation, providing patient education, drug information provision, and/or providing a pharmacy consult. Eight different DRP categories were reported with the most frequent being the need for additional drug therapy (49%) followed by non-adherence (12.5%). DRPs were shared with the patients' PCP when appropriate.

Conclusion: Pharmacy and dental students successfully collaborated to provide patient care through this interprofessional dental APPE in order to provide impactful interventions and identify drug related problems which may lead to improved patient outcomes.

Yasmin Nasser

Impact of Fourth-Year Advanced Pharmacy Practice Experiences (APPEs) on Cultural and Social Determinants of Health (SDOH) Knowledge and Skills Development

Authors: Yasmin Nasser, PharmD Candidate; Mary Beth O'Connell, PharmD

Faculty Mentor: Mary Beth O'Connell PharmD

Abstract

Introduction: Pharmacy accreditation requirements include cultural competency and SDOH skills. The impact of APPEs on these areas has been minimally explored and not within the same cohort.

Objective: To quantify changes in cultural and SDOH knowledge and skills after APPEs.

Method: Pharmacy students completed the Self-Assessment of Perceived Level of Cultural Competence (SAPLCC) survey with anonymous codes at the end of their third-year capstone course (required) and APPEs (optional). SAPLCC consists of 75 items (4-point Likert scale) within six domains and one global score (total 300 points). Five demographic survey items were included. Average domain scores were classified as low (<2), moderate (2-3) and high (>3). Sum scores are domain items added together. Matched surveys were analyzed with descriptive statistics and paired T-test for sum scores with SPSS v29; p<0.05 significant.

Results: Seventy-three students completed both surveys (75% response). Matched cohort was 25.4±3.7 years old, 74% female, 86% White, 40% Arab-American, 46% Christian, and 25% Muslim.

Domains	Knowledge	Skills	Attitudes	Encounters	Abilities	Awareness	Global
No. items.	16	11	15	11	13	9	75
Max sum points	64	44	60	44	52	36	300
Post P3 sum.	50.3	36.9	55.0	34.3	45.0	31.5	252.9
Post P4 sum	50.3	37.0	54.0	35.0	45.6	31.2	253.2
P4 % max points	78.5%	84.2%	90.1%	79.6%	87.8%	86.6%	84.4%
P4 % self-classifying	51%	70%	82%	54%	78%	70%	77%

as high scores

All domain and global sum scores after APPEs were not statistically different from pre fourth-year scores.

Conclusion: Cultural and SDOH knowledge and skills did not increase after APPEs. Self-assessed knowledge and encounter domains were the lowest after APPEs. Potentially enhancing APPE training in these areas could increase student abilities.

Sandi Nuzha

The Sweet Truth: Optimizing Insulin Infusion Protocols for Enhanced Glycemic Control Across a Health System

Authors: Sandi Nuzha, PharmD Candidate 2024; David Wilpula, PharmD, BCPS; Lana Alkhwaji, PharmD

Abstract

Introduction: Managing glycemic control in hospitalized patients presents a complex challenge, with previous observational studies indicating that both hypoglycemia and hyperglycemia can detrimentally impact patient outcomes, irrespective of comorbidity severity. However, validated and readily available insulin infusion protocols remain limited. Insulin infusions are a crucial medical intervention in hospitals for managing blood glucose. The percentage of time spent outside a target glucose range, known as time in therapeutic range (TIR), has been associated with adverse clinical outcomes. Corewell Health East (CHE) currently employs nine distinct insulin infusion protocols, each tailored to specific patient populations.

Objective: To assess the appropriateness and effectiveness of existing insulin infusion protocols of a health system using measured protocol adherence and TIR to identify the need for additional nursing education.

Methods: A multi-center, retrospective, observational medication use evaluation involving patients aged 18 and older who received an insulin infusion according to CHE protocols. A searchable database will be queried to identify patients who received diabetic ketoacidosis, intensive care unit care, cardiovascular surgery, or obstetrics insulin infusion protocols between July 2022 and July 2023. A convenience sample of 50 patients per protocol was selected from each site. Glucose control was assessed using Time in Therapeutic Range (TTR), defined as the proportion of time that glucose values remained within specified target ranges during insulin infusion. TTR is further categorized into time below therapeutic range, time in therapeutic range, and time above therapeutic range, reported in hours. Hypoglycemia incidence among patients was assessed and reported as events per 100 patient days. Protocol adherence was determined through an adherence score, calculated by evaluating the number of protocol-compliant assessments and reported as a percentage. Electronic medical records were reviewed to evaluate adherence by examining dose titration and compliance with protocol guidance.

Results: Pending completion of data collection and analysis.

Conclusion: Pending completion of data collection and analysis.

Carolina Orzol

Potential Cost Savings in the Reversal of DOAC Associated Bleeding

Authors: Carolina Orzol, BS, PharmD; Lindon Nikolajj, BS, PharmD; Vince Procopio, PharmD, BCCCP; Norm Buss, PharmD, BCPS

Abstract

Introduction: Direct oral anticoagulants (DOACs) are a cornerstone of therapy in treatment and prevention of deep vein thrombosis, pulmonary embolism and other thromboembolic disorders. Despite their favorable safety profile, patients are still at an increased risk of intracranial hemorrhages (ICH), gastrointestinal (GI) and/or fatal bleeding. Two agents commonly used in DOAC associated bleeding include andexanet-alfa and four factor prothrombin concentrate complex (4F-PCC). Reversal agent selection is determined by cost, presentation, and several studies.

Objective: Evaluate adherence to Henry Ford Health System (HFHS) 2023 “Tier 1: Anticoagulation Reversal Guidelines” and determine cost efficiency in the management of DOAC-associated bleeding with andexanet-alfa.

Methods: This is a single-center, retrospective, cohort study that included patients admitted to a HFHS hospital and received andexanet-alfa between June 2022 and June 2023. Included patients were aged 18 years or older, on apixaban or rivaroxaban at home, and had a bleeding event requiring reversal of DOAC with andexanet-alfa. Pregnant women were excluded. Patients were grouped on appropriate or inappropriate usage of andexanet-alfa according to HFHS’s anticoagulant reversal guideline(s). Primary endpoint is the percentage of patients based upon the new 2023 guidelines would have qualified for prothrombin complex concentrate. Secondary endpoint is to determine the total cost savings if the new guidelines had been implemented before and completely followed through. Descriptive statistics were utilized to analyze the primary and secondary endpoints.

Results: In total, about 21% of patients received andexanet-alfa for GI bleeds and could have qualified for 4F-PCC instead under the 2023 HFHS guidelines. 4F-PCC is about \$3,211 cheaper than low-dose andexanet-alfa and would have resulted in a cost saving of \$41,743 in a 12-month period.

Conclusion: 4F-PCC is an effective and economical reversal agent in DOAC-associated GI bleeds. There are significant cost-savings opportunities by following the 2023 anticoagulation reversal guidelines at a HFHS.

Wiam Ouahab

Building Pharmacy Student Empathy Through a Decision-Making Game

Authors: Wiam Ouahab, PharmD Candidate; Alison Lobkovich, PharmD; Insaf Mohammad, PharmD, BCACP; Sheila Wilhelm, PharmD, FCCP, BCPS.

Faculty Mentor: Sheila Wilhelm, PharmD, FCCP, BCPS.

Abstract

Introduction: Doctor of Pharmacy programs are charged with developing students' empathy based on the 2016 Accreditation Council for Pharmacy Education (ACPE) Standard 3 and the 2022 Curriculum Outcomes and Entrustable Professional Activities (COEPA). While empathy is essential to optimal patient care, its subjective nature makes it challenging to teach and therefore literature is lacking on best teaching practices. We developed a novel simulated approach to teach and assess empathy in a pharmacy classroom. Our study aimed to utilize a validated empathy scale to quantify the impact of this learning experience on students' empathy development.

Objective: To assess whether a simulated decision-making game in a pharmacy skills lab course will impact empathy in pharmacy students.

Methods: We completed a cohort-based quality improvement project in which third year pharmacy students participated in a classroom empathy game experience that simulated a month in a patient's life and issues related to the cycle of poverty. Prior to the game, students completed a voluntary, anonymous baseline demographics survey. They also completed a pre- and post-survey of the validated empathy tool, the Kiersma-Chen Empathy Scale (KCES-R) to measure the change in the scale score following the decision-making game. Students also provided free-text comments in the post-survey. Statistical tests used included descriptive statistics for demographic data, Shapiro-Wilk test of normality and Wilcoxon Signed-Rank test for survey scores (SPSS Version 29).

Results: Pharmacy students (n=37) showed a statistically significant improvement in empathy with an overall increase in composite KCES-R scores ($z = -5.071$, $p < 0.001$) after participating in the empathy game class session. Each of the 14 KCES-R items showed a significant increase ($p < 0.05$) after the learning experience. Students' free-text responses indicated the activity was insightful and effective for developing empathy in pharmacy students.

Conclusion: The empathy game simulation was a successful approach to increase empathy in third-year pharmacy students.

Macy Shupp

Desirability of Outcome Ranking (DOOR) Analysis of T2 Rapid Diagnostic for Candida in the Bloodstream in Intensive Care Patients

Authors: Macy Shupp, PharmD Candidate; Kaylee Caniff, Pharm.D., BCIDP; Dana Holger, Pharm.D., AAHIVP; Thomas Walsh, MD, PhD (Hon), FIDSA, FAAM, FECMM; Michael Veve, PharmD, MPH; George Alangaden, MD; Michael J. Rybak, Pharm.D., MPH, PhD

Faculty Mentor: Michael Rybak, Pharm.D., MPH, PhD

Abstract

Introduction: Bloodstream infections (BSI) due to *Candida* spp. are considered a major cause of morbidity and mortality in healthcare environments. The time to appropriate therapy has been previously documented as a risk factor for mortality. Currently, blood cultures can take up to 72-96h to identify *Candida* spp. while the T2Candida takes 3-5h resulting in a rapid time to appropriate treatment.

Methods: This is a retrospective, multicenter, cohort study of patients diagnosed with candidemia at Henry Ford Hospital (HFH) and the Detroit Medical Center (DMC) from 2016-2022. Included patients were adults with a positive T2Candida or blood culture at participating centers, or in the ICU within 72h of a positive T2Candida. Patients were excluded if they had bacterial BSI or a fungal BSI other than *Candida* species, if patients died or were discharged to hospice/palliative care within 48h from T2Candida, pregnant/breastfeeding, prisoners, and COVID-19 positive during admission. Statistical tests were performed using SPSS. Desirability of Outcome Ranking was used to determine the benefits of T2Candida test in the clinical setting and evaluate patient outcomes.

Results: Overall, 106 patients were included; 56 patients received traditional blood culture testing (DMC) and 50 patients received the T2Candida test (HFH). There were no significant differences between groups in clinical outcomes. However, there were significant differences between groups when comparing baseline demographics, risk factors such as APACHE II score (25.5vs 20.9 $p<0.002$), organism (*C.albicans*/*C.tropicalis* 32.1%vs74% $p<0.001$, *C.krusei*/*C.glabrata* 46.4%vs22% $p<0.008$), and interventions performed (Ophthalmological exam 76.8%vs94% $p<0.005$). The DOOR analysis showed significant results between groups. The probability that a randomly selected patient who is assigned to the T2Candida group will have a better outcome is 56.6% (95% CI 51.3%-61.9%)

Conclusion: In patients with Candidemia, patients assigned to the T2Candida group are more likely to have an overall better outcome. To our knowledge, this is the first study specifically using DOOR analysis in reviewing Candidemia infections, more studies are needed for further evaluation.

Caroline Simko

A Qualitative Analysis of an Interprofessional Musical Educational Workshop Focusing on Non-Verbal Communication Skills

Authors: Caroline Simko, PharmD Candidate 2024; Aline Saad, PharmD; Georgiana Marusca, MD; Diane Levine, MD.

Faculty Mentor: Dr. Aline Saad, PharmD

Abstract

Introduction: The importance of non-verbal communication with patients is established to optimize care. However, few health professional curricula teach these skills. Musicians, particularly quartets, employ non-verbal communication in various intricate ways beyond the musical piece. These expressions contribute to an ensemble's cohesion, synchrony, and artistic interpretation.

Objective: To evaluate the impact of observing musicians' use of non-verbal communication on health professional students' understanding of these skills and their application in interprofessional teams.

Method: A total of 65 medical and 50 pharmacy students attended a workshop with a string quartet. Following a performance by the musicians, students and musicians engaged in activities to practice the non-verbal communication strategies employed by the quartet to optimize their delivery.

Authors provided pre-and post-surveys, which included closed and open-ended questions to assess understanding of underlying themes of non-verbal communication with patients and interprofessional teams. An inductive qualitative analysis was performed on open-ended questions to identify emergent non-verbal communication themes.

Results: Of the 115 students who attended the workshop, 105 students (91%) completed the pre-survey, and 94 students (82%) completed the post-survey. 52% medical and 29.5% pharmacy students had prior instrumental or vocal musical training. Comparison demonstrated significant improvement in students' knowledge in appreciating the influence of nonverbal communication with patients and teams (60.5% pre vs 72% post-workshop).

Before the workshop, students identified the most important nonverbal communication cues they look for in patients' interactions as eye contact (96.5%), body language (79.8%), facial expressions (45.6%), and emotional intelligence (20.7%). After completion of the workshop, emerging nonverbal communication strategies emphasized team rehearsal/planning (59.7%) and paralinguistics (38.6%).

Conclusion: Healthcare professionals and musicians employ similar strategies to perform in teams and deliver specialized tasks; effective nonverbal communication is crucial to both. Engagement with musicians may serve as a vehicle to instruct students on non-verbal communication.

Niharika Thota

Investigating the Synergistic Potential of Bacteriophage, Combined with LL-37 and/or Antibiotics against *Enterococcus faecium*

Authors: Niharika L.S. Thota, BS, PharmD Candidate 2025; Callan R. Bleick, PharmD, PhD Candidate 2027; Samantha Vader, BS; Biswajit Biswas, MS, PhD; Cesar A. Arias, MD, PhD, MS; Susan Lehman, PhD; Michael J. Rybak, Pharm D, MPH, PhD

Faculty Mentor: Michael J. Rybak, Pharm.D., MPH, PhD

Abstract

Introduction: Multidrug-resistant (MDR) *E. faecium* (E_{fc}m) infections pose a substantial threat, causing approximately 54,000 hospitalizations and 5,400 fatalities annually in the US. LL-37, a human derived cationic antimicrobial peptide alongside bacteriophages (phages) which infect, replicate, and lyse bacterial cells, serve as potential novel strategies to eliminate foreign pathogens when combined with antimicrobials.

Objective: To assess the percent bacterial survival of two MDR E_{fc}m strains against the combination(s) of either: LL-37, phages, and/or antibiotics over 2h and 4h.

Methods: Two MDR E_{fc}m strains resistant to daptomycin (DAP) and/or ampicillin (AMP), R-497 and HOU-503-01 were utilized. Phages, NV-503-01 and NV-497, were quantified and propagated to MOI of 0.01 and 0.1 respectively. LL-37 was diluted to a suboptimal concentration of 0.5uM (survival rate 70-80%) to detect a synergistic interaction more easily. The experiment was conducted in triplicate and after 24h of incubation at 37°C samples were drawn and plated at 2h and 4h. Data was analyzed using one-way ANOVA test and Tukey-HSD.

Results: At 2h, when combined with phages and antimicrobials, LL-37 demonstrated the lowest bacterial survival rate against both E_{fc}m strains ($P < 0.05$) versus all other combinations. Moreover, at 4h, phage showed the lowest bacterial survival rates when combined with antibiotics DAP/AMP at 1/2-1/16th MIC respectively, with or without the addition of LL-37.

Conclusion: Despite LL-37's presence in the 4h assay, it did not make a significant impact on lowering the bacterial survival rate over the time-period when compared to phage alone +/- antimicrobials ($P > 0.05$). This outcome could be due to multiple factors including phage antagonism, LL-37 resistance, optimal timing of phage killing/replication in respect to its lytic cycle, and LL-37's sensitivity to physiological environments. Further investigating the interaction of LL-37 with multiple phages, antibiotics at 1-2x their MICs, and higher LL-37 concentrations, could provide deeper insights into the synergistic interactions among these combinations.

Victoria Tutag Lehr

Naloxone public access for metro Detroit communities: the NaloxBox®; pilot program

Authors: Victoria Tutag Lehr, PharmD; Lauren Meloche, MS; Ja'Lea Echols MPH candidate; Denise Kolakowski, MS; Robert Dunne, MD, FAEMS, FACEP; Umar Khan, PharmD candidate; Varun Vohra, PharmD, DABAT

Abstract

Introduction: Opioid overdose deaths in Michigan remain among the highest in the United States. The etiologies of the growing number of drug overdose deaths are complex and multifactorial, requiring a multifaceted response including expanded naloxone access. Prompt bystander administration of naloxone for opioid overdoses in community settings helps prevent death. However, naloxone must be readily available in high-vulnerability areas for immediate administration. A NaloxBox® is a container that includes free, ready-to-use naloxone doses for bystander administration in publicly accessible locations. Our Wayne State University team collaborated with AmeriCorps to pilot a NaloxBox program to increase public access to naloxone within Wayne, Oakland and Macomb counties.

Objective: 1) To characterize community locations, including demographics and social vulnerability, for NaloxBox placement across metro Detroit; and 2) to evaluate the number/rate of opioid overdose deaths at locations pre- and post-NaloxBox placement.

Methods: We developed an electronic survey to identify community partners willing to place a NaloxBox at their site. Sites for n=100 NaloxBoxes will be secured using survey data and Emergency Medical Services overdose hotspot data. AmeriCorps members will install, monitor, and refill boxes at locations. Quick Response (i.e. QR) codes on the NaloxBox will capture voluntary de-identified naloxone utilization data. Social vulnerability, assessed using the Social Vulnerability Index (SVI), representing national percentiles of county-level SVI, will inform NaloxBox® placement at locations of high risk. Chi-Square analysis will compare overdose deaths pre- and post-NaloxBox placement.

Results: Survey distribution to partners within Wayne, Oakland, and Macomb counties started September 1, 2023, 11 community partners (business, pharmacy, nonprofit/service agency, school, residential, and community space) committed to NaloxBox placement. Assessment of locations, unit placement, and outreach for additional locations is ongoing.

Conclusion: NaloxBox implementation is expanding public access of naloxone within metro Detroit communities. Anticipate installation completion in October 2023. Analysis of overdose deaths to follow.

Shahad Zaytouna

Pharmacist-Driven Antimicrobial Preoperative Prophylaxis Impact on Patient Outcomes

Authors: Sarah Hassani, PharmD (PGY-1 Resident), Dmitriy Martirosov, PharmD, BCIDP

Faculty Mentor: Safana Atwan, PharmD, BCCCP

Abstract Introduction: Surgical site infection (SSI) is one of the most common types of hospital associated infections (HAIs) that pose significant challenges to patient health and healthcare systems worldwide. The CDC estimates that SSIs account for 20% of all HAIs and cause a 2-to 11-fold increase in risk of mortality¹. They are also very costly, increasing hospitalization costs by around \$20,000 per admission and extending hospital length of stay by 9.7 days². Colorectal and hysterectomy procedures have a high occurrence of SSI postoperatively. Colorectal surgeries are associated with 15% of all HAIs, which should raise concerns to prevent infection. A prospective cohort study of 1075 patients by Falconer found that implementation of SSI colorectal bundle reduced overall SSI rate from 15.9% to 9.4%³. Furthermore, a meta-analysis by Zywoot observing pre- and post- implementation data SSI bundles for colorectal surgeries was associated with an SSI risk reduction of 40%⁴. Abdominal hysterectomy surgeries come with the highest incidence of SSI compared to laparoscopic or vaginal approaches⁵. A retrospective study by Guo reported 2 SSIs post-bundle implementation out of 532 hysterectomies performed and in a single-center prospective study that involve 2,809 consecutive patients who underwent resection of the colon only 134 patients (4.7%) were diagnosed with surgical site infections (SSI) after receiving preoperative antibiotics^{6,7}.

Objectives: Primary Outcome(s): difference in guideline concordance with respect to antibiotic selection, dosing, and timing between groups. Secondary Outcome: difference in risk of surgical site infection between groups

Methods: This is a single center, retrospective cohort study of patients who underwent gynecologic or colorectal surgery at Corewell Health Dearborn Hospital between January 2016 to June 2023. Patients who are younger than 18 years of age, have a history of antimicrobial resistance to preferred surgical prophylaxis regimens within the preceding 12 months, pregnant or immunocompromised will be excluded. An intervention that granted pharmacists the ability to order pre-operative surgical prophylaxis occurred in October 2013. A system was put in place to ensure pharmacy notification of add-on cases. If pharmacy is not notified of add-on cases, the provider is to place orders for the appropriate preoperative antibiotic. Patients who had scheduled surgery between January 2016 through June 2023 and received antibiotics ordered by a pharmacist will be included in group 1. Patients who had emergent surgery between January 2016 through June 2023 and received antibiotics ordered by provider outside of pharmacy will be included in group 2. Patients will be identified with an NMSN procedure code of "COLON SURGERY" or "ABDOMINAL HYSTERECTOMY" via a report in the electronic health record. This study is expected to enroll 150 patients, evenly divided into two groups. Data collection variables are listed separately but generally include patient demographics, surgery type, operating surgeon, renal function status, risk factors for surgical site infection, allergies, and pre-operative prophylaxis. Results: pending

Hiba Almoussa

THE EFFECTS OF ISOMETRIC ANKLE TRAINING WITH VISUAL FEEDBACK IN INDIVIDUALS WITH CHRONIC STROKE

Authors: Hiba Almoussa, SPT, Anna Krinkie, SPT, Kathryn Gordon, SPT, Tamara Simjanoski, SPT, Sara Maher, PT, PhD, DScPT, Vicky Pardo, PT, DHS.

Faculty Mentor: Dr. Vicky Pardo, PT, DHS.

Abstract

Introduction: The NuStep Transitt recumbent stepper allows subjects to work on limb movements while in a safe seated position. The Transitt provides real-time feedback during interactive games. The purpose of this study was to determine the effect of isometric dorsiflexion-plantarflexion training using the NuStep Transitt Paddle ball game in subjects with chronic stroke. Specifically, its effect on gait, functional mobility, strength, balance, coordination, visual scanning, and endurance. **Methods:** Twenty-two participants (11 female, 14 right hemiparesis, mean age 60.6 +/-11.4) with chronic stroke were recruited. Participants completed pre- and post-evaluations (visits 1 and 10), which included gait on the GAITRite (normal and fast speeds), Dynavision (visual scanning), maximum voluntary contractions of knee extension/flexion and ankle dorsiflexion/plantarflexion, Lower Extremity Functional Scale, Four-Square Step Test (FSST), Five Times Sit to Stand (5xSTS), 6-Minute Walk Test (6MWT), and lower extremity motor/sensory Fugl-Meyer assessment. Visits 2-9 consisted of 45 minutes of training twice a week. Between the 5-minute warm-up and cool-down, participants completed 5-minute bouts of Paddle Ball gaming, using isometric DF and PF to control the paddle. Demographic data were analyzed using descriptive statistics followed by parametric or non-parametric tests for each pre- and post-outcome measure. Independent t-tests were run for all comparisons except for the 5xSTS, FSST, 6MWT, and Dynavision measures where Wilcoxon signed ranks were used due to non-normal distribution. To prevent type 1 errors, Holm-Bonferroni post-hoc adjustments were conducted for all significant findings. **Results:** There were significant changes for 5xSTS [15.56 to 13.73 seconds ($p = 0.017$)], 6MWT [887.54 to 1001.64 ft ($p = 0.013$)], and FSST [22.56 to 19.54 seconds ($p = 0.025$)]; moderate to small effect sizes were found. Significant changes in fast gait included non-hemiparetic step and stride length ($p=0.004$), hemiparetic step length ($p=0.005$), and normalized velocity ($p=0.005$). There were significant changes for the Dynavision average reaction time [1.82 to 1.51 seconds ($p = 0.01$)], total number of hits [35.27 to 42.27 hits ($p = 0.005$)], and upper hemiplegic quadrant average reaction time [1.78 to 1.39 seconds ($p = 0.013$)]. Large and moderate effect sizes were found for the gait and Dynavision results. **Discussion:** Training with the Paddle Ball game on the NuStep Transitt is an engaging and challenging method of improving LE function, endurance, balance, and visual scanning. The significant changes in 5xSTS, FSST, 6MWT and gait parameters may translate to safer transfers, decreased fall risk, and improved functional mobility. Significant changes in the Dynavision scores can translate to improved visual scanning, which is particularly important for driving. **Conclusions:** Ankle training with visual feedback using an interactive Paddle Ball game on the NuStep Transitt had clinically relevant effects on functional mobility and visual scanning for individuals with chronic stroke. **Acknowledgements:** The authors wish to thank NuStep LLC for their support of this project.

Christina Ambrozy

CAFFEINE EXPECTANCY DOES NOT INFLUENCE THE PHYSICAL WORKING CAPACITY AT THE FATIGUE THRESHOLD (PWCFT)

Authors: Christina A. Ambrozy, SPT, Nicole E. Hawes, SPT, Olivia L. Hayden, SPT, Isabella Sortzi, SPT, and Moh H. Malek, PhD

Faculty Mentor: Moh H. Malek, PhD

Abstract

The placebo effect occurs when a desired outcome is experienced due to the belief that a treatment is effective, even in the absence of an active ingredient. One explanation for this effect is based on a person's expectations of a drug or supplement. While caffeine's effects on sports performance have been studied, little is known about how expectations of caffeine affect neuromuscular fatigue during continuous muscle action. The physical working capacity at the fatigue threshold (PWCFT) can be used to assess neuromuscular fatigue non-invasively using surface electromyography. Thus, the purpose of this study was to investigate whether caffeine expectancy influences PWCFT. We hypothesized that regardless of expectancy, caffeine consumption would delay neuromuscular fatigue. The study involved eight healthy college-aged men (mean \pm SEM: age, 25.6 \pm 1.0 y) who visited the laboratory on four occasions, each separated by seven days. The subjects completed four experimental conditions, in random order, where they were told they were consuming caffeine or placebo, and either received caffeine or placebo. After consuming the drink, the subjects remained in the laboratory for an hour and then performed an incremental exercise test. The results showed that the condition where subjects were told they were consuming caffeine and received caffeine had significantly higher mean values for maximal power output [$F(3,21) = 11.75$; $p < 0.001$], PWCFT [$F(3,21) = 12.28$; $p < 0.001$], PWCFT (%maximal power output) [$F(3,21) = 8.75$; $p < 0.001$], heart-rate at end exercise [$F(3,21) = 8.75$; $p < 0.001$], and heart-rate at end exercise (%predicted) [$F(3,21) = 3.83$; $p = 0.025$] compared to the two conditions where placebo was received. However, no statistically significant mean differences were found from the condition where subjects were told they were consuming placebo, but consuming caffeine. This suggests that a person's expectancy and potential somatic response may serve as a cue for how an ergogenic aid or placebo could affect subsequent performance.

Sarah Bishop

Caregiver Voices: “This was my life; My new life.”

Authors: Sarah Bishop, OT Student; Shanjana Chowdhury, OT Student; Alex Corneau, OT Student; Madison Thomas, OT Student, Fredrick Pociask, PT, Ph.D.

Faculty Mentor: Rosanne DiZazzo-Miller, Ph.D., FAOTA, OTRL

Abstract

Introduction: The role of caregiving is widely stigmatized as burdensome and undesirable, with variance across this perspective being examined only through the lens of differing cultural expectations.

Objective: This phenomenological study aims to understand caregivers' lived experiences based on the perceived “burden” on caregiving for aging individuals with chronic conditions to inform practice.

Methods: Twenty-five phenomenological interviews captured feelings and experiences associated with caregiving for the aging. Qualitative content analysis using a data-driven inductive approach established codes and themes derived from the data. Researchers revealed a consensus level greater than 95%. Member checks and investigator triangulation were implemented to add rigor and validity.

Results: Three main themes emerged, including life-changing in terms of positive outlooks and life balance dynamic; role strain in terms of time and responsibility, processing grief, and lack of resources and support; and role reversal advocacy, as in coming full circle, preconceived notions, and lack of choice.

Conclusion: These findings stress the critical need for providing relevant resources immediately after diagnosis. Healthcare professionals must also focus on exploring how positive experiences can aid in caregiver stress management and improve life-balance dynamics.

Savannah Carr

Occupational Therapy Life Skills Programming for Mothers Experiencing Homelessness

Authors: Savannah Carr, MOT student; Talia Rebottaro, MOT student; Jordan Wozniak, MOT student; Shumaya Zaman, MOT student; Doreen Head, PhD, OTRL; Regina Parnell PhD

Faculty Mentor: Doreen Head, PhD, OTRL; Regina Parnell PhD

Abstract

Introduction: In the United States, nearly 80% of women experiencing homelessness are single mothers. Occupational therapists can aid in their family's transition from homelessness to assisted or independent housing by providing life skills training.

Objective: This research sought to explore the usefulness of various occupation-based life skills interventions with (n=45) mothers residing in homeless shelters. Life skills education modules were provided for these mothers to determine which components of the program effectively addressed the needs of women and their families.

Methods: Occupational therapists and occupational therapy students provided didactic and hands-on life skills modules to three cohorts of mothers residing in homeless shelters, during 2017, 2019, and 2023. Four topics were covered: coping skills, money management, social support and self-esteem. The instruments used included an intake interview and a pre- and post-tests for each topic. Participant received a \$10 CVS gift card per life skill session as an incentive to participate.

Results: Participants were predominantly African American; average age 27 years old. The majority had never married and had two children. Most were unemployed with an income less than \$5,000. Many had 1-2 previous temporary housing placements in the last year and had been at COTS five months. Most had no car and largely relied on public transportation.

Conclusions: To date, overall quantitative outcomes for self-esteem, coping skills, and money management showed higher scores on post-test, than pretest, indicating participants identified increased knowledge following most life skill sessions. Qualitatively, the mothers reported feeling more confident and competent and express plans to use new life skill knowledge in various settings. Study limitations include missing data due to inconsistent participation of this transient population and milieu distractions due to inadequate childcare. Also, it is unknown if participants utilized study information in their future decision-making. Lastly, findings cannot be generalized to others who are experiencing housing insecurity.

Brianne Droste

A Comprehensive Review of Cocaine-Related Autopsy Findings: A Case Study and Literature Review

Authors: Brianne Droste

Abstract

Cocaine use exerts a devastating impact on the human body. Autopsy findings serve as a crucial window into pathologic and anatomic cocaine-associated changes. This article presents a case study and literature review aimed at consolidating and analyzing autopsy data to elucidate the pathological effects of cocaine. The case involves a 60-year-old African American male with multiple possible comorbidities that highlight the multifaceted interplay of cocaine abuse such as hemorrhagic stroke, aortic dissection, and coronary artery disease, ultimately resulting in a fatal cerebrovascular event. A comprehensive search across multiple electronic databases was used to support or dismiss these findings. It illuminates the importance of staying educated on evolving patterns in substance abuse. This article provides insights into the effects of cocaine, reinforcing the importance of autopsy findings and ongoing research.

Megan Hofman

Hand function following nerve transfer surgeries combined with hand training interventions in patients with spinal cord injuries: a scoping review

Authors: Megan Hofman, MOT Student; Kyle Racho, MOT Student; Deanna Sandven, MOT Student; Alexis Staff, MOT Student

Faculty Mentor: Dr. Gino Panza, Ph.D.

Abstract

Introduction: Trauma to the spinal cord can cause significant loss of upper extremity function negatively impacting one's ability to perform many activities of daily living (ADLs) and quality of life (QoL). Nerve transfer surgery combined with hand therapy is an emerging practice which may be a beneficial approach to restore hand function and improve ADLs and QoL. However, therapy modalities following nerve transfer surgeries are not well described creating a disconnect between evidence based interventions and clinical practice.

Objective: To provide a scoping review of hand function following nerve transfer surgeries combined with hand training interventions in patients with spinal cord injuries (SCI). Secondly, we aimed to provide a description of the various hand training protocols following the nerve transfer surgery.

Methods: A literature search was conducted using a PC (Population, Concept) approach. Occupational therapy students conducted a PubMed search of original research articles involving outcomes related to hand function following combinatorial nerve transfer surgery and hand training in those with SCI.

Results: The search from 2018-2023 yielded 61 articles. 8 articles were included that performed tendon and nerve transfers with hand training. 53 articles were excluded because they were not original research articles or did not fit the inclusion criteria. Overall, nerve transfer surgery in combination with hand training resulted in hand function improvements. However, details regarding hand therapy were ambiguous.

Conclusion: Nerve transfer surgery with combinatorial hand training interventions in those with SCI are promising. However, the current literature does not describe the hand training interventions, making it difficult to recreate training conditions. Also, the lack of detailed information regarding hand training may be confounding the outcomes following this combinatorial training. Increased details regarding training could improve reproducibility and provide an opportunity for improved training methods following surgery, resulting in improved hand function and QoL for these individuals.

Miki Kamiya

ASSESSING NON-COGNITIVE SKILLS WHEN INTERVIEWS ARE NOT POSSIBLE: A PILOT STUDY OF THE CANA-HP

Authors: Daniels D'Asia, SPT; Dorais Sierra, SPT; Kamiya Miki, SPT; McLean James, SPT; Maher Sara, PT, PhD, DScPT, OMPT

Faculty Mentor: Sara Maher PT, PhD, DScPT, OMPT

Abstract

INTRODUCTION: Health professionals lack racial and ethnic diversity and may not adequately handle the predicted shift of diverse patients in the next decade. Applications to health professional programs rely heavily on cognitive markers (e.g., grade point average (GPA)), while non-cognitive attributes (e.g., motivation or social skills) may be overlooked. This study examined psychometric properties of a novel methodology designed to assess non-cognitive attributes called the Computer-Based Assessment of Non-cognitive Attributes of Health Professionals (CANA-HP). Specific research questions focused on internal consistency (reliability), construct validity, item difficulty / discrimination, and bias of the methodology. **METHODS:** A convenience sample was used and consisted of applicants invited for remote interviews into a midwestern Doctor of Physical Therapy program. Applicants who met inclusion criteria and consented to the study completed a demographic survey followed by 12 situational judgment tests (six multiple choice and six open-ended (i.e., short answer). Situational judgement tests assess the ability of an applicant to respond to workplace situations. **DATA ANALYSIS:** All data were analyzed using SPSS v. 27.0 or Iteman v. 4.3. Statistical significance was set prior at $p < .05$. In addition to descriptive and frequency statistics, Cronbach's coefficient alpha calculated internal consistency reliability, and Pearson's correlation coefficients were calculated between CANA-HP scores and GRE and GPA scores for construct validity. Item difficulty, item discrimination and bias were analyzed using mean average (P), Rpbis, and Fisher's exact tests, respectively. **RESULTS:** Fifty students participated in the study with an average age of 22.5 years (+ 3.4). The students were primarily female (66.7%), Caucasian (76.5%), and not first-generation college students (92.2%). Internal reliability was poor for the multiple-choice stations ($\alpha = 0.576$), but acceptable for the open-ended stations ($\alpha = 0.739$). No correlation was found between the CANA-HP total scores and standardized cognitive assessments (GRE and GPA scores). The open-ended questions had adequate item difficulty (mean P = 3.04 to 4.72), with low item discrimination for four items (0.02 to 0.19), and poor discrimination on the remaining two items (-0.12 to -0.14). Multiple choice questions were slightly easier (mean P = 4.84 to 12.64) with poor discrimination on four items (-0.05 to -0.25), low discrimination on one item (0.02) and adequate discrimination on the final item (0.25). The instrument was free of bias in the categories of gender, race, first generation status, Pell grant status, and income. **DISCUSSION:** The use of open-ended questions is recommended to assess non-cognitive attributes of applicants into health professions as these items had acceptable internal consistency and item discrimination. In addition, they were not correlated with standard cognitive measures which means they test something different from cognitive skills. Traditional multiple-choice questions need further refinement. Predictive validity

of the tool is still needed. **CONCLUSIONS:** Physical therapists in educational settings could consider adding open-ended ethical questions to the application process when interviews are not feasible.

Anaya Lechnar

Reliability and Validity of the Step Test Evaluation of Performance on Stairs (STEPS) in Persons with Chronic Stroke

Authors: Anaya Lechnar, SPT; Zoey Bezilla, SPT; Cece Findlay, SPT; Bri Pajakowski, SPT

Faculty Mentor: Andrew Moul, PT, DPT, NCS; Nora Fritz, PhD, DPT, NCS; Victoria Pardo, PT, MHS, DHS

Abstract

Introduction: After a stroke, individuals experience neurological changes that make stair climbing challenging. The STEPS outcome measure was created to assess the quality of stair climbing in individuals with Huntington's disease. The establishment of a reliable outcome measure to assess stair navigation in the chronic stroke population would be beneficial to improve patient function and safety.

Objective: The purpose of this study was to determine the reliability and validity of the STEPS tool in the chronic stroke patient population.

Methods: Twenty-four participants with chronic stroke with an average age of 58.96(11.17) years old, an average of 8.29(6.39) years since stroke, and 11 of which were females were recruited and completed walking, balance, and lower extremity measures, including the STEPS tool. The STEPS tool was evaluated by three in-person raters (1 physical therapist (PT) and 2 student PTs). A recording of STEPS performance was assessed by four raters (2 PTs, 2 student PTs) at two time points, 7 days apart.

Results: The STEPS tool demonstrated excellent interrater (ICC = 0.975) and intrarater (ICC = 0.958) reliability, excellent concurrent validity with Four Square Step Test ($r = -0.855$) and Tinetti POMA ($r = 0.811$), and good concurrent validity with Fugl-Meyer LE Score ($r = 0.707$). The STEPS tool had good to excellent concurrent validity with gait velocity across three conditions including normal ($r(22)=0.753$), fast ($r(22)=0.756$), and backward velocity ($r(22)=0.835$), and with gait parameters, like hemi double support times for backward conditions ($r(22)=-0.750$).

Conclusion: The STEPS tool is a valid and reliable outcome measure to assess stair navigation in the chronic stroke population that may be incorporated in the clinical setting.

Mary McLaughlin

Health and Wellness Education Positively Impacts Residents of Low-Income Housing Communities

Authors: McLaughlin M, Holcomb J, Plonka J, Wingett J, Maher S, Dickson J

Faculty Mentor: Dr. Dickson, Dr. Maher

Abstract

INTRODUCTION: The Center for Disease Control (CDC) defines noncommunicable diseases (NCDs) as any condition not directly transmissible from one person to another. NCDs are classified as an epidemic with evidence suggesting that lower income populations are at greater risk. It is within the physical therapist's (PTs) scope of practice to educate on NCDs that impact functional mobility. **OBJECTIVE:** Investigate the impact of PT-led health and wellness workshops (HWWs) to residents of low income housing communities (LIHCs) in metro Detroit. **METHODS:** A quasi-experimental repeated measures design with convenience sampling was used. Each HWW included a presentation about a specific NCD, movement session, and educational handout. Participants completed a pre-workshop survey to document demographic information and answer questions relating to physical activity, exercise selection, nutrition, and healthy lifestyle choices. The post-workshop survey included the same questions with two additional questions regarding ease of incorporation and interest in future workshops. Statistical analysis included Wilcoxon Signed Ranks, ANOVA, and Mann Whitney U. **RESULTS:** Participants included 36 residents from 3 LIHCs in metro Detroit. Knowledge of CDC physical activity guidelines statistically improved ($Z=-2.89$, $p=.004$, $r=.37$) from pre- to post-workshop. Confidence in choosing specific exercises to improve health ($Z=-2.65$, $p=.008$, $r=.33$), select foods based on nutritional content ($Z=-2.95$, $p=.003$, $r=.37$), and identify lifestyle choices that influence health ($Z=-2.89$, $p=.004$, $r=.36$) yielded statistically significant results. No significant differences were found between groups. Ninety-five percent of participants reported interest in attending future PT-led workshops. **CONCLUSION:** PT-led HWWs positively impacted residents of LIHCs in metro Detroit. Resident's knowledge and confidence in identifying risk factors for NCDs significantly improved, with a majority of residents reporting it would be easy to incorporate what they learned into daily routines and interest in attending future workshops.

Karla Montgomery

Pause for Paws: A Drop-In Clinic for Graduate and Professional Students

Authors: Karla Montgomery, BS, OTS; Amber Bywater, BS, OTS; Grace Kubitz, BS, OTS; Morgan Rudolph, BS, OTS; Ciara Ginn, BS, OTS

Faculty Mentor: Dr. Christine Kivlen

Abstract

Introduction. Graduate and professional students experience mental health challenges such as stress, anxiety, and decreased well-being. Our previous research has suggested involvement in focused therapy dog programming results in positive mental health benefits among college graduate students (Kivlen et al., 2022). Furthermore, our previous research suggests a need for a drop-in therapy dog clinic and this type of clinic has not been evaluated in graduate students (Kivlen et al., 2023). **Objective.** The goal of this study is to examine feasibility and effectiveness of a drop-in therapy dog clinic on perceived stress and anxiety in graduate students. **Methods.** Over 16 weeks, participants will complete a survey with 4 outcome measures assessing stress and anxiety, before and after participating in a drop-in therapy dog clinic. We anticipate up to 300 participants, which represents 30% of college enrollment and provides 80% power to detect pre/post changes in stress and anxiety. **Results.** Our planned analysis for program feasibility will use descriptive statistics and we expect the program will be accepted, as evidenced by students from more than 75% of programs attending at least once a month. Additionally, it's anticipated participants will engage in 1-3 activities with the therapy dogs, including but not limited to petting, hugging, giving treats, talking to, and playing with toys with the therapy dog. We anticipate students will demonstrate an average frequency of 1-4x per month for 5-30 minutes/session. Our planned analysis for program effectiveness uses paired t-tests and we anticipate perceived stress and anxiety will show a statistical significance in the mean difference between pre and post-tests. **Conclusion.** Through the use of therapy dog programming, our goal is to improve graduate student's overall well-being. To achieve this goal, student's perceived stress and anxiety will decrease, and satisfaction with life will increase.

Bukelwa Nkungu

Skull Fracture Patterns in Fatal Motor Vehicle Accidents: A Case Reprint

Authors: Bukelwa Nkungu, BSc, Nicole Croom, MD

Faculty Mentor: Lou Mendes-Kramer

Abstract

Every year motor vehicle accidents affect all age groups and cause a significant number of severe injuries and deaths worldwide. There are many contributing factors that increase the incidence of MVAs, including but not limited to the age of the driver, road conditions, being unrestrained, and driving under the influence. The terminal injuries resulting from MVAs are usually due to head trauma, including skull fractures. Skull fractures of varying types occur due to the extreme amount of blunt force created by motor vehicle accidents. Specifically, hinge fractures of the base of the skull require a high impact blunt force to occur. This case report focuses on an example of the type of hinge fracture that can occur in a high-speed motor vehicle accident. The pertinent findings of the autopsy will be discussed and compared to the available literature regarding presentation and complications associated with skull fractures.

Regina Parnell

Community Leisure Programs: A MOT Service-Learning Model

Authors: Regina Parnell, PhD, OTRL

Abstract

Community Leisure Programs: A MOT Service-Learning Model

Introduction: Blending service-learning models into health-care curricula, has been shown to support both academic goals and community objectives. Service-learning allows students to apply course concepts in real-life situations and to evaluate and manage clients' occupational skills in real time. Student advocacy and leadership skills improve through collaboration with community partners when developing projects which simultaneously address student learning needs and programming gaps in community sites.

Objective: Students will...

- Collaborate with faculty and community sites to present leisure programming.
- Incorporate OT theory & practice in the community leisure programs.
- Identify areas of personal enrichment and academic growth opportunities.

Methods: Faculty, students, and community program administrators collaborated to establish service-learning leisure programming goals. Three cohorts (n=80) of first-year MOT students planned and directed leisure programs in Detroit community sites, where minoritized populations with and without disabilities were serviced. Following the service-learning presentations, students completed reflection papers focused on their overall learning experience as well as professionalism and the use of OT concepts. Community administrators provided qualitative feedback on the effectiveness of the service-learning leisure program for their community clients.

Results: Five locations: Homeless shelter; Community center; Afterschool program; Senior day program; Community mental health program. Students successfully implemented leisure programs, incorporating traditional OT therapeutic media including sewing, leatherwork, woodwork, ceramics, and paper crafts. Students identified personal enhancement in self-confidence, leadership skills, critical thinking, and cultural awareness. Opportunities for growth included clinical competence and social justice. Community administrators were delighted with the leisure programs, citing elevated client enjoyment, participation, and the desire to incorporate OT programming in the future.

Conclusions: Student academic learning and community service programming is enhanced by incorporating service-learning projects into the health-care curriculum in collaboration with community entities servicing clients across the lifespan with various abilities and needs.

Rafael Plasencia

Functional Massage Prior to Exercise Delays the Onset of the Physical Working Capacity at the Fatigue Threshold (PWCFT)

Authors: Rafael R. Plasencia, SPT, Jared VanZant, SPT, Stephen C. Charron, SPT, Nicholas M. Manderachia, SPT, Jennifer Dickson P.T., D.P.T., O.M.P.T., and Moh H. Malek, Ph.D.

Faculty Mentor: Moh H. Malek, PhD and Jennifer Dickson, PT, DPT, OMPT

Abstract

Functional massage (FM) is a soft tissue technique that incorporates non-end range joint movement with tissue compression to treat musculotendinous pain and dysfunction. FM is performed to a target muscle and its surrounding soft tissue by compressing the tissue and moving the associated joint to either shorten or lengthen the muscle. As a result, in clinical practice, FM may be used at the beginning of a treatment session to prepare the fibers of the target muscle and surrounding soft tissues for functional activity. The Physical Working Capacity at the Fatigue Threshold (PWCFT) uses surface electromyography (EMG) to demarcate between non-fatiguing and fatiguing exercise. To our knowledge, no studies have examined the efficacy of FM when performed prior to the exercise session. The purpose of this study, therefore, was to determine whether FM pre performance delays the onset of neuromuscular fatigue. We hypothesized that FM would increase maximal power output as well as PWCFT compared to the control condition. Thirteen healthy college-aged men [mean \pm SEM: age, 24.1 \pm 0.5 y; weight, 83.0 \pm 3.2 kg; and height, 1.80 \pm 0.02 m] ranging from 22 to 28 years-old volunteered for the present study. On two occasions separated by at least 7 days, subjects visited the laboratory to perform single-leg knee-extensor ergometer exercise after either receiving 7 min of FM (experimental condition) or no FM (control condition). The results indicated that the onset of neuromuscular fatigue was significantly delayed for the absolute and relative PWCFT (80%) values compared to the control condition. There was, however, no significant mean difference between FM and control for maximal power output. The findings of the present study indicated that FM was effective in delaying neuromuscular fatigue as assessed by PWCFT. These findings may be applicable to both sport and clinical settings as FM prior to exercise may be involved in priming the target muscles.

Joseph Roche

Skeletal muscle structure and function in a mouse model of spinal cord demyelination

Authors: Joseph A. Roche PhD, Gino Dagostino BS, Zaid Alshawabkeh BS, Jawad Tajaldeem BS, Devin Greger BS, Iman Manzoor BS, Alexander Gow PhD

Abstract

Introduction. Claudin-11-deficient mice have been reported to have defective spinal cord myelination, and altered motor control and muscle tone in their hindlimbs.

Objective. We compared claudin-11-deficient mice with strain-, age-, and sex-matched controls (claudin-11-sufficient mice). Our research hypothesis was that deficient mice will have reduced muscle strength and will show a greater resistance to high stretch velocities compared to their sufficient counterparts.

Methods. We studied the ankle dorsiflexor and plantarflexor muscles in deficient and sufficient mice. In a convenience sample of ten claudin-11-deficient and four claudin-11-sufficient mice (3-4 months, males). We recorded the maximum isometric contractile torque of the ankle plantarflexor and dorsiflexor muscles measured in milli-Newton-millimeter (mNmm), and the maximum contractile torque at low (100 degree/s) and high (1200 degree/s) muscle stretch velocities during eccentric contractions to assess spasticity. We also studied structural changes in muscle cross sections stained with hematoxylin and eosin.

Results. One- way ANOVAs were performed. Data are reported as mean +/- SD. Maximum plantarflexor contractile torque was 7800 +/- 1651 mNmm and 9646 +/- 2637 mNmm in deficient and sufficient mice, respectively. Maximum dorsiflexor contractile torque was 1956 +/- 347 mNmm and 2975 +/- 195 mNmm in deficient and sufficient mice, respectively. Spasticity assessed as the ratio of maximum eccentric torque measured at 1200 degree/s to 100 degree/s was 0.94 +/- 0.07 and 0.93 +/- 0.01 in the plantarflexors of deficient and sufficient mice, respectively, and 1.41 +/- 0.19 and 2.1 +/- 0.33 in the dorsiflexors of deficient and sufficient mice, respectively. Differences were not statistically significant ($p > 0.05$). Deficient mice showed no remarkable alterations in muscle structure.

Conclusion. Claudin 11 deficiency in mice does not affect maximum contractile torque and stretch-velocity dependent muscle tone when studied by robotic dynamometry under anesthesia, nor does it prominently affect muscle structure.

Joseph Roche

Muscle fiber-type assessment in a human-to-mouse muscle xenograft model

Authors: Joseph A. Roche PhD, Max Aleshire BS, Griffin Balick BS, Paolo DiMaria BS, and Alex Dusza BS

Abstract

Introduction. Muscle tissue can regenerate through muscle stem cells known as muscle satellite cells (MuSCs). MIME is a technique developed in our laboratory, through which, donor muscle tissue with MuSCs can be implanted into a host muscle to promote donor-cell-derived myogenesis.

Objective. We studied whether or not MuSCs maintain memory of the type of muscle fibers (fast or slow) with which they were associated. We hypothesized that MuSCs do not maintain memory of the fibers with which they are associated and form slow or fast muscle fibers based on the host environment.

Methods. We tested our hypothesis by implanting donor muscle, which contained mostly slow fibers, into host muscle, which contained mostly fast fibers. Implantation of donor tissue was performed by MIME. Following MIME, we injected a myotoxin into the host muscle, which induced concerted degeneration followed by MuSC-dependent regeneration. Specifically, we studied mouse tibialis anterior muscles, which were implanted with segments of human donor tibialis anterior muscle. The human TA is comprised mostly of slow fibers. The mouse TA is comprised 100% of fast fibers. This experimental paradigm is appropriate to ascertain whether or not satellite cells retain memory of the muscle fibers with which they were originally associated. We collected host mouse muscles after 12 weeks of regeneration to ascertain if there was an increase in the percentage of slow muscle fibers.

Results. Quantitative data confirmed that the cluster of human muscle fibers, which regenerated in the host mouse TA muscle had more slow (~50%) than fast (~30%) fibers (T-test, $P < 0.01$, $N = 4$ muscles/mice).

Conclusion. Contrary to our hypothesis, our data suggest that MuSCs do maintain memory of the type of muscle fibers with which they were originally associated. MuSCs give rise to fast or slow muscle fibers based on their donor origin.

Joanne Rush

Preoperative pressure pain threshold utilization in laparoscopic and robotic cholecystectomies and hernia repairs

Authors: Michael D'Agostino, DNAP, CRNA, Nami Edwards, DNAP, CRNA, Jessica Hoefft, DNAP, RNA, David Morse, DNAP, CRNA, Brigid Rojas, DNAP, CRNA, Christopher Gill, PhD, MBA, CRNA, ACNPC-AG, FACHE

Abstract

The use of opioids remains the primary treatment for patients with postoperative pain and surgery may contribute to chronic opioid use in the general population. Pressure pain threshold (PPT) can be utilized to quantify pain intensity using a dolorimeter. PPT has been studied in some surgical populations, but has not been studied in patients undergoing ambulatory robotic and laparoscopic cholecystectomies and hernia repairs. This cross-sectional observational study aimed to understand the relation between preoperative PPT measurements using a dolorimeter and postoperative opioid consumption in patients who underwent ambulatory laparoscopic and robotic assisted cholecystectomies and hernia repairs. It was hypothesized that there would be an inverse correlation of preoperative PPT measurements and postoperative opioid consumption. However, this study found that there was a weak correlation between preoperative PPT measurements and postoperative opioid consumption. This was not a statistically significant correlation.

Shanmin Sultana

Sensory Processing Challenges and Adaptive Behaviors of Children: Retrospective Analysis of Clinical Data

Authors: Christine Azzo, B.S.; Heidi Pickford, B.S.; Shanmin Sultana, B.A.; Sheena Patel, MOT, OTRL; Sandy Glovak, OTRL; Kimberly Banfill, MOT, OTRL; Preethy S. Samuel Ph.D.

Faculty Mentor: Preethy S. Samuel Ph.D.

Abstract

Introduction: One in six children and more than two thirds of children with developmental disabilities are estimated to have sensory processing disorders (SPD). While sensory processing and integration are internal neurological mechanisms that are necessary for adaptive responses, abnormal processing often manifests externally as behavioral problems. Little is known about the empirical relationship between SPD and behaviors. Therefore, the purpose of this study is to evaluate the influence of sensory processing challenges of children on adaptive behaviors.

Methods: A cross-sectional retrospective study design was used to evaluate the association of sensory processing challenges with adaptive behaviors of 143 children aged 2-11 years ($M = 6.20$, $SD = 2.49$) attending an outpatient pediatric clinic in metro-Detroit. Sensory processing challenges were evaluated using the Sensory Processing Measure (SPM) home form that measures challenges in 5 primary domains (vision, auditory, tactile, proprioception, & vestibular), and in 2 higher order domains (praxis & socialization). Adaptive behaviors of children were measured using the Behavioral Assessment System for Children (BASC-3).

Results: The most common diagnoses were poor coordination (32%) and autism (25%). All 7 SPM subscales were significantly correlated with mean adaptive behaviors. Multiple linear regression analysis indicated that an 8-factor model could explain about 51% of variance in adaptive behaviors. The significant predictors of adaptive behaviors were praxis ($\beta = -.37$, $p < .011$), socialization ($\beta = -.32$, $p < .001$), and tactile processing ($\beta = -.21$, $p = .01$) and age of child ($\beta = -.15$, $p = .01$). Negative beta indicates as sensory processing challenges increase, children have fewer adaptive behaviors (leadership, ADLs, functional communication etc.).

Discussion: Results suggest the need for interventions targeting praxis, socialization, and tactile processing to improve adaptive behaviors of children, all skills within the occupational therapy practice framework. Next steps in research include establishing validity of the SPM and BASC-3 and effectiveness of Ayres Sensory Integration therapy®.

Taylor Takla

Impaired mobility negatively impacts navigation ability and map recall in a virtual environment in persons with Multiple Sclerosis

Authors: Taylor N. Takla, BS; Alexis N. Chargo, MOT; Ana M. Daugherty, PhD; Nora E. Fritz, PhD, PT, DPT, NCS

Faculty Mentor: Nora E. Fritz, PhD, PT, DPT, NCS

Abstract

Introduction: Spatial navigation is an essential component for independent living and encompasses one's ability to travel through their environment to reach a goal location. Successful navigation relies on cognitive processing, memory of the environment, and mobility. The role of mobility in the act of navigation is clear, however, its impact on cognition supporting navigation and memory of the environment is unknown. Virtual environments have created opportunities to explore navigation abilities in individuals with mobility impairments, including individuals with Multiple Sclerosis (MS) who experience motor and cognitive deficits.

Objective: Therefore, the goal of this study was to examine relations between mobility and virtual navigation abilities in MS.

Methods: We examined performance in a virtual Morris water maze (vMWM) while seated at a computer and free recall of the environment in 23 ambulatory individuals with MS (18F, 5M, age 25 - 67 years). Mobility was assessed by forward and backward clinical walking tests.

Results: Individuals with slower backward walking velocity required longer time to navigate to the goal location in the vMWM ($r = -.493$, $p = .017$), which suggests a mobility-related cognitive impairment in navigation ability. Though not significant, individuals with slower forward walking velocity had worse map recall of the vMWM ($r = .397$, $p = .067$). Individuals with worse map recall had worse navigation efficiency (time: $r = -.440$, $p = .04$; distance: $r = -.428$, $p = .047$).

Conclusion: These results highlight the unique intersection of cognition and mobility during navigation in persons with MS. Given that the vMWM is performed while seated, evidence of any correlation with mobility suggests differences in cognitive processing that cannot be directly attributed to walking impairments. Future studies should examine navigation abilities and walking performance in a larger sample and evaluate how impairments in mobility may influence cognitive processes that support navigation to better understand this complex relation.

Georgia Young

Anesthesia Knowledge and Electronic Nicotine Delivery Systems

Authors: Aquandralyn Bajric, Adam Millar, Nicole Tront, Red Lozano, Chadley Brunk, Dr. Georgia Young and Valdor Haglund Haglund

Abstract

Electronic nicotine delivery systems (ENDS) have expanded in popularity amongst the public with 20.8% of high school students reporting using these devices in 2018. Smoking ENDS causes various health problems, including lung inflammation, impaired defense against bacterial and viral pathogens, hypertension, tachycardia, and many other negative physiological changes to the human body. Due to the recent adoption of this smoking modality, many anesthesia providers may lack adequate familiarity with ENDS and its potential deleterious effects. To provide safe, individualized anesthesia care, it is crucial for the anesthesia provider to be knowledgeable on this topic. Our research aims to explore the knowledge gap of anesthesia providers concerning ENDS and determine if this social history factor is regularly addressed during the preoperative assessment.

Keywords: e-cigarettes, electronic cigarettes, smoking, vaping, anesthesiology

Chris Armstrong

D-685 Reverses Motor Deficits and Reduces Accumulation of Human alpha-Synuclein Protein in Two Different Parkinson's Disease Animal Models

Authors: Christopher Armstrong, Dan Luo, Banibrata Das, Alope K. Dutta

Faculty Mentor: Dr. Alope Dutta

Abstract

Parkinson's disease is a neurodegenerative disease characterized by tremors, postural instability, and psychiatric and cognitive complications. These symptoms are caused by pathogenic factors that include alpha-synuclein aggregation resulting in the loss of dopamine neurons in the substantia nigra. Many people with PD suffer from dementia, which is characterized by cortical and limbic alpha-synuclein accumulation in the striatum, cortex, and hippocampus. We have developed a multifunctional dopamine agonist molecule, D-520, to target misfolded, toxic aggregates of alpha-synuclein. Its potent activity at dopamine D2 receptors is intended to provide symptomatic relief in PD. The parent molecule has produced robust inhibition against alpha-synuclein protein in in vitro experiments. However, due to the poor absorption and blood brain barrier penetration a prodrug, D-685, was developed. Analyzing whole brain lysate compared to plasma concentrations the prodrug robustly penetrated the blood brain barrier. Our studies further show that D-685 reduces toxic aggregates of alpha-synuclein and phospho-alpha-synuclein in transgenic D-line mouse model compared to the transgenic control. We have demonstrated that the efficacy of the parent drug D-520 has been further enhanced by conversion to the prodrug D-685 as demonstrated in the transgenic animal experiment and the reserpine induced symptomatic PD animal model experiment. Future studies will further examine the efficacy of the prodrug in other relevant animal models to gain further insight into its mechanism of neuroprotection.

Dima Awad

Behavioral and Genomic Responses to BTE *Daphnia pulex* Assessment of the Effects of Individual Constituents Prior to the Evaluation of Mixtures.

Authors: Dima Awad, MS; Rucha Joshi, MS; Zoha Siddiqua, PhD; David K. Pitts, PhD.

Faculty Mentor: David K. Pitts, PhD.

Abstract

Benzene (B), toluene (T), ethylbenzene (E), and xylene (X) are volatile organic compounds (VOCs) derived from petroleum. BTEX exposure may result in toxic interactions (e.g., additive, or synergistic) among the constituents which are not well characterized. The initial focus was to develop methods evaluating the toxic effects of individual constituents before examining effects of mixtures using the invertebrate model *Daphnia pulex*. Effects of exposure to the individual BTE constituents (0 to 243 ppm) on behavior were examined by (1) determining threshold concentrations that cause immobility over a 24hr period (n=10 per concentration), and (2) examining the impact of BTE exposure on *D. pulex* swimming behavior using sublethal concentrations determined by immobility assay. An innovated, sealed, single-well chamber was constructed to examine the swimming behavior of *D. pulex* using optical tracking. Each constituent induced immobility at similar concentrations. Inhibition of swimming behavior also occurred at similar concentrations (10 to 30 ppm) within 2 hrs. of exposure (n=12 for each concentration). An upgraded sealed 6-well chamber is being evaluated which increases throughput and enables more complex behavioral studies. Data derived from behavioral assays were also utilized to evaluate changes in gene expression over 24-hrs of individual BTEX constituents. Significant changes in gene expression relative to media controls were found using 3' RNA-Seq. Data from both behavioral and genomic assays will be used in future mixture toxicology studies in *D. Pulex* and the vertebrate zebrafish to establish potential human biomarkers.

Vibha Deshpande

Investigation of Inhibition of Ferroptosis process by small molecules

Authors:

Vibha Deshpande Masters student, Purba Mazumder, Dinh Luong, Muhammad Tarar, Alope K. Dutta

Faculty Mentor: Dr. Alokke Dutta

Abstract

Introduction: Ferroptosis is a caspase-independent form of regulated cell death driven by iron-induced formation of lipid peroxides that accumulate at toxic levels causing cell death. Under physiological conditions cell combats lipid peroxidation with the help of selenoprotein GPX4. It has a central role in the ferroptotic pathway as it reduces lipid peroxide to lipid alcohol. Our study uses the utility of employing the ferroptosis-inducing compound RSL3 in cellular models to study the mechanism of production and inhibition of ferroptosis. Specifically, our investigation aims to study the molecules with potential antioxidant and iron-chelating properties for their capacity to inhibit the process of ferroptosis.

Methods: Our goal is to evaluate the effect of small molecules in modulating the ferroptosis pathway in cellular models. Test compounds are evaluated in different in vitro assays in PANC-1 cell lines sensitive to production of ferroptosis in presence of ferroptosis-inducing agent RSL3. Ability of test compounds to rescue cells from toxicity and oxidative stress from treatment of RSL3 were evaluated. Both cell viability and DCFDA assays were carried out to judge the potential of compounds in modulating ferroptosis process and provide neuroprotection.

Results: The results show that dose dependent pretreatment of Panc-1 cells with multifunctional neuroprotective compounds D-512 and D-583 could protect the cells from toxicity of RSL-3 significantly compared to RSL-3 treated cells alone. The effect was found to be dose dependent. RSL-3 produces robust reactive oxygen species in Panc-1 cells. However, cells pre-treated with test compounds could dose dependently significantly reduce production of ROS upon exposure to RSL-3. The protection of level of GPX4 from exposure to RSL-3 by test compounds was evaluated.

Conclusion: In conclusion, the findings from this research present promising prospects for advancing innovative therapeutic approaches in the field of Parkinson's disease and other neurodegenerative disorders. Small molecules dopamine agonist with iron chelation and antioxidant properties are able to modulate ferroptosis process and offer a potential avenue to disease modifying therapeutics in PD.

Nikitha Gadipudi

Development of H4 Derived Peptide Inhibitors of the HAT 1-RbAp46 Complex

Authors: Nikitha Gadipudi, MS Pharmaceutical Sciences, Andrew Lipchik, PhD

Faculty Mentor: Andrew Lipchik, PhD

Abstract

Cancer is characterized by rapid cell division and proliferation. The rapid cell division results in an increased demand for nucleotides, which can be treated with agents targeting DNA replication including anthracyclines, platinum salts and taxanes. However, resistance commonly occurs with these therapies leading to disease recurrence. There is a need to develop additional agents that can target rapidly dividing tumors through novel pathways.

Chromatin, through the production of histones, is required to support DNA replication during cell division. Presently, no therapeutics target chromatin replication directly. Our prior research indicates that HAT1 serves as a critical regulator of histone H3 and H4 levels and influences cell cycle progression, findings validated in a tumor model, rendering it an attractive drug target.

While a library of small molecule inhibitors to suppress HAT1 enzymatic activity has been explored, the emergence of resistance mechanisms by other histone acetyltransferases (HATs) and poor pharmacokinetics and pharmacodynamics highlights the need for an alternative strategy. Previous studies have shown the effects of knocking down Rbap46, which enhances HAT1 catalytic activity, resulting in more potent inhibition of H3 and H4. This observation leads to the hypothesis that disrupting Rbap46's scaffolding function within the HAT1-Rbap46 complex could yield superior inhibition of H4.

In this study, we suggest the application of an alpha-helix peptide originating from H4 as a potential inhibitor for disrupting the interaction between the HAT 1-Rbap46 complex and the H3-H4 dimer, with the aim of impeding nucleosome synthesis and suppressing tumor growth. Our strategy for developing this inhibitor involves the utilization of peptide stapling. This technique induces an alpha-helical conformation by connecting two specific amino acids on the same side of the helix. To assess the characteristics of our peptide, we performed circular dichroism (CD) to evaluate its alpha-helical structure and utilized microscale thermophoresis (MST) to ascertain the binding affinity of a specific peptide, revealing a binding affinity of 210nM.

Noah Gleason

Novel Insights into roles of Small G Protein Guanine Dissociation Stimulator (smgGDS) in insulin secretion in Pancreatic Beta Cells

Authors: Noah Gleason, MS; Carol Williams, PhD; Anjaneyulu Kowluru, PhD

Faculty Mentor: Anjaneyulu Kowluru, PhD

Abstract

Introduction: smgGDS has been implicated in the regulatory control of newly synthesized small G protein prenylation signaling modules. Two splice variants of smgGDS with distinct functions have been reported. smgGDS-607 binds unprenylated small G proteins while smgGDS-558, which lacks one of the thirteen armadillo domains found in smgGDS-607, binds prenylated small G proteins. The following studies provide novel and important groundwork regarding the role of smgGDS within the pancreatic beta-cell.

Objective: The overall objective of these studies are to ascertain the subcellular distribution of smgGDS between the cytosolic and membrane fractions in pancreatic beta-cells.

Methods: Clonal insulin-secreting beta (INS-1 832/13) cells were cultured for specified periods of time in presence of basal glucose (2.5 mM) or high glucose (20 mM), membrane and cytosolic fractions were isolated using the MEM-Per Plus kit (Thermo Fischer) or confocal microscopy.

Results: Immunoblotting studies revealed that both splice variants of smgGDS are expressed in human islets, rat islets and INS-1 832/13 cells. Transfection of smgGDS-siRNA resulted in significant knockdown of both smgGDS splice variants in INS-1 832/13 cells. A significant inhibition (-52%) of glucose-stimulated insulin secretion (GSIS) was observed in INS-1 832/13 cells following siRNA-mediated depletion of smgGDS. In addition, insulin secretion elicited by a membrane depolarizing concentration of KCl (increased calcium influx), forskolin (increased cAMP generation) or IBMX (inhibition of phosphodiesterase (PDE)) was inhibited by -49%, -27%, and -28%, respectively. Subcellular distribution studies revealed no significant alterations in the abundance of smgGDS in the cytosolic and membrane fractions during the 45-minute period of stimulation of INS-1 832/13 cells by stimulatory (insulinotropic) concentration of glucose.

Conclusions: Based on these findings, we conclude that smgGDS is expressed in human islets, rodent islets, and clonal beta cells, and that it plays regulatory roles in insulin secretion derived from glucose metabolic events, including calcium- and cAMP-dependent signaling steps.

Rucha Joshi

Behavioral and Genomic Responses to Xylene in *Daphnia pulex*

Authors: Rucha Joshi M.S., Dima Awad M.S., Zoha Siddiqua PhD, David K. Pitts PhD

Faculty Mentor: Dr. David K. Pitts, PhD.

Abstract

Human exposure to volatile organic chemicals (VOCs) is known to have harmful effects, but our knowledge of toxic mechanisms and our ability to diagnose exposure is limited due to the lack of biomarkers of exposure. Exposure to volatile petroleum products like BTEX is of particular concern. This study aimed to determine the toxic behavioral endpoints and transcriptomic changes resulting from xylene exposure using the invertebrate animal model *Daphnia pulex*. An immobility assay (IM) was done to determine xylene's potency and sublethal behavioral toxicity.

IM10 values were calculated as the concentration that produces immobility in 10% of the animals.

40 ml EPA vials with xylene dissolved in COMBO culture media (0 to 50 PPM) were used to evaluate immobility. The mobility of each Daphnid was visually recorded at specified time points over 24 hrs.

When averaged across all time points, the IM10 value for xylene was found to be approximately 20 ppm. This IM10 value was then used to inform genomic studies and keep concentrations in the sublethal range. A genomic assay utilizing EPA vials exposed animals over a 24-hour period to 10 ppm xylene.

Xylene inhibits swimming behavior and causes 10% immobility at 20 ppm. Significant changes in gene expression at 10 ppm relative to COMBO controls were found using Quantseq. The analysis of the significantly altered genes is ongoing. Data from both behavioral and genomic assays will be used in future studies to examine BTEX mixture toxicology in *D. pulex* and zebrafish to establish potential human biomarkers.

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 Gadameedi, PhD; Andrew Lipchik, PhD

Faculty Mentor: Andrew Lipchik, PhD.

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 were characterized using circular dichroism. Membrane permeability of the peptides were assessed with a cellular uptake assay in the C2C12 cell line. Insulin sensitization was determined by measuring Akt activation via phosphorylation status in a cellular model of IR in the C2C12 cell line.

Results: Pak1 derived peptides displayed alpha helical properties in an induced fit binding model. They also exhibited robust displays of membrane permeability with the use of the cell penetrating peptide Xentry. Additionally, treatment with the Pak1 peptides was sufficient to restore insulin sensitivity in vitro in the skeletal muscle model of IR.

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

Ashley Pall

The Characterization of Iron Targeting Drugs in Treating Friedreich's Ataxia

Authors: Ashley Pall B.S.; Danielle Bailey, PhD; Daniel Kosman, PhD; Timothy L. Stemmler, PhD

Faculty Mentor: Timothy Stemmler, PhD.

Abstract

Cytotoxic accumulation of iron in the mitochondria is the primary pathogenic event driving the rare and fatal neurodegenerative movement disorder, Friedreich's Ataxia (FRDA). Clinically, early age of onset and rapid disease progression met with poor standard of care highlights the urgent need for FRDA therapeutics. Modulating mitochondrial iron overload using iron chelating drugs that have been clinically approved for the treatment of systemic iron overload diseases is an attractive approach to address the critical need for FRDA therapeutics. However, to date, these drugs are reported to disrupt intrinsic iron homeostasis in FRDA and therefore fail to move past early phase FRDA clinical trials. Promisingly, novel iron chelators in clinical development exist to treat other intracellular iron overload disorders such as Parkinson's and Alzheimer's Disease but have yet to be investigated in the context of FRDA. Moreover, the biophysical characterization of both traditional and novel iron chelating drugs is largely absent, underscoring a fundamental disconnect between disease treatment and understanding of outcome. Here, we use an in vitro approach to investigate the iron binding properties of both traditional and non-canonical iron chelating compounds. Our studies indicate, that the novel iron chelator PBT434 possesses unique iron binding properties relative to traditional iron chelators, thus advocating PBT434 as an ideal proponent for applications in treating intracellular iron overload and further supporting continued analysis as a potential FRDA therapeutic.

Arifur Rahman

Proteomic profiling of PNPLA3 mutants in human hepatocytes reveals potential pathways in non-alcoholic fatty liver disease

Authors: Arifur Rahman, M. Pharm.; Xiangmin Zhang, PhD; Ruchi Jaiswal; Zheyun Peng; Wanqing Liu, PhD; and Zhengping Yi, PhD.

Faculty Mentor: Zhengping Yi, PhD; and Wanqing Liu, PhD.

Abstract

Non-alcoholic fatty liver disease (NAFLD) has emerged as the most prevalent chronic liver disease and a significant health concern worldwide. Approximately 80 million individuals in the United States are suffering from NAFLD. However, the underlying molecular mechanism of NAFLD formation is still poorly understood. Most importantly, there are no FDA-approved therapeutics available for NAFLD management yet.

Patatin-like phospholipase domain-containing protein 3 (PNPLA3) plays a crucial role in lipid metabolism, particularly in hepatocytes. Genome-wide association studies (GWAS) have identified a prominent variant of the PNPLA3 gene, denoted as I148M, which can affect the liver's ability to process lipids. The 148M allele leads to lipid droplet formation by accumulating triglycerides in the liver, increasing the risk of liver cirrhosis and fibrosis as well. Meanwhile, another PNPLA3 variant, S453I, more common in African Americans, was associated with a reduced risk of developing NAFLD.

We hypothesize that mutations of PNPLA3 lead to differentiated interactions between PNPLA3 and other proteins in human hepatic cells, which may further result in a different capacity of hepatocytes to modulate lipid homeostasis. The overall goal aims to address this knowledge gap by performing a proteomic analysis to discover the interactome of each PNPLA3 isoform using in vitro cell studies. We now report the preliminary findings of comparative proteomics experiments examining how PNPLA3 and its mutations affect protein abundance patterns overall. Our analysis revealed a total of 4503 proteins with at least 2 unique peptides and a confidence level exceeding 99.99%. By considering a 2-fold change and a P-value <0.001 between the groups, we have pinpointed 42 proteins that exhibit substantial variation between the 148I and the 148M isoforms. Gene ontology and pathway enrichment analyses demonstrated significant enrichments in cellular proliferation, catabolic processes, and lipid metabolism pathways. With regard to their molecular functions, lipid binding and glutathione transferase activity were the most prevalent. According to pathway analysis using KEGG and Reactome, these proteins are primarily involved in lipid and glutathione metabolism. More studies are ongoing in the group.

Amirreza Samarbakhsh

Discovery and Development of Broad-spectrum Antiviral Therapeutics by Targeting PL-Protease

Authors: Amirreza Samarbakhsh, MS; Hariprasad Aruri, PhD; Dineshsinha Chauhan, PhD; Abdullah Al-Homoudi, MS; Ladislau Kovari, PhD; Pawan Singh, PhD; Navnath Gavande, PhD

Faculty Mentor: Navnath Gavande, PhD.

Abstract

The transmission of betacoronaviruses from animal hosts to humans has caused severe consequences formed as an outbreak and changed our lives especially during the last couple years. Severe acute respiratory syndrome (SARS-CoV-2) originates from a group of betacoronaviruses known as subgroup 2b. Therefore, 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. It was revealed that the papain-like protease (PLpro) has narrow substrate specificity for K48 polyubiquitin and ISG15 originating from certain species, which its inhibition could stop the 2b members biological pathway. To design the candidate molecules to act as PLpro inhibitors, computational docking helped to understand the interaction between inhibitor binding pocket of PLpro with the hit molecules (GRL-0617, GRL-0667, Compound 19), and our designed molecules. After the development and synthesis of the potential inhibitors, we assessed percent inhibition and IC50 using FRET based assay with a ubiquitin-based substrate. The lead compounds were then tested for antiviral and cytotoxic activities which showed moderate improvement compared to the parent compounds.

Angel Schilke

The Design, Synthesis, and Inhibition of *Clostridioides difficile* Spore Germination by Bicyclic Tertiary Amide Analogs of Chololate

Authors: Angel R. Schilke; Shiv K. Sharma, Ph.D.; Jacqueline R. Phan, Ph.D.; Christopher Yip, Ph.D.; Prateek V. Sharma, Ernesto Abel-Santos, Ph.D.; and Steven M. Firestine, Ph.D.

Faculty Mentor: Steven M. Firestine, PhD.

Abstract

Clostridioides difficile infection (CDI) is a major identifiable cause of antibiotic-associated diarrhea. In our previous study (*J. Med Chem*, 2018, 61, 6759-6778), we have identified N-phenyl-cholan-24-amide as a potent inhibitor of spore germination. The most potent compounds in our previous work are N-arylamides. We were interested in the role that the conformation of the amide plays in activity. Previous research has shown that secondary N-arylamides exist exclusively in the coplanar trans conformation while tertiary N-methyl-N-arylamides exist in a non-planar, cis conformation. The N-methyl-N-phenyl-cholan-24-amide was 17-fold less active compared to the parent compounds suggesting the importance of the orientation of the phenyl ring. To lock the phenyl ring into a trans conformation, cyclic tertiary amides were prepared. Indoline and quinoline cholan-24-amides were both inhibitors of spore germination; however, the indoline analogs were most potent. Isoindoline and isoquinoline amides were inactive. We found that the simple indoline derivative gave an IC₅₀ value of 1 μ M, while the 5'-fluoro-substituted compound (5d) possessed an IC₅₀ of 400 nM. To our knowledge, 5d is the most potent known spore germination inhibitor described to date. Taken together, our results indicate that the trans, coplanar conformation of the phenyl ring is required for potent inhibition.

Marcella Sharma

A Fragment-Based Thermal Binding Screen for the Identification of Binders of Bacterial N5-CAIR Mutase

Authors: Marcella F. Sharma; Aaron Robida, PhD; Nick Santoro, PhD; Steven M. Firestine, PhD.

Faculty Mentor: Steven M. Firestine, PhD.

Abstract

Annually, the United States encounters 2.8 million antimicrobial resistant infections that results in 35,000 deaths per year. Alarmingly, six of the top 18 antimicrobial resistance threats are costing the U.S. more than \$4.6 billion dollars annually. In addition, we are no longer in the Golden Age of antibiotic drug discovery to keep up with this demand. This is putting microbes at an advantage, a terrifying reality that we cannot afford. Our research is aimed at using target-based drug discovery to identify novel bacterial enzyme inhibitors. It has been shown that bacteria rely on the de novo purine biosynthesis pathway to produce the necessary biomolecules to support bacterial survival. Within this pathway, we are focusing on the step where 5-aminoimidazole ribonucleotide (AIR) is enzymatically converted to 4-carboxy-5-aminoimidazole ribonucleotide (CAIR) using two unique bacterial enzyme, N5-CAIR synthetase (PurK) and N5-CAIR mutase (PurE). In higher eukaryotes, this conversion occurs, but through a different mechanism where AIR is directly carboxylated by AIR carboxylase to produce CAIR. Because of this deviation, we can selectively target the bacterial pathway, making it a very attractive antimicrobial target. Our interest lies in the development of PurE inhibitors since there is strong evidence supporting the critical role of this enzyme in bacterial survival. To find novel PurE binders, we dedicated our efforts to developing and optimizing a sensitive thermal binding assay that has a Z' of 0.89 that was used to identify fragments that bind to PurE. This assay overcomes the shortcomings of previously used absorbance and fluorescence-based activity assays and can also be used for a high-throughput screen. We present the results of a 4500 fragments screen that was conducted at the University of Michigan's Center for Chemical Genomics (CCG) along with follow-up dose dependence studies in the thermal binding and an activity assay.

Elizabeth Slane

Flame Retardant-Induced Neural Cell Death

Authors: Elizabeth Slane, M.S.; Brian Cummings, Ph.D.

Faculty Mentor: Dr. Brian Cummings, PhD.

Abstract

Flame Retardants (FRs) prevent the growth of fire and are used in many consumer and industrial products. Numerous FRs are linked to decreased neurological function, including learning and memory, which is partially mediated by the hippocampus. Recent studies from our laboratory demonstrate that FRs alter lipid metabolism in the hippocampus. Lipins are phosphatidic phosphohydrolases that regulate lipid metabolism by mediating the conversion of phosphatidic acid to diacylglycerol. The overall goal of this research is to understand the role of lipin in the mechanism of FR-induced neural cell death. Towards this we tested the toxicity of different classes of FRs in vitro in HT-22 cells (mouse hippocampal), and NE-4C cells (mouse neural stem cells). Both lipin 1 and 2 expression were detected in both cells as demonstrated by immunoblot analysis. Treatment of both neural cells with the lipin inhibitors propranolol and atenolol did not induce toxicity as determined by cell and nuclear morphology, and MTT staining. In contrast, curcumin induced time- and concentration-dependent toxicity. Further, both brominated (BFRs) and organophosphate flame retardants (OPFRs) induced toxicity. While all BFR's tested induced cell death, OPFRs had variable effects on toxicity, with tris (2-ethylhexyl) phosphate and triphenyl phosphate causing little to no toxicity in HT-22 cells, and all OPFRs tested inducing concentration-dependent toxicity in NE-4C cells. These data demonstrate that BFRs and OPFRs induce neural cell toxicity, but that OPFRs are less toxic than BFRs. Further research will define the role of lipin in FR-induced neural cell death.

Li Tao

A modified method to extract DNA from FFPE samples

Authors: Li Tao, M.Sc.; Yang Jiang, MD; Wanqing Liu, Ph.D.

Faculty Mentor: Wanqing Liu Ph.D.

Abstract

Formalin-fixed paraffin-embedded (FFPE) samples have proven to be a feasible source for genomic (gDNA) extraction, sequencing and genotyping. However, the current protocols for extracting gDNA from FFPE tissues require relatively large sample amount, limiting the usage of FFPE samples with small quantity. We aim in this study to improve the yield of DNA extraction from FFPE samples. Specifically, we optimized the deparaffinization, protein digestion, and gDNA lysis steps and tested in extracting DNA from FFPE liver samples with different sample quantity. Our findings indicated that with standard commercial kits, an extended heating step combined with a manual removal of paraffin significantly increased the DNA yield by % (how much percentage?) without affecting the DNA quality. Our improved technique provides an improved strategy for isolating gDNA from FFPE samples, increasing the chance of sample usage when the quantity of biospecimen sample is limited.

Jacob Tartamella

Design and Synthesis of Small Molecule Covalent Inhibitors for SARS-CoV-2 PLpro

Authors: Jacob Tartamella, MS; Narva Kushwaha, PhD; Abdullah Al-Homoudi, PhD; Ladislau Kovari, PhD; Navnath Gavande, PhD.

Faculty Mentor: Navnath Gavande, PhD.

Abstract

Papain-like protease (PLpro) is a viral protease essential for the viral replication of SARS-CoV-2 due to the proteolytic cleavage of polypeptide 1a (pp1a) and polypeptide 1b (pp1b) causing the release of non-structural proteins (NSPs) that have various essential functions for the production and release of new virions. In addition to the importance of PLpro for viral replication, the viral protease also aids in the evasion from the host immune response by cleaving Interferon Stimulated Gene product 15 (ISG15) off host and viral proteins which promotes the interference of viral proteins in host translational machinery and the proper formation of mature virions among other functions. Moreover, the nucleotide sequence of PLpro is highly conserved in the coronaviridae family with a sequence homology around 80% adding to its attractiveness as a therapeutic target. As a result of the important function of PLpro in viral replication, suppression of the host immune response, and its highly conserved amino acid sequence, PLpro has been recognized as a viable and attractive target for the development of both noncovalent and covalent inhibitors. In this project, we seek to further develop covalent inhibitors for SARS-CoV-2 PLpro by synthesizing compounds based on the non-covalent inhibitor, GRL-0617, due to its favorable and unique interactions with PLpro previously determined in crystallography studies. To date, we have synthesized a few covalent inhibitors based on our structure-based drug design approach and assessed their PLpro inhibitory and anti-viral activities using FRET-based and cell-based assays, respectively.

Duy Long

Tumor Stroma-Penetrating Oligomicelles Containing Combination Payload for Reversal of Drug Resistance and Immune Modulation in Kidney Cancer

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

Faculty Mentor: Arun Iyer, PhD

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.

Jyotsna Jajula

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

Authors: Jyotsna Jajula, Salma Althobaiti, Prahlad Parajuli, Samaresh Sau, Navnath Gavande and Arun K. Iyer

Faculty Mentor: Arun 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. **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 pH-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.

Hariprasad Aruri

Development of novel and effective hydroxyquinoline analogs for the treatment of Zika virus

Authors: Hariprasad Aruri, Ph.D; Sneha Singh, Ph.D; Susmita Das, Ph.D; Prahlad Parajuli, Ph.D; Pawan Kumar Singh, Ph.D; Ashok Kumar, Ph.D; Navnath S. Gavande, Ph.D.

Faculty Mentor: Dr. Navnatah Gavande, PhD.

Abstract

Zika virus (ZIKV) is an emerging RNA virus which not only causes neurological but also ocular abnormalities in infants. In infected cells, ZIKV exploit autophagic processes to enhance its replication and spread. Thus, a range of autophagy inhibitors have emerged as promising strategies to combat RNA virus infections, with hydroxychloroquine (HCQ) being one of the most promising. In this study, we synthesized and assessed the antiviral activity of HCQ analogs and determined the underlying mechanisms. Among the ten synthesized compounds, two novel drug candidates, GL-287 and GL-382, displayed potent antiviral effects against ZIKV infection in human ocular cells, primarily by inhibiting autophagy. The two analogs surpassed the antiviral efficacy of HCQ and other promising autophagy inhibitor drugs like ROC-325, GNS561, and DC661. Moreover, unlike HCQ, these drugs did not exhibit cytotoxicity in the ocular cells. Treatment with compounds GL-287 and GL-382 in ZIKV-infected cells increased the abundance of LC3 puncta, indicating an accumulation of autophagic vacuoles, which suggests a disruption of the autophagy process. Furthermore, compounds GL-287 and GL-382 effectively inhibited the ZIKV induced antiviral and inflammatory response in ocular cells. Collectively, our study demonstrates antiviral potential of novel compounds 287 and 382 against ZIKV via inhibiting autophagy.

Zhao Fei

Mild Intermittent Hypoxia Improves Hand Function in a Participant with Motor Incomplete Cervical Spinal Cord Injury

Authors: Fei Zhao, Ph.D.; Megan Hofman; Lexi Soltesz; Haya Javaid; Orena Koka; Jack Smith; Gino Panza, Ph.D.

Faculty Mentor: Gino Panza, PhD.

Abstract

Introduction: Individuals living with spinal cord injury (SCI) have a decline of hand function. Mild Intermittent Hypoxia (MIH), as a developing intervention, may improve hand function in people with SCI.

Objective: To determine the effect of 8 days of MIH on hand function in participants with motor incomplete SCI.

Methods: Three individuals with motor incomplete SCI (C4, T1, C7. AIS: 1 D, 2 C) aged 44 +/- 3.61 (2 Male, 1 Female) with signs and symptoms of autonomic dysfunction. Individuals underwent MIH each morning. MIH consisted of twelve two-minute bouts of hypoxia interspersed with two-minutes of normoxic recovery. Slight hypercapnia (+2 mmHg) was maintained throughout the entire protocol after an initial 10 minutes of breathing normoxic air. MIH was administered for 8 days over 2 weeks. The primary outcome is the Graded Redefined Assessment of Strength, Sensibility, and Prehension (GRASSP). Comparisons were made at baseline, following MIH on day 1 and 8, and after 8-day MIH (post-MIH). Data for right and left arm were averaged as a fraction of baseline.

Results: Small increases in strength (1.05 +/- 0.05), sensation (1.14 +/- 0.18), and prehension performance (1.04 +/- 0.04) were found following Day 1's MIH. However, small improvements were only found for strength (1.11 +/- 0.07) and prehension performance (1.07 +/- 0.04), but not sensation at post-MIH. The largest increase was found in the morning at the 8th day. Following 8 days of MIH, increased strength (1.17 +/- 0.05), sensation (1.24 +/- 0.12) and prehension performance (1.09 +/- 0.06) were found.

Conclusions: MIH increases hand function as evidenced in 3 individuals with motor incomplete SCI. The last day following MIH shows the largest improvements. Acute exposure may result in increased strength, sensation, and prehension performance, but repeated MIH exposure may not augment this effect.

Narva Deshwar Kushwaha

Development of small-molecule inhibitors of SOS1-KRAS interactions for cancer therapy

Authors: Narva Deshwar Kushwaha, PhD, Hariprasad Aruri, PhD, Jeremy M. Kelm, Pharm.D, Evan Malin, BS, Navnath S. Gavande, PhD.

Faculty Mentor: Navnath S. Gavande, PhD.

Abstract

Kirsten rat sarcoma viral oncogene homolog (KRAS) is a prevalent oncogene causing pancreatic, colorectal, and non-small cell lung cancers making it a prime target for the development of small molecule inhibitors for decades. The interaction between son of sevenless 1 (SOS1) gene and KRAS is crucial for activating signals of growth and survival through the mitogen activated protein kinase (MAPK) pathway in a range of cancers. So inhibiting SOS1, a KRAS activator and important feedback node, represents an effective approach to treat KRAS-driven cancers. Since, efforts to directly target KRAS have been largely unsuccessful due to its high affinity for GTP/GDP, and the lack of a clear binding pocket. Recently a highly potent, selective, and orally bioavailable small-molecule SOS1 inhibitor (BI-3406) that binds to the catalytic domain of SOS1 has been developed. BI-3406 has been shown to significantly reduce formation of GTP-loaded KRAS (activated KRAS), thereby inhibiting downstream MAPK signalling to prevent the growth and survival of tumor cells. Herein, we synthesized a diverse library of SOS1 inhibitors and examined their activity using HTRF assay and western blot analysis.

Zhenjie Liu

Co-inhibition of FADS1 and SCD-1 Synergizes Suppression of Renal Cancer Cell Growth Via Induction of ER Stress

Authors: Zhenjie Liu, Ph.D.; Jiang Yang, M.D.

Faculty Mentor: Wanqing Liu, Ph.D.

Abstract

Desaturated fatty acids, including monounsaturated fatty acids (MUFAs) and polyunsaturated fatty acids (PUFAs), play a pivotal role in cancer cell growth by maintaining function of bio-membrane system, supplying energy, generating intermediate metabolites and signaling molecules. Fatty Acid Desaturase-1 (FADS1) is a key enzyme involved in PUFA metabolism, while Stearoyl coenzyme A desaturase-1 (SCD-1) catalyzes MUFA production. We and others have demonstrated that both FADS1 and SCD1 play important role in cancer cell growth and proliferation. Inhibiting each of them induces ER stress and demonstrates anti-cancer effects. We hypothesize that lipid desaturation to produce MUFA and PUFA is alternatively required to maintain ER homeostasis and cancer cell growth. In this study, we treated renal cancer cells (786-O, ACHN, and A498) with inhibitors respectively targeting FADS1 and SCD-1 alone or together, followed by evaluation of cell proliferation and apoptosis. Remarkably, our findings demonstrated that treatment with FADS1 and SCD-1 inhibitors synergistically impeded the growth and proliferation of renal cancer cells and induced cell apoptosis. Moreover, our results revealed that inhibiting each of the enzymes induced the expression of another. While each inhibitor induces increased ER stress, co-inhibiting significantly synergizes this effect. Collectively, our study indicates that intracellular MUFA and PUFA production is key to maintain ER homeostasis and co-inhibition of both lipid desaturation pathways is potentially synthetic lethal to cancer cells by inducing unresolvable ER stress. This data provides novel insights into the therapeutic potential of targeting FADS1 and SCD-1 in the treatment of renal cancers and beyond.

Patrick Monaghan

Measurement Properties of Backward Walking and its Sensitivity and Feasibility in Predicting Falls in Persons with Multiple Sclerosis.

Authors: Patrick G. Monaghan, PhD; Taylor N. Takla, BS; Alexis N. Chargo, MOT; Erin M. Edwards, PhD; Biaohua Yu, MS; Emily Myers, BS; Ana M. Daugherty, PhD; Nora E. Fritz, PhD, DPT

Faculty Mentor: Dr. Nora Fritz, PhD, DPT

Abstract

Introduction: People with Multiple Sclerosis (PwMS) experience mobility impairments elevating fall risk. The adverse consequences of falls highlight the need to identify clinical measures that accurately predict falls in PwMS. Backward walking (BW) better differentiates fallers from non-fallers in PwMS. However, no studies have evaluated psychometrics of the Backward Walking Timed 25 Foot Walk (BW-T25FW) or BW outcome measures such as BW velocity, nor have evaluated the predictive utility of BW for prospective fall risk in MS or its association with activity level.

Objective: This study aimed to assess the reliability and responsiveness of the BW-T25FW and BW metrics, including BW velocity. Additionally, it sought to investigate the feasibility of using BW for predicting falls at three and six months and examine its associations with activity levels.

Methods: 23 PwMS completed the forward (FW) and BW-T25WT. Spatiotemporal measures of FW and BW were also recorded. To assess test-retest reliability, participants completed two study visits, separated by one week. Falls and activity levels were tracked for the subsequent six months. Test-retest consistency was estimated with an intraclass correlation coefficient, and the minimum detectable change was also computed. Correlation analyses assessed the relationship between BW and prospective falls and activity levels.

Results: BW-T25WT and BW velocity exhibited excellent test-retest reliability. Large effect sizes to interpret clinically meaningful change in the BW-T25WT and BW velocity were also found. Both metrics demonstrated modest negative correlations with falls at 3 and 6 months and correlated strongly with very active minutes at 3- and 6-months post-study.

Conclusion: The BW-T25W and BW velocity are effective and reliable in clinical use for evaluating functional mobility in PwMS, highlighting that they are sensitive to subtle changes and may be an impactful marker for tracking disease progression and treatment efficacy.

Prahlad Parajuli

Encapsulation of CD40 agonist antibody (CD40a) in tumor-targeted smart nanolipid reduces tumor growth and enhances anti-tumor immune activity while minimizing systemic toxicity

Authors: Prahlad Parajuli, Salma Althobaiti, Duy Luong, Arun Iyer, Navnath Gavande

Faculty Mentor: Navnath Gavande, Ph.D.

Abstract

Pancreatic ductal adenocarcinoma (PDAC) is refractory to immunotherapy because the dense desmoplastic stroma hinders immune cell infiltration. Agonistic CD40 mAb (CD40a) is capable of inducing immune cell activation, tumor infiltration, and attenuation of desmoplasia. However, therapeutic studies with CD40a have shown only modest efficacy and high systemic toxicity due to lack of tumor-targeted delivery. Here, we report that encapsulation of CD40a in low extracellular pH (pHe)-triggered membrane adhesive nanoliposomes (pHTANL-CD40a) sequesters CD40a from systemic circulation and enables sustained release in the tumor intracellular space upon cell membrane adhesion. Treatment of PDAC (Panc02) transplanted mice with pHTANL-CD40a reduced tumor growth, enhanced tumor immune infiltration/activation, and conferred a survival advantage compared to vehicle and free-CD40a. Importantly, pHTANL-CD40a treatment also resulted in significantly lower systemic toxicity as indicated by minimal loss of body weight, minimal kidney and liver deformity, and reduced serum levels of liver enzyme alanine transaminase (ALT) and inflammatory cytokine IL-6. This study demonstrates that encapsulation in smart nanolipid enhances in vivo efficacy of CD40a, reduces systemic toxicity, and will potentially sensitize pancreatic cancer to immunotherapy using checkpoint inhibitors.

Rola Raychouni

Performance of ChatGPT for Pharmacy Education Questions.

Authors: Rola Raychouni PharmD., Wanqing Liu Ph.D.

Faculty Mentor: Dr. Wanqing Liu Ph.D.

Abstract

Introduction: Many fields of science have been quickly embracing artificial intelligence (AI) and it has already impacted many aspects of our daily life, changing the way we think and approach questions. It remains debatable how OpenAI chat bot can be utilized as a tool facilitating medical and pharmacy education and learning. Literatures examining the accuracy of Open AI chatbots in response to pharmacy questions and their impact on pharmacy education are scarce.

Objective: To test the accuracy of ChatGPT in answering general pharmacy education questions that are expected to be part of pharmacists' or pharmacy students' knowledge.

Method: The experiment tested how ChatGPT answered general pharmacy education questions that were gathered from online NAPLEX practice exams and continuing education articles. Fifty questions were divided into broad categories including: pharmacotherapy, pharmacovigilance, and dosing. The questions tested analytical intelligence and were rated by difficulty level as basic, analytical, or creative.

Results: In answering all 50 questions, ChatGPT had an average accuracy rate of 58%. The accuracy rate decreased as the questions became more difficult: the accuracy rates are 69% (22/32), 45% (5/11), and 29% (2/7) for questions defined to basic, analytical, and creative levels, respectively. ChatGPT performed well in answering pharmacotherapy and pharmacovigilance questions, with an accuracy rate of 70% (21/30). However, calculations can be identified as a weakness with ChatGPT when answering dosing questions with only 40% accuracy rate (8/20). ChatGPT is subject to be confused with complex wording. It demonstrated limited comprehension of hidden messages embedded in questions and depends on clear, simple, and straight forward information. Its capacity is also largely limited in making decisions and reverting to general answers like following directions of the physician when asked to choose an appropriate plan. Its responses are also unpredictable, with often answering simple questions wrong while other complex questions correctly.

Conclusion: This preliminary study should serve as a warning to pharmacists and pharmacy students to exercise caution and verify answers provided by ChatGPT as its responses cannot be trusted to be accurate at the present status of the Chatbot.

Bassil Adam

Targeted remodeling of the extracellular matrix with a branched peptide PD-1 agonist as immunotherapy for Type 1 Diabetes (T1D)

Authors: Bassil Adam; Jitender Dev Gaddameedi, PhD; Andrew Lipchik, PhD.

Faculty Mentor: Andrew Lipchik, PhD

Abstract

Introduction: T1D is an autoimmune disorder characterized by the loss of insulin production due to T-cell-dependent destruction of beta cells. Currently, there are no curative therapies for T1D. While allogenic beta cell transplants offer promise, autoimmunity persists. Therapies must be developed to protect beta cells and maintain insulin production. Programmed Cell Death Protein 1 (PD-1), a key regulator of immune suppression, maintains self-tolerance by interacting with its ligand PD-L1. This interaction inhibits inflammation and leads to T-cell anergy. Enhancing PD-1:PD-L1 signaling holds promise for preserving beta cell survival and restoring tolerance.

Objective: We aim to reinforce PD-1:PD-L1 signaling by remodeling the extracellular matrix. We propose using a branched peptide with a PD-1 peptide agonist and dibenzocyclooctyne (DBCO) for direct conjugation to beta cells via click chemistry with a metabolically incorporated azide-sugar. The branched peptide allows control over agonist levels, broad surface coverage, and flexible binding. After confirming peptides' incorporation into the extracellular matrix, we'll assess their impact on beta cell survival and T cell activity which we hypothesize will prevent T cell-mediated beta cell death.

Methods: We used microwave-assisted solid-phase peptide synthesis to produce a series of branched peptides with PD-1 peptide ligand and DBCO for cell surface labeling. Azide incorporation in the beta cell extracellular matrix was achieved through metabolic labeling with azide-containing sialic acid precursor (ManNAc). Compound presence was confirmed using fluorescent microscopy, and we tested T-cell cytotoxicity using the insulinoma cell line, INS-1, and primary murine T cells.

Results: Three branched peptides with varying PD-1 agonist stoichiometries (two, four, and eight) were synthesized. Control peptides with scrambled sequences were also made. Our peptides were incorporated into the beta cell extracellular matrix leading to T-cell inhibition.

Conclusions: In conclusion, our branched peptide PD-1 agonist shows promise as a T1D therapeutic which warrants further development.

Shaylyn Avery

Impact of Sequential Administration of Ampicillin and Daptomycin along with Bacteriophage against *Enterococcus faecium*

Authors: Shaylyn Avery, Undergraduate student; Callan R. Bleick, PharmD; Samantha Vader, BS; Sumaiya Mohib, Undergraduate student; Biswajit Biswas, MD; Cesar A. Arias, MD, MSc, PhD; Michael J. Rybak, PharmD, MPH, PhD

Faculty Mentor: Dr. Michael Rybak, PharmD, MPH, PhD

Abstract

Introduction: The combination of Daptomycin (DAP), and ampicillin (AMP) has been an effective therapy against multidrug-resistant *E. faecium* (Efc_m). Bacteriophage (phages) in combination with antibiotics has been shown to exhibit synergistic activity.

Objective: We aim to assess the relationship between phage and Efc_m while administering antibiotics sequentially during the phage lytic cycle by observing 4h bacterial survival assays via spectrophotometric analysis.

Methods: *E. faecium* clinical isolate, HOU503, was utilized with bacteriophage, NV-503-01, provided by the Naval Medical Research Center. Phage was quantified and propagated to a MOI of approximately 10⁸-9. AMP and DAP were prepared at a final concentration of 128mg/L and 1mg/L, respectively. HOU503 grew to stationary phase in BHI and cells were harvested the next day by centrifugation, washed in PBS, and read via spectrophotometer to an OD₆₀₀ of 1.0 (1x10⁸ CFU/mL). Each reaction was set up in a 1.5mL microcentrifuge tube in triplicate. Organism stock and phage were diluted with a solution of RPMI and calcium for a final volume of 500uL after the addition of the antibiotics. Samples were incubated at 37°C. 50 uL of each DAP and AMP were added to applicable tubes at time points of 1h, 2h, and 3h. Samples were plated in triplicate on BHI agar after 4-h of incubation. After 24h of incubation, colonies were counted and analyzed. Data is expressed as mean percent survival. Samples were spectrophotometrically analyzed to identify concentrations of HOU503 over 24h. Data was expressed as growth suppression curves.

Results: AMP and DAP administration with phage at 0h accomplished the targeted bacterial survival rate against Efc_m. AMP, DAP, and phage combined with HOU503 simultaneously resulted in significantly ($p < 0.05$) lower bacterial survival compared to administration at 1, 2, and 3h.

Conclusion: Utilizing bacterial survival assays via spectrophotometric analysis, we observed considerable enhancement in the eradication of multi-drug resistant Efc_m with the addition of AMP, DAP, and phage simultaneously. Further investigating sequential dosing with phages in combination with various isolates and antibiotics will shed light on the impact this interaction has in antibiotic administration with phage.

Anna Ganey

Radiation Induced Second Malignancies

Authors: Anna Ganey; Amna Alzuad; Zach Adkins; Melana Beavers; Mackenzie Heilman; Peyton Hodgson; Matthew Leone; Jessica Li; Taylor Makowicki; Chloe McKenzie;

Abstract

Introduction: Radiation used in the treatment of malignancies is an effective treatment choice which can decrease recurrence and improve site specific disease. Despite this, it has the potential to induce an adverse late side effect, radiation induced secondary malignancies. In this systematic review, we will summarize the occurrence of radiation induced secondary malignancies (RISM) with specific focus on its causality and methods to reduce its incidence.

Methods: The Wayne State University Library System and database PubMed were used to conduct an optimized search for studies, systemic reviews, and meta-analysis of RISM from creation to August 15, 2023. Studies including any association to RISM were screened, and those particularly associated with Hodgkin Lymphoma, breast malignancy, and pediatric malignancy were included for further analysis.

Results: Factors contributing to RISM include age, diagnosis, and treatment type, among other low risk factors. Pediatric populations are more susceptible to RISM with evidence from multiple studies and literature reviews. Increasing age is also a contributing factor, which increases the probability of RISM as a patient ages. Patients who are diagnosed and treated for Hodgkin's Lymphoma have a higher risk of developing RISM, as well as breast cancer patients. In addition, it was found that chemotherapy agents may increase the susceptibility for RISM in some patients. Radiation treatment modalities, such as 3DCRT, IMRT, VMAT, and PBRT, also play a role in RISM.

Conclusions: Radiation therapy for malignant tumors has the risk of producing secondary malignancies in patients. In order to advance the field of radiation therapy, it is imperative that the contributing factors are identified and minimized to reduce late side effects.

Robert Kina

Staphylococcus aureus propagation through filtration membranes

Authors: Robert Kina, undergraduate student; Paula Smolenski, BS. MS.; Andrew Berti, Pharm.D. Ph.D.;

Faculty Mentor: Andrew D Berti, Pharm.D. Ph.D.

Abstract

Introduction: Staphylococcus aureus bacteremia is a major healthcare issue due, in part, to its ability to cause difficult-to-treat osteomyelitis. Microbial invasion of the osteocyte lacuna-canalicular network (OLCN) enables it to evade the body's immune system and establish a chronic infection. Designing effective therapies requires replication of OLCN conditions. A commercial microfluidic silicon membrane canalicular array (uSiM-CA) is cost-prohibitive for routine screening and analyses. In this study, we designed a cost-effective alternative model using variant syringe filter membranes in replicating the propagation of *S. aureus* of the OLCN.

Methods: Methicillin-resistant *S. aureus* (MRSA) strain LAC was cultivated in Mueller-Hinton Broth. Filtration membranes tested included: surfactant-free cellulose acetate (SFCA) 0.2 μm , Nalgene Polyethersulfone (PES) 0.45 μm , and Titan3 glass microfiber (GMF) 0.7 μm . Bacteria ($\sim 10^8$ cfu/mL) were added to the upper chamber and incubated for up to 48 hours. Media in the lower chamber was supplemented with resazurin (50 $\mu\text{g/mL}$) to provide colorimetric detection of viable bacteria. Where indicated, media were supplemented with Tween 80 to inhibit biofilm production. Following incubation, all model components were cultured, and viability was verified via microscopy and lysostaphin if growth occurred.

Results: PES 0.45 μm membranes permitted *S. aureus* propagation into the intermediate tube, confirmed via microscopy, and lysostaphin enzyme. However, both the SFCA 0.2 μm and Titan3 GMF 0.7 μm membranes only permitted a faint resazurin color change with no viability in the intermediate tube.

Conclusions: Implementing the microfluidic silicon membrane is a vital tool in replicating the OLCN. However, current limitations such as cost hinder its ability to be widely used and studied. Our model, while cost-effective, does not replace the necessary membrane in replicating the OLCN conditions.

Hainan Li

Inhibition of G protein-coupled receptor 35 accelerates wound healing through augmenting endothelial function

Authors: Hainan Li, MS; Liping Xu, BS; Jie-Mei Wang, MD, PHD.

Faculty Mentor: Jie-Mei Wang, MD, PHD.

Abstract

Introduction: G protein-coupled receptor 35 (GPR35) is associated with various pathologies, including diabetes, but the precise function and underlying mechanisms are less understood. Oxidative stress responsive 1 (OXSR1) is a serine/threonine protein kinase involved in various processes, such as response to environmental stress, acting as a regulator of angiogenesis and blood pressure. We hypothesized that the inhibition of GPR35 pace wound healing by augmenting endothelial function by targeting OXSR1.

Methods and Results: Human dermal microvascular endothelial cells (HDMVECs) from healthy subjects and type 2 diabetic patients at passage 5-7 were cultured in vitro. The GPR35 knockdown by siRNA in HDMVECs improved cell migration (Modified Boyden Chamber assay, n=5) and proliferation (BrdU assay, n=5), and these were reversed by simultaneously knocking down OXSR1. Fluorescent staining suggested that the decreased OXSR1 in HDMVECs exposed to high glucose (25 mM) for 72 hours was reversed by GPR35 siRNA (n=5, p<0.05). Meanwhile, the transfection of adenovirus carrying GPR35 gene (Ad-GPR35) diminished OXSR1 protein expression (Western Blot, n=5). In the in vivo study, topical delivery of GPR35 siRNA onto the wounds accelerated wound closure in type 2 diabetic mice (7-mm full-thickness excisional wound, n=4-5, p< 0.05).

Conclusions: Our data suggested that the inhibition of GPR35 can accelerate wound closure, possibly through activation of OXSR1 signaling in endothelial cells. This study provided novel evidence for a potential therapeutic target in tissue repair in hyperglycemia.

Evan Malin

Biological Analysis of Potent and Novel USP10 Inhibitors for the Treatment of FLT3-ITD-Positive Acute Myeloid Leukemia and Non-Small Cell Lung Cancer (NSCLC)

Authors: Evan Malin (B.Sc.); Huy Nguyen (MS), Amirreza Samarbakhsh (PhD); Hariprasad Aruri (PhD); Prahlad Parajuli (PhD); Navnath S. Gavande (PhD)

Faculty Mentor: Navnath Gavande, PhD

Abstract

Ubiquitin-specific peptidase 10 (USP10) has been shown to be implicated in a number of different cancers including breast cancers, prostate cancers, leukemia, and lung cancer. While its role in cancer isn't fully understood, its ability to prevent proteasomal degradation of target proteins via the cleaving of ubiquitin tags allows oncogenic proteins to become stabilized when they otherwise wouldn't. As such, stabilized and mutated proteins are allowed to flourish and contribute to the proliferation of tumors. Our objective is to analyze the efficacy of novel USP10 inhibitors developed in our lab and to compare them against reported nonselective USP10 inhibitors like Wu-5, P22077, and HBX19818. We have performed viability assays by alamarBlue and MTT assays and quantitative analysis of HDAC6 and FLT3 in non-small cell lung cancer (NSCLC) and acute myeloid leukemia (AML) cell lines, respectively using Western Blots. We analyzed downstream effectors of HDAC6 in NSCLC such as alpha-tubulin and the autophagy markers LC3B-I and LC3B-II to evaluate the mechanism of action of our new inhibitors. The results herein demonstrate outstanding potential for one of our developed USP10 inhibitors with an IC50 of 10 uM in both USP10 enzymatic and viability assays. One of our lead compounds exhibit significantly better USP10 inhibition than the previously reported inhibitors Wu-5, P22077, and HBX19818. The inhibition of USP10 allows for ubiquitinated proteins to become degraded by the proteasome which leads to anti-proliferative effects in tumors.

Shelby Schons

Simulated Urine Cases for Laboratory Teaching of Clinical Laboratory Science Students

Authors: Shelby Schons, MaryAnne Stewart, Ed.D., MLS (CSMLS)

Faculty Mentor: MaryAnne Stewart, Ed.D., MLS (CSMLS)

Abstract

Simulated urine samples are used as a safe and reliable alternative to real patient samples for clinical laboratory science students to analyze and diagnose. This study aims to create effective simulated urine samples for the purpose of education and to evaluate the quality of the samples created in this exercise. Three samples were created, a normal sample, a diabetes mellitus case, and a urinary tract infection case. These samples were simulated using chemicals and cells that mimic physical, chemical, and microscopic properties of these three conditions. The results showed that the samples were consistent with the conditions they aimed to imitate in all three categories with few exceptions. While this exercise produced satisfactory results the methods for creating simulated urine samples require further study as it is an invaluable tool in clinical laboratory science education.

Lexi Soltesz

8 Days of Mild Intermittent Hypoxia Improves Autonomic Dysreflexia and Orthostatic Hypotension in Individuals with Motor Incomplete Spinal Cord Injuries

Authors: Lexi Soltesz; Fei Zhao, Ph.D.; Megan Hofman; Haya Javaid; Jack Smith; Orena Koka; Gino Panza, Ph.D.

Faculty Mentor: Gino Panza, Ph.D.

Abstract Introduction: Individuals with spinal cord injury (SCI) experience autonomic dysfunction resulting in autonomic dysreflexia (AD) and orthostatic hypotension (OH) which are uncontrolled rises and drops in blood pressure (BP). Objective: To investigate the impact of mild intermittent hypoxia (MIH) on Autonomic Dysreflexia (AD) and Orthostatic Hypotension (OH) in individuals with motor incomplete spinal cord injury (SCI).

Methods: Three individuals with motor incomplete SCI (C4, T1, C7/T5, AIS: 1 D, 2 C) aged 43 +/- 3.461 (1 Male, 2 Female) with signs and symptoms of autonomic dysfunction. Individuals underwent MIH each morning which consisted of twelve two-minute bouts of hypoxia interspersed with two-minutes of normoxia. Slight hypercapnia (+2 mmHg) was maintained throughout the entire protocol after an initial 10 minutes of breathing normoxic air. MIH was administered for 8 days over 2 weeks. Individuals with sleep apnea were treated with continuous positive airway pressure throughout the 2 weeks. Autonomic dysreflexia (AD) and Orthostatic Hypotension (OH) were measured before, the day after, and 2 weeks following the completion of the MIH protocol. AD was elicited by inflating a tourniquet to 300-mmHg around the participants' thighs for 6 minutes. OH was elicited with a sit-up test. AD and OH were calculated as the max and minimum, respectively, blood pressures (BP) compared to a 3-minute normoxic baseline. Blood pressure was measured with a finger beat-to-beat blood pressure device.

Results: Thigh occlusion resulted in an increase in systolic and diastolic BP of 19.72 +/- 1.86 and 15.67 +/- 4.14 mmHg, respectively. Sit-up test resulted in a reduction in systolic and diastolic BP of 30.32 +/- 10.15 and 14.45 +/- 4.79 mmHg, respectively. Following 8 days of MIH the magnitude of systolic and diastolic BP during thigh occlusion was 10.96 +/- 2.84 (P = 0.03) and 10.00 +/- 2.82 (P = 0.07) resulting in a 46 +/- 0.10 and 36 +/- 0.06 percent improvement. Likewise, the improvement in AD was maintained for up to 2-weeks following MIH for systolic BP (13.16 +/- 3.19, P = 0.048) but not diastolic BP (11.11 +/- 3.87, P = 0.12). Following MIH, systolic and diastolic BP during the sit-up test improved from - 30.32 +/- 10.15 to - 0.60 +/- 13.06 (P = 0.01) and - 14.45 +/- 4.79 to 6.08 +/- 7.93 (P = 0.076) resulting in a 133 +/- 55 and 169 +/- 56% improvement. However, following 2 weeks systolic and diastolic BP during the sit-up was -8.79 +/- 6.81 (P = 0.31) and -1.06 +/- 6.86 (P = 0.37) which was a 53 +/- 28 and 59 +/- 51 percent improvement. No significant differences were found for heart rate during AD (9.23 +/- 9.34 vs 15.58 +/- 10.36 vs 5.61 +/- 1.49) or OH (-3.01 +/- 6.16 vs 1.35 +/- 4.97 vs - 4.50 +/- 4.41) for pre-, post- and 2 weeks following MIH, respectively.

Conclusion: 8 days of MIH improved the BP changes associated with both AD and OH during in-lab provocation. These data suggest that partial improvement in these outcomes may be sustained for at least 2 weeks following MIH.