EUGENE APPLEBAUM COLLEGE OF PHARMACY & HEALTH SCIENCES

16th Annual Research Day

Wednesday, October 16, 2019

Table of Contents

Organizing Committees

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Diane Adamo (Chair ex efficio)

Kyle Burghardt

Kathleen Chardenet

Fei Chen

Malcolm Cutchin (Serving Associate Chair)

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Paul Kilgore (Chair)

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Michael J. Rybak

Timothy Stemmler (Assoc Dean of Research)

MaryAnne Stewart

Research Forum Administrative Committee

Marissa Rossman

Daisy Wright

Ayushi Kumar

Agenda

8:00 AM	**Poster Setup**
9:00 AM	**Student Poster Presentations**
10:45 AM	**Transition to Auditorium for Award Ceremony**

11:00 AM — **Welcome**

Catherine Lysack, Ph.D., Interim Dean

Denise Figlewicz, Ph.D., Assistant Vice President for Research Enhancement and Development

11:06 AM — **Keynote Address**

Introduction, Jiemei Wang, MD, Ph.D.
Keynote Speaker, Timothy Billiar, MD

12:00 PM — **Presentation of Awards**

POSTER AWARDS

Paul E. Kilgore, MPH, MD, FACP	Malcolm Cutchin, Ph.D.
College Research Committee Chair	Research Committee Assoc Chair

COLLEGE FACULTY RESEARCH RECOGNITION AWARDS

Tim Stemmler, Ph.D.	Diane Adamo, Ph.D., M.S., OTR
Associate Dean for Research	Research Committee Chair *ex officio*

12:30 PM — **Lunch**

Lunch is provided for those who registered for the event. Thank you!

12:30 – 3:00 PM — **Poster Display and Presentation**

Guest Speaker: Timothy R. Billiar, MD

Dr. Timothy Billiar is the George Vance Foster Professor and Chair, Department of Surgery, Vice-President and Chief Academic Officer, University of Pittsburgh Physicians and Associate Medical Director, UPMC International.

Timothy R. Billiar, M.D. received his undergraduate degree from Doane College in 1979 and a medical degree from the University of Chicago in 1983. He then completed training in general surgery at the University of Minnesota and the University of Pittsburgh. This included a four-year research training fellowship.

In 1992, Dr. Billiar joined the faculty of the Department of Surgery University of Pittsburgh as a trauma surgeon. Since 1999, Dr. Billiar has served as Chair of the Department of Surgery at the University of Pittsburgh and the George Vance Foster Endowed Chair. Dr. Billiar has a long standing clinical and research interest in trauma, shock and sepsis. In research that has been funded by the National Institutes of Health since 1989, Dr. Billiar's laboratory has contributed to fundamental discoveries on the mechanisms leading to dysfunction of the immune system after injury or severe infection. His laboratory has also contributed to discoveries on the regulation and function of the inducible nitric oxide synthase.

Dr. Billiar is past President of the Society of University Surgeons, the Nitric Oxide Society, the Surgical Infection Society, and the Shock Society, USA. In 2006, Dr. Billiar was inducted into the National Academy of Medicine, USA and in 2011 was named Distinguished Professor of Surgery at the University of Pittsburgh. He is also past recipient of the Flance-Karl Award and the Medallion for Scientific Achievement from the American Surgical Association and the Award for Scientific Achievement from the Shock Society. In 2016, he received the Friendship Award from the People's Republic of China and a Distinguished Service Award from the University of Chicago. In 2018 he was awarded the Jonathan E. Rhoads Medal from the American Philosophical Society and the Sheen Award from the American College of Surgeons.

Abtracts

Faculty

ABSTRACT NO. 1	
Name	MaryAnne Stewart
Category	Faculty
Title	Clinical Laboratory Science and Nursing Co-Curricular Interprofessional Education Simulation
Authors	MaryAnne Stewart, EdD; Erik Carter, PhD; Elizabeth McQuillen, PhD
Abtract	Introduction: The impact that interprofessional education has on health care professions is profound, which ultimately leads to better patient outcomes. Although Clinical Laboratory Scientists and Nurses work closely together within the healthcare team there has been little to no research done on interprofessional education as students between these two professions. To address this, simulated hospital scenarios, based on patient cases and test results, have been created in a team role-play experience. The primary focus was to build on communication and collaboration between two disciplines: Nursing students (n=78) and Clinical Laboratory Scientist students (n=24). Methods: The main research question focused on exploring if interprofessional education using a peer-peer problem-based learning approach enhances learning for cohort Clinical Laboratory Science and Nursing students. This mixed-methods approach utilizes pre and post quantitative survey results on interprofessional professionalism and a qualitative reflection portion that incorporates professional development. Results: Results showed that the student's readiness to participate and attitudes improved following participation of the IPE simulation. Survey results also showed a significant increase in respect and understanding for each other's profession following the IPE simulation. Students reported that the greatest benefit to this experience was in their communication skills using patient-case scenarios. Conclusion: Creating an IPE simulation between nursing and clinical laboratory science students improved their understanding and attitudes of the other respective profession. Further evaluation of the impact of this exercise on learning outcomes is warranted. Key Words: simulation, interprofessional education, nursing, clinical laboratory science

ABSTRACT NO. 2	
Name	Doreen Head
Category	Faculty
Title	Occupational Therapy Life Skills Programming for Mothers Experiencing Homelessness
Authors	Doreen Head, PhD, OTRL; Regina Parnell, PhD, OTRL; Alyssa Ouellette, MOTS; Karly Schrader, MOTS; Amber Severin, MOTS
Abtract	Over the years deinstitutionalization and the outsourcing of mental health services from hospitals to community settings are among many factors that have severely reduced the number of medical model mental health settings for occupational therapy (OT) fieldwork opportunities. Understandably, there has also been a sharp decline in the number of occupational therapists choosing to practice in mental health settings. Despite these challenges, the field has maintained its commitment to this practice area by requiring that students have at least one fieldwork experience with a psycho-social focus "that influences engagement in occupation" (AOTA, 2016). Fortunately, the profession has expanded treatment into new practice arenas and supported the development of alternative fieldwork education options, however strategies needed to secure non-traditional mental health placements remain complex (American Occupational Therapy Association [AOTA], 2010; Scheinholtz, 2010). There is limited evidence on effective interventions for enhancing the occupational performance of mothers experiencing homelessness. Studies suggest some individuals living in homeless shelter's lack knowledge and abilities to perform basic life skills such as money management, maintaining permanent housing, acquiring gainful employment, good nutrition, and effective coping mechanisms. There is an urgent need for more research to demonstrate the effectiveness of OT interventions with this population. Literature suggests that OT has an appropriate role. It is likely that mothers residing in transient housing would benefit from an occupation based life skills training program. However, research is needed to determine which life skill training modules would be advantageous, Thomas et al. (2011). This study seeks to explore the effectiveness of various occupation based life skills interventions with mothers residing in a homeless shelter to determine which components of life skills programming best addresses the needs of women and families experiencing homelessness. This poster presentation will describe the steps taken by the WSU Master of Occupational Therapy (MOT) program to cultivate relationships with community partners. This multi-year project at The Coalition On Temporary Shelter (COTS) addressed the life-skill needs of women and children experiencing homelessness. The mothers participated in the Life-Skills workshop; covering 4 topics; coping, social support, self-esteem building, and financial management. The 90 – 120 minutes life-skills sessions included worksheets, discussion, and hands-on activities. Participants completed pre-tests and post-tests to measure quantitative and qualitative effectiveness of the intervention. Demographic information was also collected. Participants were compensated with a $10 CVS gift card for each completed life skills topic, up to $40 for participation. To date positive quantitative trends are noticed in each of the four life skills, despite relatively small sample size (N - 33). Qualitative analyses reveal that participants felt they increased their overall knowledge in each of the life skills, with financial management unit being described as the most helpful. Because of the longstanding relationship between faculty and COTS administrators, students have had opportunities to volunteer and assist faculty on this research project. The setting exposes students to the role of OT in a community based organization, provides an opportunity to develop clinical reasoning, assessment and task analysis, research protocol, apply communication skills and enhance cultural awareness.

ABSTRACT NO. 3	
Name	Martha Schiller
Category	Faculty
Title	Interprofessional Collaboration Assessment of Students in Physical Therapy at Wayne State University
Authors	Martha Schiller, DPT; Kristina Reid, DPT
Abtract	Introduction: Interprofessional collaboration (IPC) is needed for Interprofessional collaborative practice (IPCP) for all health care professionals. Physical therapist (PT) students need to develop the skills of interprofessional collaboration (IPC) as part of their academic and clinical curriculum. Starting in 2018, this became a requirement for PT Programs according to the Commission on Accreditation in Physical Therapy. Programs need to assess student readiness for entry level IPC to ensure the behaviors required are met before graduation. The purpose of the study was to assess interprofessional collaboration behaviors of DPT students in their final clinical experiences across a variety of settings using the Interprofessional Collaborator Assessment Rubric (ICAR). Subjects: Subjects consisted of 57 clinical instructors (CIs) of 55 DPT Students METHOD: Students and CIs were informed of the study by the Director of Clinical Education with an introduction to the ICAR. CIs working with consenting students during their final clinical experiences in 2017/18 and 2018/2019 were invited to participate. CIs completed the ICAR for their students using a 9 point scale in 6 areas of IPC including communication, collaboration, roles and responsibilities, collaborative patient/client-family centered approach, team functioning and conflict management. A rating of 5 was defined as "expected" performance with 0 being well below expected performance and 9 being well above expected performance. CI education was provided using email instruction to all CI's including an optional training session. Data was analyzed using descriptive statistics for CI demographics and IPC behaviors using SPSS, version 25. Results: CIs were a mean age of 36.2 + 9.8 with a range from 27-63 years. Previous CI training was reported by 74%. More than 10 years of practice was reported by 42%, and 33% had been a CI for over 10 years. CIs represented multiple settings, including acute care, rehabilitation, outpatient and pediatrics. Mean ratings for all collaborative behaviors were above 5: communication (7.1 + 1.5), collaboration (6.8 + 1.7), roles and responsibilities (6.6 + 1.7), collaborative patient/client-family centered approach(7.0 + 1.5), team functioning (6.9 + 1.6), conflict management (6.5 + 2.2), collaboration ability compared to other students (7.0+ 1.7). Ranges were from 2-9, and all behaviors had a low range below 5. Discussion: Although mean ratings for all collaborative behaviors were above 5.0, not all students met the expected standard. Students rated below the expected standard may not be prepared for real world clinical practice. Differences in rating below expected level between cohorts may indicate the addition of intentional teaching and student self-assessment in the clinical and academic environments enhances student readiness for IPCP. To ensure all students are prepared for interprofessional collaborative practice, assessment of IPC may be beneficial to include as part of their terminal course assessment. CONCLUSIONS: Interprofessional collaborative IPC behaviors are being demonstrated in multiple settings by most students in their final year of clinical education. However not all students met the expected level of 5 in all areas indicating a need for didactic and clinical interprofessional collaborative practice education and experiences to prepare PT students for clinical practice. Acknowledgements: Funding through WSU Program Assessment Grant

ABSTRACT NO. 4	
Name	Wangqing Liu
Category	Faculty
Title	Genetic and Developmental Variation of the Pharmacogenome in Children
Authors	Zhipeng Liu, Xiaokun Wang, Wanqing Liu
Abtract	Background: Dynamic changes happen in Drug-Metabolizing Enzymes and Transporters (DMET) function in children at the genome-wide level. However, how age and genetic factors together determine the variation of DEMT function remains incompletely understood. Aim: To investigate the effects of age and genetic factors on DMET expression during human development. Method and Materials: We collected a cohort of pediatric liver samples (n = 109) with different developmental stages. Whole-genome genotyping and RNA-seq were performed to obtain the genetic variations and mRNA profiling of each sample. ANOVA was used to identify genes whose expressions are significantly different among different age groups. The effect of the interaction between age and genetic factors on gene expression was evaluated by a linear regression model. Due to the drastic difference of gene expression patterns between prenatal and postnatal livers, we analyzed the two groups separately and compare the results afterward. Results: We identified 177 genes that are significantly associated with age in prenatal livers (FDR < 0.05), among which 13 genes are key pharmacogenes and 94 are GWAS related genes. Significant age-genetics interactions were found to affect 2099 gene expressions (FDR < 0.05), among which 21 are pharmacogenes and 438 are GWAS genes. For the postnatal child livers, there are 236 genes found to be significantly correlated with age, among which 7 genes are pharmacogenes and 127 are GWAS genes. Similarly, we found 1695 significant Gene X Age eQTLs in the postnatal group (FDR < 0.05), among which 4 are pharmacogenes and 274 are GWAS genes. Conclusion: Age broadly affects gene expression, and many key pharmacogenes and disease-related genes are significantly affected by both age and genetic variants.

ABSTRACT NO. 5	
Name	Zhihui Qin
Category	Faculty
Title	Isothiocyanate-containing hybrid androgen receptor (AR) antagonist depletes AR and induces ferroptosis in GSH-deficient prostate cancer cells
Authors	Zhihui Qin, Liping Xu, Siyu Ou
Abtract	Purpose: Androgen receptor (AR) over-expression, mutation and the emergence of AR splice variants (AR-Vs) promote disease-driving AR signaling in castration-resistant prostate cancer (CRPC). In addition to the sustained AR activation, apoptosis evasion adds extra hurdle for treating hormone refractory disease. To overcome these challenges, we firstly designed isothiocyanate (ITC)-containing hybrid AR antagonist (ITC-ARi) and then rationally combined ITC-ARi with glutathione (GSH) biosynthesis inhibitor buthionine sulphoximine (BSO) to efficiently downregulate AR/AR-V and induce ferroptosis (an alternative cell death mechanism) in CRPC cells.

Methodology: Naturally occurring ITCs (e.g., sulforaphane) display pleiotropic anti-PCa activities. A representative ITC-ARi 2-63 is designed by incorporating ITC into an AR ligand scaffold. The sulfhydryl reactivity of ITC is transiently masked as N-acetyl cysteine (NAC) conjugate that gradually releases parental free ITC in aqueous solution. Because the anticancer effects of ITC/ITC-NAC conjugate are attenuated by GSH-participated conjugation or thiol exchange, we rationally combined 2-63 with BSO for enhanced anti-PCa activities.

Results: Hybrid drug 2-63 antagonizes AR transactivation, downregulates AR/AR-V7, and upregulates cellular stress markers Hsp70 and heme oxygenase-1 (HO-1), indicating the disruption of heat shock proteins (Hsps) and the activation of Nrf2 pathway. More importantly, 2-63 and BSO combination synergistically reduces viability of multiple PCa cell lines, and the noncancerous prostatic RWPE-1 cell is much less affected. Because 2-63 plus BSO does not upregulate typical apoptosis markers, we investigated alternative cell death mechanism in this combinatorial treatment. Drug combination-caused cell viability loss is effectively rescued by iron chelator (deferoxamine, DFO), antioxidants (α-tocopherol (α-Toc), ferrostatin-1 (Fer-1)) or the inhibitor of HO-1 (Zinc (II) protoporphyrin IX, ZnPP). Both Fer-1 and α-Toc are potent radical scavengers blocking lipid hydroperoxide generation, and ZnPP suppresses HO-1-catalyzed upregulation of intracellular Fe^{2+}. The reverse of growth suppression by DFO, antioxidants and ZnPP supports the induction of ferroptosis, a regulated non-apoptotic cell death caused by reactive oxygen species (ROS)- and iron-dependent lipid peroxidation. 2-63 and BSO also more efficiently downregulate AR/AR-V than 2-63 alone in Enz-resistant PCa cells. Interestingly, ferroptosis-preventing DFO and Fer-1 do not rescue AR/AR-V7 and are unable to suppress the upregulation of Hsp70 and HO-1.

Conclusion: Our results suggest that the synergism of 2-63 and BSO occurs through increasing drug accessibility to cellular targets, expanding availability of iron and potentially affecting glutathione peroxidase 4 (GPX4) activity, the most important cellular defense to eliminate lipid hydroperoxide. Combining ITC-ARi and GSH-depleting agents could be a new concept leading to effective CRPC treatment. |

ABSTRACT NO. 6	
Name	Xiangmin Zhang
Category	Faculty
Title	Insulin Receptor Catalyzes PLCG1 Phosphorylation
Authors	Xiangmin Zhang, M.D, Ph.D; Aktham Mestareehi; Berhane Seyoum, Ph.D; Zhengping Yi, Ph.D
Abtract	Phospholipase C, gamma 1 (PLCG1) is a signal transducer of tyrosine kinases and is activated in multiple receptor tyrosine kinase signaling pathways. PLCG1 interacts with the insulin receptor (IR) via its pleckstrin homology domain and plays a role in insulin-stimulated glucose uptake in adipocytes. Tyrosine phosphorylation of PLCG1 has been shown to regulate PLCG1 activity and plays a key role in various downstream signaling pathways. To determine the role of PLCG1 in skeletal muscle insulin resistance, we identified a site-specific PLCG1 tyrosine phosphorylation at 771 (pTyr771) which was positively correlated with insulin sensitivity. Using in vitro differentiated human skeletal muscle myotubes, we found that PLCG1 pTyr771 was indispensable to two well-known insulin-stimulated phosphorylation events (pSer473 and AS160 pSer588). To identify the upstream regulator of PLCG1, we carried out in vitro kinase assay by incubating PLCG1 with IR. The PLCG1 was expressed and purified from E. coli. The IR (active cytoplasmic terminus) was expressed and purified from insect cells. After incubating PLCG1 with IR in vitro for 30 min with ATP provided, PLCG1 phosphorylation was determined by HPLC-ESI-MS/MS. PLCG1 that was not incubated with IR was used as the control. The result showed that IR preferentially phosphorylated tyrosine residues, especially Tyr771 of PLCG1. Other major stimulated sites included pTyr783 and pTyr470/pTyr472. We then confirmed the findings by western blot using pTyr771 and pTyr783 specific antibodies. Our findings suggest that PLCG1 is regulated by the insulin receptor through site-specific phosphorylation.

ABSTRACT NO. 7	
Name	Justine Gortney
Category	Faculty
Title	Evaluation of Professional Growth in a Matched Pharmacy Student Cohort Using a Faculty Advising Assessment Rubric
Authors	Minakshi Lahiri, Ph.D.; Heba Saleem, Pharm.D. Candidate; Chris Giuliano, Pharm.D., MPH
Abtract	Objectives: To evaluate the personal and professional growth of a matched cohort of P1 through P3 students using a novel faculty advising assessment. Methods: Representatives from the Pharmacy Program Assessment Committee developed the Faculty Advising Assessment for Advisees (FAAA) to assist with longitudinal assessment of students on professionalism and personal development. The FAAA is a 5-item rubric with questions about values, engagement, self-awareness, professionalism, and leadership that is linked to mandatory student-faculty advising meetings and the students' self inventory. Faculty advisors rate students after each winter semester advising meeting using the FAAA. Cohort and individual data was extracted from the user data management system, E*Value. Individual FAAA scores were matched based on each school year and deidentified. This cohort of student data from P1 through P3 years were analyzed to determine maturation of personal and professional behaviors. An overall score was determined for each student per year based on the anchors to the FAAA questions listed as not engaged=1, beginning=2, emerging=3 or engaged=4. IRB designated this study as exempt. Results: Data was analyzed for 93 students from the Pharm.D. class of 2020. Overall scores for winters of 2017 through 2019 increased based on matriculation throughout the curriculum and were 13.66 ± 2.7, 16.81 ± 2.43, 17.87 ± 2.21. Using repeated measures ANOVA, a significant difference on overall score was seen between matched students of P1 compared to P3 year ($p<0.01$). Differences for mean score for each rubric item was also observed escalating from P1 through P3 year indicating positive growth. Conclusions: A simple to use 5-item, advising-based rubric showed cohort growth in personal and professional development between the beginning of the Pharm.D. program and then end of the didactic curriculum (P3). The results of the FAAA analysis indicate that students are maturing in their personal and professional behavior throughout the curriculum and are likely benefiting from advising, co-curriculum and other mentored experiences in the program.

ABSTRACT NO. 8	
Name	Melissa Lipari
Category	Faculty
Title	Systemic Corticosteroid Dosing in the Treatment of Moderate Acute Exacerbation of COPD
Authors	Melissa Lipari, PharmD, BCAC; Steven Kulesza, PharmD Candidate; Gabriella Karmo, PharmD; Dina Maskoni, PharmD
Abtract	Introduction: Systemic corticosteroids are the standard of care for treatment of mild to moderate COPD exacerbations. The REDUCE trial demonstrated a 5-day treatment of oral corticosteroids was non-inferior to a 14-day treatment in terms of preventing re-exacerbation within 6 months. The benefit to a shorter duration of therapy is a decreased exposure to corticosteroids and the ensuing adverse effects associated with this exposure. Despite clear evidence to support a 5-day duration of therapy, there is a lack of data evaluating the adherence to this recommendation in outpatient practice. The purpose of this study is to evaluate the dosing and duration of therapy being used to treat mild to moderate COPD exacerbations in an outpatient setting. Hypothesis: For the treatment of moderate COPD exacerbations, systemic corticosteroids are inappropriately prescribed. Study Design: Single center, retrospective observational study Methods: Patients 18 years or older treated between January 2014 through October 2018 were included if they were treated as an outpatient with an ICD-9 diagnosis code of 491.21 or ICD-10 diagnosis code of J44.9 for COPD with documentation of a mild to moderate exacerbation or symptoms of an exacerbation. Patient demographics, smoking history, antibiotic therapy, vaccination history, and systemic corticosteroid therapy were collected. Appropriate corticosteroid therapy was defined as 40mg/day of oral prednisone (or equivalent) for 5 days. Descriptive statistics were used to characterize guideline adherence using Microsoft Excel. Results: A total of 70 patients were included in the analysis. The majority of patients were female (57.1%), Caucasian (82.9%), and had a mean age of 65.6 (SD ±10.7; range 35-89) years. Thirty-five patients (48.6%) were current smokers, 41.4% former smokers and 10% had no history of smoking. Thirty-two out of 70 (45.7%) patients received appropriate systemic corticosteroid doses, while 10/70 (14.3%) and 27/70 (38.6%) received lower and higher than recommended doses, respectively. Conclusion: Systemic corticosteroids are inappropriately prescribed in the treatment of mild to moderate COPD exacerbations.

ABSTRACT NO. 9	
Name	Victoria Tutag Lehr
Category	Faculty
Title	Policies requiring Prior Authorizations or Pharmacy Safety Edits for Opioids: Michigan 2012-2018
Authors	Victoria Tutag Lehr, PharmD; Cynthia L Arfken, PhD
Abtract	Purpose: Pharmacists play a critical role in ensuring safe opioid prescribing. In Michigan opioid prescription per capita peaked in 2012 and then declined. Actions encompassing laws, regulations and insurance policies to promote appropriate opioid prescribing have been implemented since 2012, including the 2016 Guideline for Prescribing Opioids for Chronic Pain. However, there were no mentions of prior authorizations (PA) or safety reviews in the Guidelines, actions that pharmacists perform as required by payers. These actions may promote appropriate opioid prescribing, yet they can also limit access to required pain medication and increase workload. The aim of this analysis was to determine the number and temporal association with Guidelines publication in requiring these actions in one state.

Methodology: As part of a larger study, we collected and categorized policies on opioid prescriptions by large commercial (n=7) and Medicaid fee-for service payers in Michigan from 2012 - first quarter 2018. Policies were categorized into 12 different actions with multiple actions per policy possible. In this analysis, we focus on 1) PA (verifies opioid medication is necessary and patient meets criteria for use for initial prescription, refills, higher potency or extended release dosage forms) and 2) pharmacy safety review (pharmacist review required prior to dispensing medication, or documentation of trial and failure of first line therapies, intolerance/allergy/adverse reaction to first line therapies, or prescribing limited to specialists). Policies related to substance use disorder treatment or overdose prevention were not included.

Results: During the time period, there were 48 different safety reviews implemented that included every payer and every year. The number of reviews per payer ranged from one to 12 (median=5) with Medicaid implementing 4 different reviews. Temporally, 2.9 reviews per quarter were implemented prior to Guidelines publication versus 2.6 per quarter after publication (2 implemented concurrent with publication). There were 132 different PAs implemented that included every payer and every year. The number of PAs per payer ranged from 6 to 31 (median=16.5) with Medicaid implementing 16 PA requirements. Temporally, 3.6 reviews per quarter were implemented prior to Guideline publication, 4 concurrent and 9 per quarter after publication. Of the required PAs, 48.5% were for initial prescriptions, 24.2% for long acting/extended release opioids, 14.4% for refills and 12.9% for opioids with higher potency.

Conclusion: Pharmacy safety reviews and PAs for opioid prescriptions were implemented by every large commercial payer and Medicaid fee for service in one state during the examined time period, starting at the peak of opioid prescribing per capita (2012). These two requirements were separately implemented by each payer and occurred every year examined. There was no evidence that commercial payers were acting similarly or that Medicaid varied from the commercial payers. However, the number of policies requiring PAs greatly exceeded those requiring safety reviews. Furthermore, there was a noticeable trend in more PAs required after Guidelines publication than before, in stark contrast to the lack of a trend for safety reviews. The impact of these policies on prescribing and patient access to necessary opioid medication requires further examination.

Funding Source: Blue Cross and Blue Shield of Michigan Foundation |

Postdoctoral Scholars

ABSTRACT NO. 10	
Name	Ying-Ling Hu
Category	Postdoctoral Fellow
Title	Detecting pre-frailty status: Comparison of clinical judgments and the Paulson Lichtenberg Frailty Index
Authors	Yi-Ling Hu, PhD.; Heather Fritz, PhD.
Abtract	Nearly 50% of U.S. elders are prefrail and at risk for frailty. Identifying prefrail elders and escalating care could attenuate frailty progression. Screening tools are seldom used in practice. Thus, clinical judgment may be a realistic way to ensure widespread frailty screening. No studies, however, have assessed the validity of clinicians' judgment in identifying prefrail elders. This study explored the level of agreement between clinical judgments of frailty status and status categorizations made using the validated Paulson Lichtenberg Frailty Index (PLFI). Older Blacks (n = 202) recruited from a primary care clinic were first categorized as healthy, pre-frail, or frail using the PLFI. Next, geriatric physicians and nurses categorized participants into one of the same categories based on clinical judgment. Clinicians could use medical records to make determinations. We used Cohen's Kappa to determine the level of agreement of both approaches. We used descriptive statistics to explore if any of the 5 PLFI indicators explained discordant categorizations. Of the 202 participants (mean age: 76.7 8.6), 52 (26%) were prefrail and 57 (28%) were frail based on the PLFI. Physicians' judgments aligned with the PLFI in 43% of prefrail and 65.7% of frail cases. Nurse judgments aligned with the PLFI in 43.9% of prefrail and 17% of frail cases. There was slight to fair agreement between clinical judgments and PLFI (physicians Cohen's κ = .23; Nurses Cohen's κ = .59). No specific PLFI indicators independently explained discordant categorizations. Findings suggest that clinical judgments did not align well with PLFI categorizations.

ABSTRACT NO. 11	
Name	Chunna Guo
Category	Postdoctoral Fellow
Title	A proteomic and phosphprotoemic approach to identify genes and pathways potentially Mediating the impact of Cadmium on liver cancer
Authors	Chunna Guo, PhD; Nicholas Carruthers, PhD; Supuni Thalalla Gamage, PhD; Namhee Shin; Judy Westrick, PhD; Paul Stemmer, PhD; Wanqing Liu, PhD
Abtract	Background: Heavy metal accumulation in human tissues has a significant impact on human health. Cadmium (Cd), a metal that has been classified as a human carcinogen, can cause damage to various human tissues. Evidence indicates that Cd has role in both the initiation and the progression of cancer. However, the mechanisms underlying these actions have yet to be fully elucidated. Both hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA) are aggressive liver cancers for which Cd exposure has been implicated in the disease. In this study, we evaluated Cd burden in human liver samples and established proteome profiles in order to identify key proteins and signaling pathways associated with cancer development Method: We analyzed 11 paired cancerous and non-cancerous human liver tissues (4 HCC, 6 CCA and one mixed HCC-CCA) by Orbitrap-Fusion LCMS/MS. Proteomics and phosphoproteomics quantitative analyses were performed using tandem mass tags (TMT). ICP-MS was used to quantify the levels of 26 trace heavy metal elements in each tissue sample. Statistical analysis was done in R. Results: A total of 5,561 proteins were confidently identified in proteomics, of which 15 proteins were differentially expressed between tumor and adjacent tissues (paired moderated t-test, q <0.1). After the enrichment analysis, 424 signaling pathways (PIANO, q <0.1). were over-expressed and 54 signaling pathways (q <0.1) under-expressed in cancerous compared with non-cancerous liver tissues. Phosphoproteomics quantification analysis identified a total of 5,699 phosphosites of which 47 showed differential expression between tumor and adjacent tissues (moderated t-test, q <0.1). Among these, 15 signaling pathways increased and 4 signaling pathways decreased between tumor and adjacent tissue (PIANO, q<0.1). The levels of Cd, Mo, Co, Pb, Fe, Zn and Mn in the cancerous human liver were significantly lower than those in the non-cancerous (paired t-test p<0.05). A total of 834 proteins were correlated with Cd in non-tumor tissue (p < 0.05, Spearman rank correlation) in proteomics, of them, 211 differentially expressed between tumor and non-tumor tissues (p < 0.05). For phosphoproteomics, 286 phosphorylation sites were correlated with Cd in non-tumor tissue (p < 0.05), 87 of them differentially expressed between tumor and non-tumor tissues (p < 0.05). Of these proteins, serine/threonine-protein kinase PAK2 exhibited the high correlation with Cd in both total and phosphoproteomics. Full-length PAK2 that was found stimulating cell survival and cell growth, has an increased expression in tumor compared to non-tumor samples. Interesting, PAK2–ser141 phosphorylation as detected in our study was reported to be important for maintaining cytostatic state of cells, demonstrated a decreased level in tumor compared to non-tumor. These results were also confirmed by western blotting. Conclusions: PAK2 acts as a downstream effector of the small GTPases CDC42 and RAC1 may mediate the carcinogenic impact of Cd on hepatic cancer. Further studies are ongoing to confirm these results and to explore the potential mechanism.

ABSTRACT NO. 12	
Name	Vijayalakshmi Thamilselvan
Category	Postdoctoral Fellow
Title	P-Rex1, a Guanine Nucleotide Exchange Factor for Rac1, Regulates Glucose-and Mastoparan-Induced Insulin Secretion
Authors	Vijayalakshmi Thamilselvan, PhD; Suhadinie Gamage, MS; Sri Aneesha Chundru, BS; Anjaneyulu Kowluru, PhD
Abtract	

Background: Published evidence suggests that Rho-family of small GTPases (e.g., Rac1) play key roles in regulating cytoskeleton reorganization, contributing to glucose-stimulated insulin secretion (GSIS) in pancreatic beta-cells. Small GTPases act as molecular switches, regulated by several regulatory proteins/factors, including guanine nucleotide exchange factors (GEFs) and GDP-dissociation inhibitors (GDIs). Phosphatidylinositol 3, 4, 5-trisphosphate (PIP3)-dependent Rac exchanger 1 (P-Rex1), a known GEF for Rac1, is a multi-domain protein which activates Rac1, and has also been shown to have activity toward Rho G. In the present study, we investigated regulatory roles for P-Rex1 in Rac1-mediated signaling events in pancreatic beta-cell function. Since, Rho G links GEF families including P-Rex1 and functions upstream of Rac1 activation in a variety of systems, we also determined whether RhoG is required for GSIS in beta-cells.

Methods: INS-1 832/13 cells, rat islets and human islets were cultured under normal glucose condition. For GSIS experiments, cells were incubated with low (2.5 mM) and high glucose (20 mM) or mastoparan (30 µM) for 45 minutes in KRB buffer. Total lysates and subcellular fractions were analyzed for the expression and distribution of P-Rex-1, Rac1, and Rho G by western blot analysis. Silencing of endogenous P-Rex1 and Rho G protein expression was done by siRNA transfection. Rac1 activation and GSIS were quantified by Rac1 pull-down assay and ELISA, respectively.

Results: Western blot analysis indicated that P-Rex1, Rac1, and Rho G are expressed in INS-1 832/13 beta cells, normal rat islets and human islet and localized mainly in the cytosol. siRNA- mediated knockdown of P-Rex1, significantly reduced GSIS in INS-1 832/13 cells. Furthermore, siRNA-P-Rex1 significantly attenuated mastoparan (an activator of G proteins)-induced insulin secretion from INS-1 832/13 cells. However, siRNA mediated knockdown of RhoG showed no significant changes in GSIS. Consistent with its regulatory roles in GSIS, targeted depletion of P-Rex1 in INS-1 cells by RNA interference significantly inhibited glucose-induced Rac1 activation.

Conclusions: These results demonstrate for the first time the presence of P-Rex1 in pancreatic beta-cells and offers a novel insights into regulatory roles of this GEF in glucose-induced Rac1 mediated insulin secretion. Our findings also suggest that P-Rex1 is involved in the regulation of a mastoparan-sensitive G protein(s) that might be involved in insulin secretion. Studies are in progress to identify the downstream signaling steps involved in P-Rex1-Rac1 signaling axis, which are critical for insulin secretion.

ABSTRACT NO. 13	
Name	Xiaokun Wang
Category	Postdoctoral Fellow
Title	Reduced Function of Fatty Acid Desaturase1 (FADS1) Activates Hepatic Stellate Cell and Disturbs Glucose Metabolism
Authors	Xiaokun Wang, PhD.; Wanqing Liu, PhD.
Abstract	

Purpose: Polyunsaturated fatty acids (PUFAs) regulate a broad set of physiological processes and have a major impact on human health. Fatty acid desaturase 1 (FADS1, encoding Δ-5 desaturase) is widely recognized as one of the key rate-limiting enzymes for PUFAs conversion. Genetic alleles at the FADS1 locus lead to reduced FADS1 expression in the liver. Our previous studies have shown that genetic polymorphisms of FADS1 are significantly associated with hepatic fat accumulation. However, the role of FADS1 in NASH are not clear.

Methods: FADS1 expression was reduced by stably transfecting short hairpin RNA in hepatic stellate cells LX2. The proliferation and migration were detected by Hoechst33342 staining and transwell assay, respectively. The expression of genes was examined by qRT-PCR and western blotting. Cofocol microscopy was used for evaluating neutral lipids accumulation and mitochondria membrane potential.

Results: Here, we found FADS1 knockdown significantly activated LX2 cells, caused increased cell proliferation and migration. Meanwhile, decrease of FADS1 expression increased the accumulation of neutral lipids as detected by BODIPY staining. FADS1-knockdown also leads to increased expression of profibrotic markers α-SMA, collage type I, ET1, and CTGF. Further studies found that the production of ATP and lactate/pyruvate ratio were increased after FADS1 was decreased. Meanwhile, the expressions of some key enzymes that contribute to glycolysis, such as HK2, PKM2 and LDHB, were elevated after inhibiting the FADS1. Knockdown of FADS1 also led to decreased mitochondrial membrane potential and caused an increase in intracellular reactive oxygen species (ROS) levels. RNA-Seq data from FADS1-KO mice indicated that PI3K-AKT, MAPK, HIF-1 and Ras signaling pathways may be involved in this process, which need further validation.

Conclusions: Our study shows that suppression of FADS1 may activate hepatic stellate cell by modulating mitochondrial oxidative stress and disturbing the glucose metabolism, which may increase the susceptibility to the development and progression of nonalcoholic fatty liver disease (NAFLD).

ABSTRACT NO.14	
Name	Ahmar Mohd Rouf
Category	Postdoctoral Fellow
Title	Bio-mediated synthesis of 5-FU based nanoparticles employing orange fruit juice: a novel drug delivery system to treat skin fibrosarcoma in model animals
Authors	Ahmar Mohd Rouf
Abtract	Nano-sized drug delivery systems (NDDS) have been widely exploited to achieve targeted delivery of pharmaco-materials. Traditional pharmaceutical approaches, implied in the synthesis of nano-formulations, are obscure owing to the incompatible physico-chemical properties of the core drug as well as some other factors crucial in development of NDDS. In fact, most of the existing methods used in development of NDDS rely on usage of additives or excipients, a special class of chemicals. Barring few exceptions, the usage of synthetic excipients ought to be curtailed because of several associated undesirable features. Such issues necessitate strategies that lead to development of the synthetic excipient free drug delivery system. Plant based extracts have great potential to induce synthesis of nano-sized particles. Considering this fact, here we propose a prototype employing orange fruit juice (OJ) to facilitate bio-mediated synthesis of nano-sized supra-molecular assemblies of 5-fluorouracil (5-FU), a potent anticancer drug. The as-synthesized 5-FU Nanoparticles (NPs) retained the anti-neoplastic efficacy of the parent compound and induced apoptosis in cancer cells. The novel 5-FU NPs formulation demonstrated enhanced efficacy against DMBA induced experimental fibrosarcoma in the mouse model when compared to the micro-sized crystals of parent 5-FU drug.

ABSTRACT NO. 15	
Name	Jacinda Abdul-Mutakabbir
Category	Postdoctoral Fellow
Title	The Evaluation of the Utility in Using Different Synergy Testing Methods to Predict the Activity of Antibiotic Combinations Against Acinetobacter Baumannii
Authors	Jacinda Abdul-Mutakabbir, PharmD, AAHIVP; Juwon Yim, PharmD, MPH; Logan Nguyen Kyle Stamper, BS; Phillip Maassen, BS; Michael J. Rybak, PharmD, MPH, PhD
Abtract	Background: Acinetobacter Baumannii possess inherent and acquired resistance mechanisms that have rendered most antibiotics inactive. Dual therapy including COL given in combination with meropenem (MEM) or tigecycline (TGC) has been shown to be successful in eradicating A. baumannii infections complicated by Multidrug-Resistance (MDR). Numerous methods exist to evaluate in vitro synergy; with time-kill analysis (TKA) and checkerboard testing (CB) being most widely used. Purpose: The purpose of this study was to assess and compare the synergy presented through various synergy testing methods including minimum inhibition concentration (MIC) testing of antimicrobials in combination, CB, and TKA in 50 A. baumannii strains. Methods: Fifty MDR A. baumannii strains from the Anti-infective Research Laboratory library were evaluated. MIC testing was performed for COL in the presence of MEM and TGC as well as; MEM and TGC in the presence of COL. The COL+MEM or TGC combinations were assessed in both 24h TKA and CB. A fractional inhibitory concentration index (FICI) of < 0.5, and a reduction of ≥ 2 $\log_{10}$ CFU/ml considered synergistic in the CB and TKA testing methods, respectively. Results: The MIC testing of COL in the presence of MEM or TGC showed a >2- fold reduction in 96% and 80% of the 50 strains for each combination, respectively. CB revealed synergy in 64% of strains utilizing the COL+MEM combination, while synergy was observed in 22% of the strains with the COL+TGC dual therapy. In TKA, synergy was observed in 90% and 64% of the strains with the use of the COL+MEM and COL+TGC combinations, respectively. Conclusion: Among the methods tested, TKA was the most consistent in demonstrating synergy for both the COL+MEM and COL+TGC combinations. Nevertheless, the results of this study show different synergy methods produce differing results. Further research is warranted to establish the best synergy testing modality for determining in vivo success.

ABSTRACT NO. 16	
Name	Sara Alosaimy
Category	Postdoctoral Fellow
Title	Impact of Vancomycin Area Under Curve on Persistent Methicillin-Resistant Staphylococcus aureus (MRSA) Bloodstream Infections (BSI)
Authors	Alosaimy, S.; Jorgensen, S.C.J.; Lagnf, A.M.; Zasowski, E. J.; Trang, T.D.; Mynatt, R.P.; Pogue J.M., Rybak M.J.
Abtract	Background: Persistent Methicillin-resistant Staphylococcus aureus (MRSA) bloodstream infections (BSI) are associated with significant morbidity, mortality and health care expenditures. Vancomycin (VAN) remains the treatment of choice for invasive MRSA BSI. Current guidelines for the treatment of MRSA BSI recommend a VAN AUC24h / MIC ratio (400-600). The Detroit Medical Center (DMC) imposes a 2-level AUC guided dosing strategy, which is the most common method of VAN monitoring. However, data on the association between AUC24h and clinical outcomes in MRSA BSI are limited. We aimed to evaluate the association between VAN AUC24h and persistent bacteremia (PB) among patients with BSI.

Methods: Multi-center, retrospective cohort study from January, 2015 to August 2019. We included adult patients with MRSA bacteremia treated with VAN for which AUC24h / MIC monitoring was performed. Patients who were pregnant or incarcerated were excluded. The primary outcome was GO defined as ≤ 72 hours bacterial eradication and absence of acute kidney injury (AKI). Classification and Regression Tree (CART) analysis was performed to determine the AUC24h breakpoint (BP) most predictive of GO in the cohort. Mann-Whitney and Fischer exact tests were used for univariate analysis. The independent association between AUC24h, dichotomized at the CART derived cut-point, was then examined through multivariable logistic regression analysis.

Results: Overall, 140 patients were included. The median age was 58 (4-67) years, 66.4% male, and 22.1% intravenous drug users. The most common sources of BSI were skin/soft tissue (36.4%) and pneumonia (25.7%). The Median APACHE II score was 13 (8-18). Patients with AUC24h ≤ 510 were more likely to have positive GO compared to those with AUC24h > 510 (63.4% and 36.6%, respectively; P=0.24). Patients with AUC24h > 381 were more likely to have positive GO compared to those with AUC24h ≤ 381 (81.7% and 18.3%, respectively; P=0.12). After controlling for prior hospitalization history, skin/soft tissue and endocarditis as sources; an AUC within the (381-510) target (aOR 2.05, 95% CI 1.0-4.30) and endocarditis (aOR 0.3, 95% CI 0.10-0.92) were independently associated with positive GO. In AUC ranges of (510-600), (600-700), (≥ 700); negative GO were related to AKI in 5.3%, 33.3%, 50.0%, respectively.

Conclusion: In patients with MRSA BSI, an AUC24h within a target of (381-510) was independently associated with GO. Our findings underscore the importance of VAN dose optimization to achieve timely bacterial clearance and VAN safety in patients with MRSA bacteremia. |

ABSTRACT NO. 17	
Name	Taylor Morrisette
Category	Postdoctoral Scholar
Title	Evaluation of Omadacycline Alone and in Combination with Rifampin against Biofilm-producing Staphylococcus aureus and Staphylococcus epidermidis
Authors	Taylor Morrisette, Pharm.D.; Katherine Lev, M.S.; Razieh Kebriaei, Ph.D.; Jacinda C. Abdul-Mutakabbir, Pharm.D.; Michael J. Rybak, Pharm.D., M.P.H., Ph.D.
Abtract	Purpose: Despite advances in bioengineering and perioperative antimicrobial prophylaxis, indwelling medical devices and their associated infections represent a substantial cause of morbidity. Two of the most common pathogens associated with infections of orthopedic implants include Staphylococcus aureus and Staphylococcus epidermidis. Importantly, S. aureus and S. epidermidis are among the most common biofilm-producing bacteria. Owing to frequent failures in the treatment of S. aureus and S. epidermidis-associated biofilm infections, there is an urgent need for novel therapeutic approaches. Moreover, the lack of data evaluating omadacycline (OMC), a novel aminomethylcycline, against the most common biofilm-producing organisms associated with infections of indwelling medical devices necessitates the need of this information for the practicing clinician. The objective of this study was to evaluate OMC alone and in combination with rifampin (RIF) against biofilm-producing strains of S. aureus and S. epidermidis.

Methodology: Eight randomly selected clinical strains of S. aureus (five strains) and S. epidermidis (three strains) with various levels of susceptibility to OMC and RIF were evaluated for OMC alone and OMC in combination with RIF. Vancomycin (VAN) was used as a reference antimicrobial. The potential for synergy in the planktonic and biofilm state was assessed by combination minimum inhibitory concentration (MIC) testing for all strains and a 24-hour biofilm time-kill analysis for one randomly selected strain of S. epidermidis (NRS 101) at 0.5x and 1x biofilm MIC (bMIC).

Results: In the presence of biofilm, VAN MICs increased 2- to 4-fold and 1- to 4-fold for S. aureus and S. epidermidis, respectively. OMC demonstrated potent activity with low MICs against the evaluated strains (0.125-0.5 mg/L), with a slight increase of MICs in the presence of biofilm (0.25-2 mg/L). In the planktonic state, RIF reduced OMC MICs in 60% of S. aureus stains and 33% of S. epidermidis strains, while RIF reduced OMC bMICs in 100% of S. aureus strains (2- to 3-fold reduction). RIF did not appear to impact OMC bMICs for the evaluated S. epidermidis strains, however, at 0.5x MIC and 1x MIC, synergy (> 2-log10 CFU/mL kill compared to the most effective agent alone at 24 hours) and bactericidal activity (≥ 3-log10 CFU/mL reduction at 24 hours compared to the starting inoculum), respectively, was observed in NRS 101 with the combination of OMC and RIF.

Conclusions: Based on these encouraging results, further research is needed to evaluate the combination of OMC and RIF for biofilm-associated infections. |

Clinical Doctorate in Health Care Sciences

ABSTRACT NO. 18	
Name	Morgan Albertson
Category	Health Science
Title	The Effects of Visual Feedback during Recumbent Stepping in Patients with Chronic Stroke
Authors	Lyndsey Crosbie, SPT; Marina Bacus, SPT; Morgan Albertson, SPT; Karen Sharkey, SPT; Victoria Pardo, PT, DHS
Abtract	Introduction/Clinical Relevance: The NuStep recumbent stepper is commonly used by clinicians for clients with neurological disorders, since it is a safe and effective method of improving cardiovascular fitness. The latest model (NuStep Transitt) has a tablet display with real-time feedback of performance. There is currently no evidence on the effects of regular training on this new device, and thus the purpose of this study was to investigate the effects of intermittent visual feedback during recumbent stepping on strength, balance and functional mobility in individuals with chronic stroke Methods: Eleven participants (7 female, 9 right hemiparesis, mean age 58.7 ± 13.6 years) 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), Maximum Voluntary Contractions (MVC) of knee extension (KE) and flexion (KF), ankle dorsiflexion (DF) and plantarflexion (PF), rhythmic weight-shifting on the BalanceMaster, the Five Times Sit to Stand (5xSTS), and the lower extremity motor and sensory Fugl-Meyer assessment. Visits 2-9 consisted of 45 minutes of training on the NuStep twice a week. Between the 5 minute warm-up and cool-down, participants stepped 5 minutes with and then without visual feedback about left/right percentage effort, for a total of 35 minutes of training with appropriate rest breaks. A descriptive analysis was performed followed by nonparametric Wilcoxon paired samples testing to compare pre and post values for each participant. Results: There were no significant changes in rhythmic weight shifting on the BalanceMaster. There was a significant change in 5xSTS from 32.0 to 17.8 seconds (p=0.007). There was a significant change in plantarflexion MVC on the hemi side from 41.5 to 48.2 lbs (p=0.027), with KE strength on the hemi side approaching significance (p=0.087). Fast gait showed significant changes for stride length on the hemi (p=0.024) and non-hemi leg (p=0.019), step length on the non-hemi side (p=0.024), with gait speed approaching significance (p=0.053). Normal gait showed significant changes for step (p=0.042) and stride (p=0.034) length on the non-hemi side. Discussion: Decreased use of the hemi leg is often a problem for individuals post-stroke. Being able to educate the participant about this imbalance and give them real-time feedback about the percentage of use of the hemi leg is a valuable tool for clinicians. Stepping on the NuStep with visual feedback about left/right percentage of effort leads to significantly improved hemi PF strength. The significant changes in 5xSTS in this study translates to safer transfers and mobility and a decrease in fall risk. The changes in gait parameters, which are likely affected by the changes in PF strength, leads to a more normalized and energy efficient gait pattern. Conclusions: This intervention study has demonstrated that the addition of visual feedback about left/right percentage effort while exercising on the NuStep has significant and clinically relevant effects on the strength and functional mobility of individuals with chronic stroke.

ABSTRACT NO. 19	
Name	Natalie Brikho
Category	Health Science
Title	Medication Related Problems in Post-Discharge Hemodialysis Patients
Authors	Natalie Brikho, Bachelors of Health Sciences; Chantale Daifi, PharmD; Pia- Allison Roa, Bachelors of Health Sciences; Caren El-Khoury, RPh; Mohammad Alawieh, RPh
Abtract	Background: On average, dialysis patients are on 9-10 oral medications and 2-3 parenteral medications, placing them at higher risk for DRPs [1]. Clinical pharmacy services such as medication therapy management (MTM) are implemented into dialysis clinics to identify and resolve DRPs as well as improve medication therapy outcomes. The clinical pharmacist is implemented into the existing dialysis clinical team to offer a variety of pharmaceutical care services. Existing literature of clinical pharmacists implemented in hemodialysis clinics showed that of the nearly 1600 DRPs identified, the predominant types were inadequate laboratory monitoring (23.5%), over-dosing (20.4%), underdosing (16.9%), unneeded medication (14.9%) [2]. Additional literature showed that in medication reviews for 64 dialysis patients conducted over a 6-month period, DRPs were present in 92% of dialysis clinic patient. [3]. While there is some data to show the role of a clinical pharmacist in identifying drug-related problems in dialysis patients, there is a lack of studies showing the specific impact on post-discharge patients. In observing the current standard of care, there showed to be an increase number of discrepancies in post-discharge patient's medication list from the discharge summary and the medications they take. While the clinical pharmacist is currently implemented into the existing dialysis teams, we have identified the need to evaluate the specific role the clinical pharmacist has in identifying and resolving drug-related problems specifically in patients post-discharge from inpatient hospital admission.

Methods: This is a prospective descriptive study measuring the effectiveness of a pharmacist clinical service in post-discharge dialysis patients by identifying drug related problems. The clinical pharmacist performed standard of care medication therapy reviews within 1 week after patient returns to dialysis following discharge from the hospital. Pharmacy interns collected data describing drug related problems uncovered and resolved by the clinical pharmacist and assist the clinical pharmacist as needed. Results/Conclusion: Data collection and analysis are ongoing. An interim analysis will be presented at the WSU Research Day.

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ABSTRACT NO. 20	
Name	Emily Denn
Category	Health Science
Title	Age Related Differences in Physical Function and Cognitive Performance
Authors	Emily Denn, SPT Bria Kamdem Kwakam, SPT Emily Kwasniak, SPT Diane Adamo, PhD, MS, OTR Nora Fritz, PhD, PT, DPT, NCS
Abtract	Introduction: Forty-seven million people currently suffer from dementia worldwide, and the amount of people with dementia is expected to increase to 76 million by the year 2030 (WHO, 2017). Cost-effective and clinically feasible tools to predict early cognitive decline are critically needed. Being able to predict cognitive decline through grip strength and physical activity is an easy and cost-effective tool to use in the clinic. The purpose of this study was to investigate the relationship between physical function (i.e. grip strength and Six Minute Walk Test (6MWT)) and cognitive function in young and middle-aged adults at two time points, one year apart. Methods: A non-experimental, longitudinal design was used to identify relationships between physical measures of grip strength and 6MWT and cognition in young and middle-aged adults. Subjects: 34 young and 19 middle aged healthy adults met the inclusion criteria to participate in the study. Procedures: Five cognitive measures consisting of the California Verbal Learning Test, Symbol Digit Modalities Test, Controlled Oral Word Association Test (COWAT), Trail Making Test, and the Stroop Test. Physical measures including the 6MWT and measurement of grip strength with a JAMAR hand dynamometer. Data was collected at two time points, one year apart. Relationships between outcome measures were assessed using Pearson's correlation. Between group and time-point differences were assessed using independent t-tests and ANOVA (repeated measures), with alpha set at 0.05. RESULTS: At both visits, middle-aged adults demonstrated poorer performance than young adults on grip strength, Stroop Interference Test, Trail Making Test, and 6MWT. Middle-aged adults demonstrated significantly reduced grip strength on visit 2 compared to visit 1. There were no significant relationships among grip strength and cognitive function in either group at either time point. Interestingly, moderate associations were found in the middle-aged group among Stroop Interference score and 6MWT at visit 2 (r=0.666). Discussion: Middle aged adults performed worse on cognitive and physical measures compared to young adults. We were unable to detect an association between physical measures and cognitive measures in young or middle aged adults. We suspect this is due to the small sample size that was included in the study. As we continue data collection, we expect to find a strong correlation between cognitive and physical measures in middle aged adults. Conclusion: The use of physical measures functional biomarkers of cognitive decline may allow health professionals to intervene earlier with targeted interventions.

ABSTRACT NO. 21	
Name	Paul Ghazali
Category	Health Science
Title	Comparison of a Novel Immediate Feedback Tool vs. Scantron on Student Retention of Knowledge
Authors	Dr. Jeniffer Dickson, Dr. Sara Maher, Dr. Tina Pa
Abtract	Introduction: Performance feedback in the academic setting is typically done in delayed format, despite research suggesting immediate performance feedback (IPF) is superior to delayed performance feedback (DPF), when assessing a student's retention of knowledge. The Immediate Feedback Assessment Technique (IF-AT) can be used to provide a student with IPF, and the effectiveness of this tool has been studied with undergraduate psychology students. To date, no research exists on the effect of using the IF-AT for IPF with graduate students, more specifically, Doctor of Physical Therapy (DPT) students. The purpose of this study was to investigate if IPF using the IF-AT is more effective than DPF for increasing retention of knowledge in DPT students.

Methods: A single subject design was used for this study. Seventy-two first year DPT students enrolled in Basic Patient Care (PT 5030) volunteered to participate, over a two-year period. Data collection tools included two surveys, a traditional Scantron for DPF and the IF-AT for IPF. Students completed a total of 8 quizzes for this study, as well as midterm and final examinations. The Scantron was used for odd numbered quizzes; the IF-AT for even numbered quizzes. On the midterm examination, 3 questions were repeated from each quiz, for a total of 12 repeat questions. The same format was followed for the final examination. SPSS 25.0 was used for data analysis with an alpha level of 0.05. Paired t-tests were used to analyze retention of knowledge by comparing responses to specific questions between a quiz and examination. A Bonferroni adjustment was completed to prevent type I error.

Results: Seventy-one subjects completed the study. Two Scantron quizzes (1 and 3) showed a significant difference for all 6 questions repeated on the midterm examination. Two IF-AT quizzes (6 and 8) showed a significant difference for all 6 questions repeated on the final examination. On the midterm examination, IPF showed a significant difference for 3 questions all from quiz 4; Q4.1 and Q4.3 p=0.000, Q4.2 p=0.007. On the final examination, DPF showed a significant difference for 4 questions; Q5.2, Q5.3, and Q7.1 p=0.000, Q7.2 p=0.002. When comparing total number of questions correct from each quiz, the total number of questions correct on the IF-AT (16.8/20) compared to the Scantron (14.4/20) was significantly different prior to the midterm examination. DISCUSSION: Students demonstrated retention of knowledge when both IPF and structured DPF, 24 hours post-quiz, were provided. Of the two questions that displayed no significance with DPF, a large number of subjects answered the questions incorrectly on both the quiz and examination, yet no retention was found. This is in comparison to the three questions that displayed no significance with IPF, where only a small number of subjects answered the questions incorrectly on both the quiz and examination. The low number of incorrect answers on these IPF quizzes makes detection of change more difficult. This suggests that IPF may be superior to DPF to improve retention of knowledge from a quiz to examination, in a single DPT course.

Conclusions: This study detected that IPF and structured DPF, within a 24-hour period, are both effective for improving retention of knowledge for 1st year DPT students. IPF was slightly superior than DPF in overall performance on assessments. Further research is needed to determine if implementing IPF and/or structured DPF consistently throughout a DPT curriculum results in better retention of knowledge, and therefore improved success on the National Physical Therapy Examination. |

ABSTRACT NO. 22	
Name	Jared Kurdunowicz
Category	Health Science
Title	The Effects of Unilateral Recumbent Stepping in Patients with Chronic Stroke
Authors	Kathryn Kelley; Jared Kurdunowicz; Gunnar Littrup; Eric Mocher,
Abtract	Introduction: The NuStep recumbent stepper is readily available and commonly used by clinicians as a warm up and/or cool down device. However, there is limited research on its use as a targeted intervention. There is currently no evidence on the specific effects of unilateral stepping training on the hemiplegic leg. The purpose of this study was to investigate the effects of a 4 week training protocol on the NuStep utilizing a unilateral stepping condition in individuals with chronic stroke. Methods: Eleven participants (7 female, 8 right hemiparesis, mean age 56.7 ± 14.1 years) with chronic unilateral stroke (>6 months) were recruited. Participants completed pre- and post-evaluations (visits 1 and 10) which included gait on the GAITRite (normal and fast speeds), Maximum Voluntary Contractions (MVC) for knee and ankle in the sagittal plane, rhythmic weight-shifting on the BalanceMaster, the Five Times Sit to Stand (5xSTS), and the lower extremity motor and sensory Fugl-Meyer assessment. Visits 2-9 consisted of 45 minutes of training on the NuStep twice a week. Between the 5 minute warm-up and cool-down, participants stepped with the unilateral hemiparetic leg or with both legs for a total of 35 minutes with rest breaks and manual assistance provided as needed. A descriptive analysis was performed followed by nonparametric Wilcoxon paired samples testing to compare pre and post values for each participant. Results: There were no significant changes in performance on BalanceMaster and Fugl-Meyer. There was a significant change in 5xSTS from 15.7 to 13.6 seconds (p=0.019). Fast gait showed significant changes in gait speed (p=0.01) from 1.27 to 1.37 m/sec. Normal gait showed significant changes for stride length on the hemi side (p=005) and the non-hemi side (p=0.009), and a change in gait speed from 0.92 to 1.04 m/sec (p=0.002). There was a nearly-significant change in dorsiflexion MVC on the hemi side from 30.9 to 34.2 lbs (p=0.051). Discussion: The improvements in 5xSTS from above to below 15 seconds is clinically significant because this is a cutoff for higher fall risk in community dwelling older adults. Changes in stride length and gait speed indicate clinically relevant improvements in functional mobility. Gait speed greater than 1.0 m/s has been suggested as a strong predictor of reduced fall risk, adverse health events, hospitalization, and dependence for ADLs. The nearly significant change in dorsiflexion strength on the hemi leg (which could be due to the active pulling up against the footstrap) is of great relevance to neurological PT since dorsiflexion is difficult to regain post-stroke. Conclusions: This intervention study has demonstrated that a targeted intervention of unilateral recumbent stepping has significant and clinically relevant effects on the strength and functional mobility of individuals with chronic stroke. Acknowledgements: The authors wish to thank NuStep LLC for their financial support of this project.

ABSTRACT NO. 23	
Name	Jacob Centella
Category	Health Science
Title	Listening to Fast-Tempo Music Delays the Onset of Neuromuscular Fatigue
Authors	Jacob Centala, SPT; Cameron Pogorel, SPT; Scott W. Pummill, SPT; Moh H. Malek, PhD
Abtract	Studies determining the effect of music on physical performance have primarily focused on outcomes such as running time to exhaustion, blood lactate, or maximal oxygen uptake. The electromyographic fatigue threshold (EMGFT) is determined via a single incremental test and operationally defined as the highest exercise intensity which can be sustained indefinitely without an increase in EMG activity of the working muscle. To date, no studies have examined the role of fast-tempo music on EMGFT. The purpose of this investigation, therefore, was to determine whether fast-tempo music attenuates neuromuscular fatigue as measured by the EMGFT. We hypothesized that listening to fast-tempo music during exercise would increase the estimated EMGFT compared to the control condition. Secondarily, we hypothesized that maximal power output would also increase as a result of listening to fast-tempo music during the exercise workbout. Ten healthy college aged men [mean ± SEM: age, 25.3 ± 0.8 y (range from 22-31 y); body mass, 78.3 ± 1.8 kg; height: 1.77 ± 0.02 m] visited the laboratory on two occasions separated by 7 days. The EMGFT was determined from an incremental single leg knee extensor ergometer for each visit. In a randomized order, subjects either listened to music or no music for the two visits. All music was presented as instrumentals and randomized with a tempo ranging between 137 – 160 beats/min. The results indicated that listening to high-tempo music during exercise increased maximal power output (No Music: 48 ± 4; Music: 54 ± 3 W; $p = 0.02$) and EMGFT (No Music: 27 ± 3; Music: 34± 4 W; $p = 0.008$). There were, however, no significant mean differences between the two conditions (no music vs. music) for absolute and relative end-exercise heart rate as well as end exercise rating of perceived exertion for the exercised leg. These findings suggest that listening to high-tempo music increased overall exercise tolerance as well as the neuromuscular fatigue threshold. The results are applicable to both sport and rehabilitative settings.

ABSTRACT NO. 24	
Name	Kimberly Morck
Category	Health Science
Title	Utilization Of Smart Phone Texting In An Interprofessional Student-Run Clinic
Authors	Kimberly Morck, SPT; Danielle Arsenault, SPT; Kristin Carl, SPT; Jordyn Welles, SPT; David Cicala, BS; Martha Schiller, PT, DPT, MSA; Anwar Najor-Durack, PhD, LMSW; Jennifer Mendez, Ph.D.
Abtract	Introduction: The Wayne State Diabetes and Wellness (DEW) Clinic is a monthly interprofessional student-run free clinic that provides education and resources for underinsured individuals with Type 2 Diabetes with representation from Medicine, Pharmacy, Physical Therapy (PT), Occupational Therapy, Social Work, and Dietetics. The purpose of the study was to assess health behaviors, knowledge and use of text messaging with individuals with Type 2 diabetes in the student-run interprofessional DEW clinic.

Methods: 29 clients with smart phones between the ages of 44-76 were enrolled in the study; 12 completed all 4 sessions. Outcome measures completed at visits 1 and 4 included: 1) Spoken Knowledge in Low Literacy in Diabetes (SKILLD), 2) Summary of Diabetes Self Care Activities (SDSCA) and 3) Health Behaviors Questionnaire. Discipline specific assessments and education were provided. PT education included foot care and exercise. Individualized goals were created. Text messages were sent throughout the month consisting of clinic reminders, motivational statements supporting goal attainment and other personalized information to support diabetes self-care. Goals were reassessed and modified at each clinic to promote client participation. Each participant received a $20 gift card after completing the study.

Results: Knowledge scores on the SKILLD increased from 6.25+/- 2.9 to 7.92+/-.90. Post scores on the SDSCA showed client's reporting increases in frequency of health habits (daily foot checks, daily exercise) by 1-2 days a week. Weight and BP measurements remained mostly the same, though one participant did move from the "Elevated" BP category to the "Normal" BP category. Post scores on the Health Behaviors Questionnaire showed little to no change. A sampling of text messages sent between a 12-month span showed 247 texts sent to clients and 101 received from client; students sent between 6 and 33 text messages to each patient and received between 1 and 26 text messages from each patient in return.

Discussions: Preliminary results from V1 to V4 included an increase of scores for the SDSCA, HBQ, and SKILLD. The upward trends demonstrated improved knowledge and behavior change for foot checks and exercise. Clients equipped with this knowledge are likely to have better control over their diabetes management. Giving diabetic clients the opportunity to use text messaging to receive health-related information was well received by most clients. Limitations included small sample size of clients attaining 4 visits, multiple researchers collecting data, technical difficulties with internet connectivity, text messaging and client cell phones.

Conclusions: The use of the smartphone allowed direct communication with clients regarding upcoming clinic visits and self-care activity goals between clinic visits. The addition of text messaging to the standard of care at the DEW clinic has not been conclusive but may be helpful to motivate diabetic patients to change their behaviors and thereby improve their health. Adding it to the standard of care for all clients at the DEW clinic requires further research.

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ABSTRACT NO. 25	
Name	Dillon Ommodt
Category	Health Science
Title	Effectiveness of Dorsavi in Determining Safe Return to Play Following ACL Repair: A Case Series
Authors	Kwesi Easley, SPT; Jaclynn Moretti, SPT; Dillon Ommodt, SPT; Sarah Sherer, SPT; Marie Pepin PT, DPT, MSPT, OMPT; Gwynne Waters PT, DPT, OMPT, SCS
Abtract	Introduction: Current outcome measures are unable to measure the many different risk factors associated with re-tear of anterior cruciate ligament (ACL). For this reason, safe return to sport after an ACL repair is difficult to determine using standard clinical measures. DorsaVi AMI is being used currently as a wearable and wireless movement sensor that tracks and measures range of movement, symmetry, balance, and time. The goal of this study is to determine if the DorsaVi AMI is a valid objective measure to determine readiness of safe return to play after ACL repair. Methods: This study is currently on-going as a case series due to the small amount of participants at this time. This study has currently had 10 participants (3 males and 7 females with a mean age of 21.2) post ACL repair with no other comorbidities and are within the inclusion and exclusion criteria. Each participant is expected to be tested on three separate days to allow motor learning and follow-up. DorsaVi's wireless motion sensors are used to analyze performance during AMI movement tests which is compared to findings of knee range of motion, the Lower Limb Symmetry Index, and strength tests. Statistical analysis will be performed using descriptive statistics due to the small sample size. Results: At this time, there are four cases presented with a left surgical leg and completed all three test sessions. Case 1 demonstrated the lowest absolute knee extension strength values for both the surgical and non-surgical limbs; but also showed the highest LLSI increase. Case 2 demonstrated the greatest surgical limb strength improvement along with the lowest risk values related to speed of motion in the frontal plane. Case 3 demonstrated a decrease in surgical knee strength along with the highest risk values of all four cases related to re-tear. Case 4 demonstrated a declining LLSI and knee extension strength; however, showed lower risk related to re-tear. Discussion: Reviewing these four cases, there may be a relationship between increased hip and knee strength as positive predictors for a reduction in the risk values associated to ACL re-tear. Only six out of ten participants have completed all three test sessions. Due to lack of repeated subjective measures, we are unable to determine convergence validity between the he DorsaVi and the previously mentioned measures. Due to the lack of participants currently, we are unable to determine if there is a significant difference between sessions 2 and 3 or the surgical limb and non-surgical limb. Risk assessment at baseline, at 24 hours, and 4-8 weeks post show most of the cases still being at risk for re-tear on surgical limb. Conclusions: This is one of the first studies to research the validity of the DorsaVi AMI and its ability to determine readiness of return to play after ACL repair. Since not all ACL re-tear risk factors can be assessed through visual observation, we hope that the DorsaVi AMI can fill in the gaps and be a useful tool in the clinic. DorsaVi provided by Team Rehab.

ABSTRACT NO. 26	
Name	Kristin Robertson
Category	Health Science
Title	The Effect of a Wearable Sensor Visual Biofeedback on the Ability to Maintain a Neutral Spine
Authors	Kristen Robertson, SPT; Rachel Smith, SPT; Marie Eve Pepin, PT; Sujay Galen, PT; Ryan Kilgore, SPT; Nicholas Mychalowych, SPT; Catherine Macleod
Abtract	Purpose: Low back pain (LBP) is one of the most common diagnoses treated by physical therapists (PTs). Stabilization exercises are a common and effective intervention for LBP1. During stabilization exercises, the patients seek to maintain the spine in neutral, a position of elastic equilibrium with the least passive tissue strain2. Extrinsic feedback has been shown to enhance motor learning in patients, but the ideal method of providing feedback is not known. Therefore, the purpose of this study is to investigate whether a single session of exercise training with visual feedback from wearable motion sensors results in a greater ability to maintain a neutral spine compared to verbal feedback. Methods: Participants with LBP were recruited and randomized into two training groups, one group receiving verbal feedback and the other receiving real-time visual feedback provided by wearable motion sensors (ViMove, dorsavi.com). A first session included a pre-test, training and a post-test. For both training and testing, the participants were asked to perform four stabilization exercises: high lift, bird dog, standing alternating toe tap, and march on ball. To assess retention, a second identical post-test was performed 48 hours later. The magnitude of lumbar lordosis and the total lumbar excursion away from neutral was recorded using wearable motion sensors. RESULTS: 34 subjects completed the study (age = 38.3 +/- 16 years; f=29). Descriptive analyses of the total spinal movement excursion in all three planes were performed for all stabilization exercises. Most subjects demonstrated decreased movements in the frontal and transverse planes after training with visual feedback. Moreover, movements in the combined frontal and transverse planes were decreased during the bird dog and standing alternating toe tap exercises. Conclusions: This preliminary descriptive analysis of data shows that a single session of visual feedback enabled individuals with low back pain to perform stabilization exercises with a better control of their spinal movements, indicated by a decrease in lateral flexion and rotation movements. Moreover, these movement patterns were retained 48 hours after the training session. Clinical Relevance: Motion sensors allow for a clinically feasible way to measure lumbar movements and provide real time visual feedback about exercise performance. Motion sensors have the potential to improve the performance of stabilization exercises in patients with LBP. 1. Gomes-Neto M, Lopes JM, Conceição CS, et al. (2017). Stabilization exercise compared to general exercises or manual therapy for the management of low back pain: A systematic review and meta-analysis. Physical Therapy in Sport 2017; 23:136-42 2. Scannell JP, McGill SM. (2003). Lumbar posture--should it, and can it, be modified? A study of passive tissue stiffness and lumbar position during activities of daily living. Phys Ther. 2003 Oct;83(10):907-17.

ABSTRACT NO. 27	
Name	Rhonda Charara
Category	Health Science
Title	The response of a mouse model of adult-onset muscular dystrophy to 12 weeks of non-injurious exercise, reveals a low threshold for myogenic activation
Authors	Rhonda Charara, BS; Timothy Humbach, BS; Dara Schramm, BS; Britany Teal, BS; Morium Begam, BS; Marie-Eve Pepin, DPT, PhD; Sujay S. Galen, PT, PhD; Joseph A. Roche BPT, PhD 1
Abtract	Background: Mutations in the DYSF gene in humans, leads to the absence or severely reduced levels, of the protein dysferlin. Dysferlin deficiency in skeletal muscle is linked to progressive muscle weakness and wasting syndromes known as dysferlin-linked muscular dystrophies or dysferlinopathies. A major challenge in the physical rehabilitative management of dysferlinopathies is preventing the complications of a sedentary lifestyle, while still protecting muscles from contraction-induced muscle damage and accelerated wasting. We hypothesized that concentrically-biased training is safe for dysferlin-deficient muscle and alters gene expression linked to muscle protection in a murine model of dysferlinopathy.

Methods: We studied the response of dysferlin-deficient mice (N = 6) and control mice (N = 6) to 12 weeks of non-injurious, concentrically-biased, forced exercise, performed with a robotic dynamometer. Each bout of exercise involved 4 sets of concentric contractions of the tibialis anterior (TA) muscle of the hindlimb (160-90 degrees of ankle dorsiflexion). Two bouts of exercise separated by 3 days, were performed each week. After 12 weeks of exercise, the mice were euthanized and their exercised (left) and unexercised (right) TA muscles were harvested and subjected to histological (H&E staining) and gene expression (array-based quantitative RT-PCR) studies.

Results: The exercised TA muscle of dysferlin-deficient mice had $0.77 \pm 0.67\%$ damaged fibers compared to $0.20 \pm 0.11\%$ in control mice. However, the exercised TA muscle of dysferlin-deficient mice had $23.8 \pm 17.3\%$ centrally-nucleated fibers (CNFs, marker of myogenic activity) compared to $2.9 \pm 1.3\%$ in control mice. Expression of the satellite cell quiescence gene Pax3 was downregulated ~11 fold in exercised versus unexercised dysferlin-deficient muscle. Gene expression changes relevant to apoptosis were ambiguous, since the pro-apoptotic gene caspase-3 and the anti-apoptotic gene ribosomal protein S6 kinase polypeptide 1 were both downregulated (~2 and ~5 fold, respectively) in exercised versus unexercised dysferlin-deficient muscle.

Conclusion: Our data suggest that, despite being non-injurious in nature, concentrically-biased exercise might still trigger myogenic activity in dysferlin-deficient muscle. The translational relevance of this work is that, in order to avoid depleting the limited regenerative potential of dysferlin-deficient muscle, maintenance exercise must be carefully adjusted and monitored, to not only prevent injury but also minimize unwanted myogenic activation. Funding to JAR from the Jain Foundation Inc., Wayne State University Startup and FRAP Awards, and NIH R03HD091648 from NICHD. |

Doctoral Candidates

ABSTRACT NO. 28	
Name	Majed Alharbi
Category	Doctoral Candidate
Title	Protein Ubiquitinome of Primary Human Skeletal Muscle Cells
Authors	Majed Alharbi, PharmD, MS; Aktham Mestareehi, MS; Berhane Seyoum, MD; Xiangmin Zhang, PhD; Zhengping Yi, PhD
Abtract	Diabetes Mellitus is one of the major health concerns worldwide. It is characterized by abnormal regulation of metabolic activities and blood glucose levels due to either an insufficient production and release of insulin from the pancreatic beta cells in response to hyperglycemia (Type I DM) or inadequate cellular glucose uptake in response to the secreted insulin as a consequence of insulin resistance, which is a major manifestation of Type II DM. Statistically, according to the last report from CDC, there were 30.3 million diabetic people in the United States in 2015, representing about 9.4% of the United States population. The report also showed that around 95% of all diabetics were Type II patients. Moreover, 87.5% of the Type II diabetes patients were overweight or obese with BMI of 25 kg/m2 or higher. Many studies have shown that insulin resistance, particularly in the major glucose utilizing tissues, precedes the development of Type II DM and may play a critical role in its pathogenesis. Furthermore, skeletal muscle insulin resistance was shown to be a primary defect in Type II DM. Protein ubiquitination is a post-translational modification that plays vital roles in many cellular processes including insulin signaling and proteasomal degradation. A dysregulated ubiquitination process may result in elimination of critical proteins or aggregation and accumulation of abnormal proteins, which leads to a wide range of human diseases including diabetes. Additionally, it has been recently reported that the ubiquitin-proteasome system is hyperactivated in the skeletal muscle cells of obese people, which can be linked to insulin resistance. However, no large scale site-specific protein ubiquitination mapping studies on primary human skeletal muscle cells have been reported. Mass spectrometry based proteomics has become a powerful tool to provide a comprehensive characterization of site specific post-translationally modified protein sequences. In this project, we have performed proteomics analysis using HPLC-ESI-MS/MS combined with immunoprecipitation of ubiquitinated peptides targeting ubiquitin remnant motif to identify ubiquitination sites of primary skeletal muscle cells derived from 3 lean-insulin sensitive participants. This method resulted in identifying 6474 ubiquitination sites assigned to 2800 proteins. Among the identified ubiquitination sites, 2093 sites were novel and have not been reported previously in humans. Interestingly, we have identified ubiquitination sites in 118 kinases/kinases subunits (e.g. AKT, MAPK, JAK, and mTOR) and 48 phosphatase subunits (e.g. PPP2R2A, PPP2CA, PPP2CB, PPP2R3B, and PPP2R3A). We further analyzed the functional annotation of the identified ubiquitinated proteins using DAVID bioinformatics tool. The results showed that many proteins were assigned to significantly enriched critical glucose metabolism pathways (e.g. regulating glucose transport, glucagon signaling pathway, and glycolysis). We also found that different protein classes (e.g. cytoskeletal proteins, ligases, and receptor proteins), biological processes (e.g. response to stimulus and metabolic processes), and molecular functions (e.g. binding and catalytic activity) were significantly enriched. In conclusion, the present study characterized the first global ubiquitinome of primary human skeletal muscle cells derived from lean insulin sensitive participants and discovered numerous novel ubiquitination sites. These findings provide new targets for studies on skeletal muscle insulin resistance in humans.

ABSTRACT NO. 29	
Name	Rami Alzhrani
Category	Doctoral Candidate
Title	Tumor Stroma Disrupting Nanoparticles for Chemo Guided Immunotherapy of Pancreatic Ductal Adenocarcinoma
Authors	Rami Alzhrani; Samaresh Sau; Amro Aboukameel; Hashem O. Alsaab;, Asfar S. Azmi; Arun K. Iyer
Abtract	Pancreatic ductal adenocarcinoma (PDAC) is the third highest cause of cancer-related death in the United States. PDAC represents one of the most challenging cancer due to its pathological characteristics, such as dense desmoplastic tissue with >90 % tumor stroma. Among all epithelial tumors, PDAC has the densest stroma that contributes to chemotherapy resistance and reduces drug delivery to the core of the solid tumor. Overexpressing of multiple surface biomarkers such as CD24+, CD44+, ESA+, and c-Met contribute in forming PDAC stroma; thus, chemotherapeutic resistance increases. Therefore, overexpressed CD44+ and c-Met receptors can be utilized to enhance drug delivery and efficacy. In this regard, we developed a dual-targeted polymeric nanoparticle (DTPNs) that can target overexpressed CD44+ and c-Met to maximize tumor penetration via active endocytosis. So far, DTPNs was tested on orthotopic PDAC model for evaluating the imaging agent efficiency. The bio-distribution of DTPNs using near Infrared (NIR) dye showed the vast majority accumulated in the tumor site. Interestingly, the tumor/liver uptake ratio study revealed that DTPNs is seven folds higher than non-targeted polymeric nanoparticles (NTPN). On the tissue level, IHC study showed that rhodamine conjugated DTPNs more colocalization with CD44 and c-Met receptors compared to NTNPs. is higher than non-targeted polymeric nanoparticles (NTPNs). The optimized Dual targeted molecule were furthered studied for its therapeutic effects; its in vitro studies revealed that Gemcitabine conjugated polymeric nanoparticles retained killing activity compared to commercial gemcitabine. Moreover, Gemcitabine conjugated nanoparticle showed a synergistic effect when it combined with Everolimus or PD1 inhibitors. Overall, the obtained results indicated that the DTPNs would open avenues for therapy and imaging-guided diagnosis in PDAC tumor.

ABSTRACT NO. 30	
Name	Sharon Batelu
Category	Doctoral Candidate
Title	Molecular & Mechanistic Details of A High Redox Potential Ferredoxin Involved in the Mitochondrial Fe-S Cluster Assembly
Authors	Sharon Batelu, PhD. Candidate; Timothy L. Stemmler
Abstract	Iron-sulfur cluster containing proteins perform various crucial enzymatic roles within cells across all forms of life. In eukaryotes, the mitochondrial iron sulfur cluster (ISC) assembly pathway generates most of the Fe-S clusters used by proteins throughout the cell. One protein essential to this pathway is Ferredoxin, which catalyzes the transfer of electrons required for successful de novo synthesis of clusters. Our lab's working hypothesis is that the ferredoxin, when in complex with the ISC protein apparatus, provides the electrons required to produce the per sulfide sulfur atom needed to make Fe-S clusters. Ferredoxins comprise a large family of low-molecular-mass proteins that are involved in many additional cellular redox processes. Ferredoxins contain a 2Fe-2S cluster themselves, and it has been shown that these are redox-active. Depletion of the gene coding for ferredoxin in yeast has been shown to lead to a 30 fold increase of iron accumulation within the mitochondria. A tandem knockout of this gene along with that of the scaffold assembly protein, on which Fe-S clusters are assembled within the ISC complex, is fatal. While it is clear that the mitochondrial ferredoxin's involvement in the ISC assembly pathway is crucial, its exact role is not. The objective of this study is expand our understanding of the role of ferredoxin within the ISC driven assembly pathway. I have isolated the yeast ferredoxin homologue and have begun the biophysical characterization of the protein to provide the atomic level details needed to clarify the activity of the protein within the ISC complex. The stability and redox cycling of the 2Fe-2S cluster, attached to the yeast homologue, have been characterized biochemically and using several spectroscopic techniques (CD, UV-Vis and X-ray Absorption Spectroscopy). We have measured the activity of the different Fe-S cluster redox states of the cofactor bound to the yeast ferredoxin ortholog in relation to ISC complex cluster assembly activity to elucidate the physiological activity of the protein in relation to its biological activity. Combined, these data paint a broader picture of the crucial role of ferredoxin in the Fe-S cluster assembly pathway.

ABSTRACT NO. 31	
Name	Ketki Bhise
Category	Doctoral Candidate
Title	Novel Hypoxia-Targeting Prodrug for Immunogenic Cell Death in Aggressive Triple Negative Breast Cancer
Authors	Ketki Bhise, MTech; Samaresh Sau, PhD; Mohd Ahmar Rauf, PhD; Arun K. Iyer, PhD
Abtract	Triple Negative Breast Cancer (TNBC) accounts for 10-20% of the total breast carcinoma cases. There is no FDA-approved targeted therapy for TNBC due to lack of the major biomarkers: estrogen, progesterone and HER-2. TNBC is difficult to treat, with a high rate of metastasis to nearby organs. Our lab has identified the role of a hypoxia biomarker, carbonic anhydrase IX (CAIX) in proliferation and metastasis of TNBC. Based on this observation, we developed a CAIX-targeted Doxorubicin (Dox) prodrug, abbreviated as CAIX-Dox. CAIX-Dox can deliver the chemotherapeutic, Dox payload selectively in tumor microenvironment, thus reducing Dox-associated cardiotoxicity. Most of the advanced stages TNBC solid tumors present themselves with oxygen-deficient, vascularized and matrix-rich core which is impermeable to most of the chemotherapy drugs. CAIX-Dox has the advantage of killing epithelial tumor cells as well as tumor-growth promoting T-cells. Recent studies showed that Immunogenic Cell Death (ICD) has vital role in resurrecting the CD8+ T-cells mediated tumor killing. Our approach is to utilize CAIX-Dox for achieving dual effect of CAIX-mediated chemotherapy in addition with induction of ICD. Preliminary studies with CAIX-Dox has profound effect of killing TNBC cells, 4T1, through induction of early phase of apoptosis. The Western Blot analysis in 4T1 treated with CAIX-Dox has proved the significant upregulation of gold-standard ICD biomarkers HMGB1 and calreticulin by greater than 3-fold compared to control. To improve the bioavailability of CAIX-Dox, we developed CAIX-Dox encapsulated nanoparticles that can hitchhike on the plasma circulating albumin. Thus, nanoparticle will travel to the tumor and deliver the CAIX-Dox at the hypoxic core of TNBC, resulting in induction of apoptosis and ICD. Inspired from this outcome, we are developing a model for coculture of cancer and T-cells for evaluating if CAIX-Dox treatment can reeducate T-cells in killing cancer cells through ICD pathway.

ABSTRACT NO. 32	
Name	Zhuoyue Bi
Category	Doctoral Candidate
Title	Arsenic activates Nrf2 and HIF1a
Authors	Zhuoyue Bi, MS; Yao Fu, MS; Priya Wadgaonkar, MS; Qian Zhang, MS; Wenxuan Zhang, MS; Bandar Almutairy, MS; Liping Xu, MS; M'Kya Rice,MS; Chitra Thakur,MS; Fei Chen, Ph.D
Abtract	Long-term exposure to arsenic, esp. the inorganic trivalent arsenic (iAs), a human carcinogen that occurs naturally in the earth's crust or work place due to industrial settings, has been linked to various types of cancers, esp. lung cancer. In the present report, we demonstrated that treatment of the human bronchial epithelial cells with the environmentally relevant concentrations of iAs induces a Nrf2-dependent HIF1a activation, and the subsequent metabolic reprogramming featured with an enhanced glycolysis and diminished mitochondrial oxidative phosphorylation (OXPHOS). Analysis of the ChIP-seq data from the control and iAs-treated cells suggested an increased enrichment of Nrf2 and/or HIF1a on a group of genes important for glycolytic metabolism, malignant transformation, and the generation of the cancer stem-like cells. Intriguingly, we identified Nrf2 binding elements at the 33kp upstream of the HIF1a gene, and HIF1a binding sites on Nrf2 and Nrf2 signaling genes, suggesting forward mutual regulation between Nrf2 and HIF1⊠. Inhibition of Nrf2 by lentiviral-based infection of Keap1, an endogenous inhibitor of Nrf2, not only blocked iAs-induced HIF1a activation, but reduced the expression of Sox2, a key stemness gene critical for the malignant transformation and the formation of the cancer stem cells. In summary, we demonstrated that Nrf2 activation is an initial upstream signal for iAs-induced HIF1a activation, which in turn leads to metabolic reprogramming and malignant transformation of the cells. The data from this study, thus, may be translated into new strategies of cancer therapy by targeting the Nrf2-HIF1a signaling. As one of the most abundant environmental carcinogens worldwide, arsenic affects about 200 million people in more than 70 countries, including the United States. The main sources of environmental arsenic, esp. the inorganic trivalent arsenic (iAs), include groundwater contamination, working place air pollution, and application of certain pesticides in agricultural activities. The greatest threat to public health comes from the direct consumption of groundwater that flows through rocks and minerals containing naturally deposited arsenic. In recent years, an emerging concern of environmental arsenic exposure is the findings that some food crops are highly capable of enriching arsenic in the grain or other edible parts from the iAs-contaminated irrigation water and soil, such as rice, fruits and certain vegetables. Extensive studies had been made in the past on how iAs, induces human cancers in lung, skin, bladder, liver, kidney, hematopoietic systems, and other organs. Through mimicking the environmental iAs exposure, we previously showed that consecutive treatment of the human bronchial epithelial cells (BEAS-2B) with 0.125 to 0.25 uM iAs (~9 to 18 ppb) for six months, induced generation of the cancer stem-like cells (CSCs). Intriguingly, extensive studies unraveled that iAs is a poorer mutagen in mammalian cells. Thus, the cancer causing effect of iAs may be achieved through its co-carcinogen or epigenetic regulations. Few reports had suggested that iAs can convert normal stem cells to CSCs through malignant transformation. However, it is largely unknown whether iAs can induce generation of the CSCs from the normal differentiated cells until our studies showing generation of CSCs through consecutive treatment of the non-cancerous human bronchial epithelial cells. Similar to the normal stem cells, the iAs-induced CSCs also exhibited increased expression of Oct4, Sox2, Klf4, myc, and several other stemness transcription factors. In addition to the tumorigenicity in mice, these CSCs also showed characteristics of self-renewal in vitro and in vivo, and resistance to chemodrug-induced apoptosis. Both 13C-glucose flux assay and untargeted metabolomics studies indicated an increased glycolysis along with a diminished mitochondrial metabolism. Unlike the normal stem cells or cancer cells that generate lactate from glycolysis, the intermediates of glycolysis in the iAs-induced CSCs are mostly shunted to hexosamine biosynthesis pathway (HBP) for protein O-GlcNAcylation, and the serine/glycine pathway linked to one-carbon metabolism and the generation of S-adenosylmethionine (SAM), the most important methyl donor for DNA and histone methylation. Due to the diminished mitochondrial metabolism, the level of a-ketoglutarate (aKG) from TCA cycle is decreased in these CSCs. aKG is a co-factor for JmjC family histone demethylases. Thus, the overall metabolic pattern in the iAs-induced CSCs favors DNA and histone methylation, which may be essential in maintaining the unique chromatin states for CSCs. This finding also provided evidence of the causative role of metabolism on the establishment of the epigenetic landscape of the chromatin in CSCs. Nrf2 was traditionally viewed as a master regulator of the cellular antioxidant response. Emerging evidence, however, suggested that Nrf2 is also a key driving factor for tissue fibrosis, cancer progression, tumor cell metastasis, and therapeutic resistance of cancers. Several genes contributing to the stemness of the stem cells have been revealed as Nrf2-regulated genes, such as ALDH and Notch1. The hypoxia inducible factor 1a, (HIF1a), on the other hand, has been shown to be able to induce human embryonic stem cell (hESC)-like transcriptional program in cancer cells. Silencing HIF1a decreased the expression of Oct4, Sox2 and Nanog, the central stemness genes in cancer cells. Both Nrf2 and HIF1a are capable of enhancing glycolysis of the cells. There are reports showing activation of Nrf2 and HIF1a by iAs, respectively. However, it is unknown whether iAs-induced malignant transformation and the formation of CSCs requires either Nrf2 or HIF1a, or both. It is also unknown whether Nrf2 and HIF1a are two independent signaling pathways or concerted together through interactions in the iAs-induced metabolic reprogramming during the formation of the CSCs. For Nrf2 and HIF1a themselves, the mechanisms of their activation by iAs remain to be fully elucidated. In the present study, we provide evidence showing that iAs induced a Nrf2-dependent activation of HIF1a, which in turn concerted with Nrf2 to promote metabolic shift from mitochondrial oxidative phosphorylation (OXPHS) to glycolysis, most notably, in the HBP and the serine/glycine pathway, the most important side pathways of glycolysis. In addition, we showed that either Nrf2 or HIF1a, or both, can participate in the transcriptional regulation of the key genes important for malignant transformation and the generation of the cancer stem-like cells.

ABSTRACT NO. 34	
Name	Erin Edwards
Category	Doctoral Candidate
Title	Cognitive Processing Speed as a Predictor of Motor Skill Learning in Healthy Adults and Persons with Multiple Sclerosis
Authors	Erin Edwards, BS; Nora Fritz, PhD, PT, DPT, NCS
Abtract	Purpose: Motor and cognitive deficits are frequently reported in individuals with Multiple Sclerosis (MS), resulting in a high incidence of neurorehabilitation enrollment. Presently, there is no way to predict whether a patient will benefit from a specific rehabilitation program and factors mediating exercise responsiveness in MS remain unknown. This pilot study aims to determine a baseline predictor of an individual's ability to benefit from a balance training program. We hypothesized that better information processing speed at baseline would result in greater automaticity at the trained task, as measured by the change in Dual-Task Cost (DTC) following training.

Methodology: 4 healthy participants and 1 MS participant (1 Male and 4 Female; age 40± 14.3 year) underwent 4 consecutive days of balance training on the Neurocom Basic Balance Master. Each day involved a single session of 20, 2-minute blocks where participants performed weight shifts on a force platform in response to targets on a screen. Participants were also evaluated pre- and post-training on their ability to perform a dual-task (Limit of Stability Test +N-back Test).

Results: Following training, all participants demonstrated improvements in reaction time (14%), movement velocity (34%), directional control (5%) and target accuracy (6%) on the challenging balance task. Improved DTC was also seen across individuals, suggesting lower extremity motor skill training is feasible. Lastly, higher baseline processing speed on the Symbol Digit Modalities Test predicted reduced motor DTC in movement velocity (r= 0.671), 95% CI [-1.00, 0.00] and directional control (r=0.783), [0.11,1.00] following training.

Conclusion: Data collection is ongoing; processing speed holds promise as a baseline indicator of the ability to benefit from a motor learning paradigm targeting postural control and balance. Identifying key variables associated with successfully recovery of motor skills is a promising driving-force for improvements in field of neurorehabilitation. |

ABSTRACT NO. 35	
Name	Sai Pranathi Meda Venkata
Category	Doctoral Candidate
Title	The role of G Protein-Couple Receptor 39 in the regulation of mitochondrial function in endothelial cells
Authors	Sai Pranathi Meda Venkata , MS; Hainan Li , MS; Megan O'Meara , BS; .Jiemei Wang , MD, PhD
Abtract	Abstract: Introduction: G protein coupled receptor (GPR) 39 is an orphan receptor differentially expressed in variety of tissues. Endothelial cells (ECs) are responsible for tissue repair and to maintain vascular homeostasis, whose dysfunction increases the risk of cardiovascular morbidity in diabetic patients. However, the role of GPR39 in regulating EC function is not known. We believe that deleting GPR39 may protect mitochondrial functions in endothelial cells in hyperglycemic conditions.

Methods and Results: Healthy human aortic endothelial cells (H-HAECs) and diabetic human aortic endothelial cells (D-HAECs) were cultured in vitro. Studies have shown reduced migration potential (modified Boyden Chamber assay) and tube formation capacity in H-HAECs transfected with adenovirus carrying human GPR39, using transfection of adenovirus carrying egfp as control (n=5-6, p<0.05). Conversely, knocking down GPR39 by siRNA in D-HAECs improved cell migration (n=5, p<0.05). Primary cultured mouse aortic ECs from global GPR39 knockout (GPR39null) mice have shown lower levels of superoxide anions (MitoSOX) and better maintained mitochondrial membrane potential (TMRM/MitoTracker ratio) than that in MAECs from control (GPR39WT) litters in high glucose treatment (25mM, 72 hours). GPR39null and GPR39WT mice were rendered hyperglycemic by low dose streptozotocin (STZ) injections. After 3 months, these animals received hind limb ischemia by left femoral artery ligation. We observed a poor blood flow recovery measured by Laser Doppler imaging in STZ-GPR39WT mice whereas there was better blood flow in STZGPR39null mice (n=10, p<0.05 vs. STZ-GPR39WT).

Conclusions: Based on our results, we believe that deletion of GPR39 protects the mitochondrial function in ECs and maintains vascular homeostasis under high glucose conditions. Thus, the endothelial cell health can be regulated by controlling the levels of GPR39 expression. GPR39 represents a potential therapeutic target in preventing vascular complications in diabetic patients. Keywords: Endothelial function; Ischemic Injury; Diabetes Mellitus; Receptors; Oxidative stress |

ABSTRACT NO. 36	
Name	Huong (Rachel) Nguyen
Category	Doctoral Candidate
Title	A metformin-methylglyoxal imidazolinone metabolite (IMZ) increases nitric oxide production and angiogenesis in primary endothelial cells
Authors	Huong Nguyen, Ph.D. Candidate; Jiemei Wang, Ph.D.; Terrence J. Monks, Ph.D.
Abtract	Endogenous dicarbonyls, such as methylglyoxal, are elevated in type-two diabetes mellitus (T2DM) patients. These highly reactive electrophiles, together with their associated non-enzymatic advanced glycation end products (AGEs) are major contributors to cellular dysfunction during diabetic cardiovascular complications. The T2DM first-line drug therapy, metformin, significantly reduces adverse diabetic endpoints and mortality more effectively than other antihyperglycemic agents. However, the exact mechanism(s) by which metformin protects diabetic patients against cardiovascular complications is not well characterized. We previously reported that metformin scavenges methylglyoxal to form a novel imidazolinone (IMZ) metabolite. Many compounds that possess an imidazoline group act as ligands for imidazoline receptors (IR) and the ⍺-2 adrenergic receptor. Activation of these receptors initiates a signaling cascade that culminates in endothelial cell protection. We therefore hypothesize that IMZ might improve endothelial cell function and contribute to the beneficial therapeutic effects of metformin. In the current studies, we examined the in-vitro effects of IMZ on endothelial cell function using primary human umbilical vein endothelial cells (HUVECs) and characterized potential signaling pathways. In functional studies, we showed that IMZ, at physiological relevant concentrations, induces the production of the endothelial derived relaxation factor, nitric oxide (NO). In addition, IMZ significantly increased network formation and cell migration compared to control cells, indicating that IMZ increases endothelial angiogenesis. Concomitant with functional studies, the signaling studies revealed that short-term treatment of HUVECs with IMZ activated the PI3K/AKT/eNOS and MAPK pathway in a concentration and time-dependent manner; maximum activation occurred between 10 to 20 minutes. Furthermore, a 24-hour exposure to IMZ induced the expression of pro-angiogenic markers in both cellular and extracellular compartments. Interestingly, IMZ-induced PI3K/AKT/eNOS; MAPK signaling and NO production were attenuated by pretreatment with imidazoline 1 receptor (I1R) and α-2 receptor (α2R) antagonists, suggesting that IMZ action is receptor mediated. Collectively, the data demonstrated that IMZ improves endothelial cell function by activating PI3K/AKT/eNOS and MAPK pathway via I1R and/or α2R modulation. Studies are ongoing to further elucidate and confirm the effects of IMZ in in-vivo models.

ABSTRACT NO. 39	
Name	Zoha Siddiqua
Category	Doctoral Candidate
Title	Endocrine disrupting chemicals (EDCs): Detection of the 'estrogenic' properties of water
Authors	Siddiqua Zoha; Tracie Baker, DVM, PhD; Camille Akemann, PhD Candidate; Manahil Monshi, MS; Lakshmi Neha Alla Reddy MS; Katherine Gurdziel PhD; Jeremiah Shields, MS; Karim Alame; Danielle Meyer, PhD Candidate; Andrea Wahls; Fadie Saad, Pharm D; Judy, El-Nachef, Pharm D; Merna Antoon, Pharm D; Raquel Nakhle, Pharm D; Emily Crofts; Nemer Hijazi; Maha Hamid, Pharm D; Husein Nasser, Pharm D; Shawn McElmurry, PhD; Donna Kashian, PhD; David Pitts, PhD
Abtract	The Detroit River receives many contaminants from treated wastewater effluent, combined sewer overflows, urban and agricultural runoff, and landfill leachate. These contaminants include contaminants of emerging concern (CECs) that are not regulated and/or monitored by the governing agencies. Some of these CECs can disrupt normal endocrine function and have been called Endocrine Disrupting Chemicals (EDCs). Feminized aquatic vertebrates have been reported all over the world, particularly near areas where there is significant urban or agricultural impact on the environment. A number of estrogenic chemical contaminants are suspected to be possible contributors to these feminizing influences on vertebrates. Little is known about the transport, fate or relative importance of EDCs responsible for estrogenic effects observed in wildlife or potential human health effects. Our over-arching hypothesis is that model aquatic organisms, Daphnia pulex (waterflea) and Danio rerio (zebrafish) can be used to develop a molecular identification model capable of detecting estrogenic and anti-androgenic activity in water using behavioral, morphologic, and differential gene expression data and that this model can be used as a tool to evaluate the "estrogenicity" of water. Nine structurally diverse CECs that are known or suspected to be estrogenic and/or anti-androgenic were studied: 4-nonylphenol, estrone, bisphenol-A, chlorpyrifos, dieldrin, metformin, triclosan, triclocarban, and atrazine. The influence of 24-hour chemical exposure on gene expression in these aquatic animals was examined using three selected concentrations and a vehicle control based on previous behavioral assay results and literature. QuantSeq was used to examine whole organism alterations in gene expression (mRNA) following chemical exposure. The two model aquatic organisms were found to be very sensitive to environmentally relevant concentrations of EDCs (parts per trillion range, ppt) and a very large number of significant alterations in gene expression were detected. Significant gene expression changes for Daphnia were found in insect hormone biosynthesis and steroid hormone biosynthesis pathways. Examples of altered gene expression include vitellogenin, cuticle proteins, serine proteases, and many others. This study has clearly demonstrated the feasibility of this two-model organism bioassay approach to identify chemicals with estrogenic and/or anti-androgenic activity in water and explore the affected pathways. The study of the effects of single chemical exposure provides the foundation for future experiments that can address the effects of exposure to chemical mixtures typically found in surface water and ground water.

ABSTRACT NO. 40	
Name	Priya Wadgaonkar
Category	Doctoral Candidate
Title	The interplay between endoplasmic reticulum stress, mitochondrial dysfunction, autophagy in arsenic-induced transformation and the generation of the cancer stem like cells
Authors	Priya Wadgaonkar; Zhoyue Bi; Qian Zhang; Yao Fu; Liping Xu; Wenxuan Zhang; Bander Alamuitary; Chitra Thakur; Fei Chen
Abtract	Arsenic is a Group 1 human carcinogen that can be found in a number of environmental and occupational settings. Drinking water arsenic contamination is one of the major sources of arsenic exposure. In the present study, we explored the mechanistic connections between endoplasmic reticulum stress, mitochondrial dysfunction and autophagy in the arsenic-induced malignant transformation of the human bronchial epithelial cells and the derived cancer stem-like cells. Treatment of the cells with trivalent arsenic (As3+) altered the morphology of mitochondria, depletion of mitochondrial DNA and decreased expression of genes involved in ER stress response and autophagy was also observed. In addition, we noted that As3+ is able to regulate the ER-related unfolded protein response (UPR), the cGAS-STING pathway, and glycolytic metabolism. We believe that these cellular responses to As3+ are critical for the transformation and generation of the cancer stem-like cells if the cells are continuously exposed to environmental As3+.

ABSTRACT NO. 41	
Name	Qian Zhange
Category	Doctoral Candidate
Title	Mdig promotes oncogenic gene expression through antagonizing repressive histone methylation markers
Authors	Qian Zhang, Chitra Thakur, Yao Fu, Zhuoyue Bi, Priya Wadgaonkar, Zhipeng Liu, Wanqing Liu, Jian Wang, Benjamin L. Kidder. Fei Chen
Abtract	Persistent exposure to environmental hazards, such as chemical carcinogens, and toxic metals, is a major risk factor for lung cancer. To investigate the molecular mechanisms of lung diseases that result from the exposure to environmental risk, we have previously reported mineral dust-induced gene (mdig) identified from alveolar macrophages of people who had been exposed chronically to mineral dusts. Mdig is highly induced in many types of cancer, including breast, lung, pancreases, etc. However, how mdig contributes to lung cancer is not clear. Previously, protein sequence alignment suggested that mdig contains a conserved JmjC domain that is a hallmark of histone demethylase. Additionally, an inverse relationship between the level of histone 3 lysine 9 tri-methylation (H3K9me3) and mdig expression was found in lung cancer patient samples. Therefore, we hypothesized that mdig can reduce H3K9me3 to increase gene expression. We knocked out mdig in human bronchial epithelial Beas-2B cells through CRISPR-Cas9 gene editing. We examined the histone methylation profiles by chromatin immunoprecipitation-sequencing (ChIP-seq) and gene expression profiles by RNA-sequencing (RNA-seq) in wild type (WT) and knockout (KO) cells. Our results showed that the knockout is caused by deletion of several nucleotides in the second exon of mdig gene. The global histone methylation analysis revealed a pronounced increase of trimethylation of lysine 9 and 27 on histone H3 (H3K9me3, H3K27me3) as well as trimethylation of lysine 20 of histone H4 (H4K20me3) in the KO cells. Importantly, gene ontology analysis indicated that the enhanced repressive histone methylation inhibits expression of genes in the oncogenic pathways of cell growth, stemness of the cells, tissue fibrosis, and cell motility. Taken together, our current data suggested that mdig is an antagonist for repressive histone methylation markers, and is a potential target for cancer therapy. More studies are ongoing to demonstrate the oncogenic effect of mdig in lung cancer by testing the tumorigenicity of WT and KO lung adenocarcinoma A549 cells in vitro and in vivo.

Clinical Doctorate in Pharmacy

ABSTRACT NO. 42	
Name	Ashley Blanchette
Category	Clinical Doctorate in Pharmacy
Title	Beliefs about medical cannabis use and its association with medication adherence: surveying patients and health care professionals
Authors	Ashley Blanchette, PharmD Candidate; Allesandra Iadipaolo; Farrah Elrahal; Christine Rabinak, PhD
Abtract	Background: Cannabis is widely used among people with chronic diseases and its use will continue to increase as legalization across states increases. As cannabis use becomes more common, it is important to understand patients' and healthcare professionals' attitudes towards use and perceived harms versus benefits. We aim to (1) characterize why patients use cannabis (recreationally, medicinally); (2) evaluate whether patients replace prescribed medications with cannabis; and (3) characterize healthcare professional beliefs about medical cannabis use and perceived implications on clinical care.

Methods: In an ongoing cross-sectional study, we are surveying patients' use and beliefs about cannabis at the Gary Burnstein Community Health Clinic in Pontiac, MI. We are using a validated 27-item survey including demographic information (e.g., age, ethnicity, gender, education), as well as Likert-scale based questions regarding medical conditions, current medications, adherence, medicinal use of cannabis, and beliefs about the benefits and harms of medicinal cannabis use. We have currently collected 17 completed patient survey and we anticipate a total sample size of 100 collected from the clinic. Additionally, we are expanding this survey nationally via online distribution to approximately 1,000 people. Preliminary data collected from the 17 respondents were analyzed using descriptive statistics.

Preliminary results: Most participants were female (65%; n= 17), Black (53%; n=9) and are an average of 46 years old (±15 years). In addition, over half the participants reported previous use of cannabis (57%; n=14 responders) and/or currently use cannabis to self-treat a medical condition (86%; n=7 responders) including: hypertension, depression, anxiety, and bipolar disorder. Half of participants believe that cannabis has a "major effect" on medical conditions (50%; n=10 responders). These are preliminary results, and more data are needed to characterize cannabis use beliefs among patients with chronic disease(s).

Conclusions: These data will inform future research about the association between cannabis use and prescription medication adherence. |

ABSTRACT NO. 43	
Name	Sara Bugamelli
Category	Clinical Doctorate in Pharmacy
Title	Evaluation of the Cancer and Aging Research Group (CARG) Chemo Toxicity Calculator in Decreasing Health Care Utilization in Colorectal and Pancreatic Oncology Patients
Authors	Sara Bugamelli, PharmD Candidate; Charlotte Wilkinson, PharmD; Jean Doh, PharmD; Angela German, PharmD, BCOP
Abtract	Purpose: The objectives of this retrospective analysis are to determine if utilizing the CARG Chemo Toxicity Calculator in adult colorectal and pancreatic patients in Henry Ford Health System (HFHS) could have predicted toxicity and potentially decreased utilization of emergency room (ER) services and hospital admissions during the first six months of chemotherapy. If the CARG Chemo Toxicity Calculator can be used to predict toxicity, then clinicians can better treat or possibly prevent adverse effects, which will make patients more comfortable and safe, as well as provide a cost-savings for both patients and HFHS. Methods: This is a retrospective, observational cohort study of patients aged 18 years or older who received first-line chemotherapy for newly diagnosed colorectal and pancreatic cancer within the HFHS from January 2016 to July 2019. Patients who previously received treatment for current primary malignancy, pregnant patients, patients who are incarcerated, and clinical trial participants were excluded. Subjects were identified based on a data pull of electronic medical records starting chemotherapy treatment plans for the described inclusion and exclusion criteria. The primary endpoint is a composite of patients who required a hospital admission and/or an ER visit within the first six months of Day 1 of Cycle 1 of chemotherapy. Secondary outcomes include OncoSTAT (oncology urgent care clinic) visits, chemotherapy dose reduction in future cycles, chemotherapy cycle/dose delays, and (6) pharmacologic interventions to treat a complication of chemotherapy. Results/Conclusion: Research in Progress

ABSTRACT NO. 44	
Name	Ryan Caputo
Category	Clinicate Doctorate in Pharmacy
Title	Use of inhaled epoprostenol for pulmonary hypertension in post-cardiothoracic surgery patients
Authors	Ryan Caputo, Pharm.D. Candidate; Brian Feldpausch, Pharm.D. Candidate; Dana Attar, Pharm.D.; Zachary Smith, Pharm.D., BCCCP, BCPS; Long To, Pharm.D., BCPS
Abtract	Purpose Cardiothoracic surgery patients complicated by acute post-operative pulmonary hypertension (PH) have increased morbidity and mortality. Inhaled epoprostenol (EPO) can be used to treat acute PH in this patient population. Parenteral EPO is used off label for this indication. Parenteral EPO is administered using a jet nebulizer attached to the mechanical ventilator (MV) circuit. Recently, Flolan®, a branded EPO product, was reformulated with a higher pH diluent to improve stability at room temperature. To date, no study has assessed the safety or efficacy of this new EPO formulation when used via inhalation. Methods This was a retrospective, descriptive study. The study included mechanically ventilated adult patients admitted to the Henry Ford Hospital cardiac intensive care unit (CICU) after cardiothoracic surgery that developed acute pulmonary hypertension for which they received inhaled EPO from March 2017 to July 2019. The primary outcome was achievement and maintenance of a >15% reduction of mean pulmonary arterial pressure (mPAP) from baseline. The secondary outcome was achievement of an mPAP of < 30 mmHg at 6 hours post inhaled EPO initiation and duration of EPO treatment. Safety outcome assessed included acute lung injury defined as a new onset PaO_2/FiO_2 of < 150, hypotension, thrombocytopenia, and rates of bleeding. Demographic characteristics collected were hospital length of stay, ICU length of stay, duration of mechanical ventilation, and cost of therapy. Descriptive statistics were used to describe outcomes assessed. Results/Conclusion Data collection and analysis are ongoing. An interim analysis will be presented at the WSU Research Day.

ABSTRACT NO. 45	
Name	Ryan Caputo
Category	Clinical Doctorate in Pharmacy
Title	What is the relationship between student attendance and course performance in a doctor of pharmacy program?
Authors	Ryan Caputo, Pharm.D. Candidate; Zachary Mueller, Pharm.D. Candidate; Nicholas Peters, Pharm.D. Candidate; Sean McConachie, Pharm.D.; Sheila Wilhelm, Pharm.D., FCCP, BCPS
Abtract	Purpose: In the Fall 2017 semester, the Wayne State University Doctor of Pharmacy (Pharm.D.) Program implemented a mandatory attendance policy applying to all second-year (P2) Pharm.D. courses. In the Winter 2018 semester, the attendance policy was lifted, and P2 Pharm.D. students were no longer mandated to attend several core therapeutics, pharmacokinetics, and social administrative course sessions. This project was designed to determine whether there is a relationship between student course attendance and performance as determined by course grades and semester grade point averages (GPA). Methods: This was a cross-sectional study evaluating the association between student attendance and semester GPA. Attendance data were collected prospectively by students enrolled in the P2 course curriculum during the Winter 2018 semester using an online spreadsheet. Semester GPA and final grades in individual courses were obtained from the university reporting and learning management system. Variables potentially associated with attendance such as commute length, outside work status, future career plans, student professional organization involvement, and student demographics were collected using an online survey tool. Baseline variables were assessed using descriptive statistics. The association between classroom attendance and semester GPA was analyzed using multivariate linear regression. For those variables associated with semester GPA, post-hoc analyses were conducted to assess their association with attendance. All study procedures were reviewed and approved by the Wayne State University Institutional Review Board. Results: For the full class of 99 P2 students, the overall semester GPA was 3.38 and attendance was 67%. Fifty-one students had complete attendance, performance, and survey data collected; their semester GPA and attendance were similar to the full group (3.37 and 71%, respectively). Semester GPA and percent attendance were not significantly associated on univariate or multivariate regression. Post graduate career plan was significantly associated with semester GPA ($p=0.032$ for residency or hospital aspirations, n=20; $p=0.029$ for unsure or other, n=16) as compared to community pharmacy aspirations (n=12). Post-hoc analysis was performed to assess whether students with different postgraduate plans differed in attendance. Students with community, hospital or residency, or other/unsure aspirations attended class an average of 60%, 83%, and 73%, respectively, which was significant (F=6.628, $p<0.01$). Pairwise testing revealed a significant difference between students with residency or hospital career plans compared with community career plans ($p<0.01$). Conclusion: Overall, there was no significant association between class attendance and semester grades. However, it appears that students who want to practice in health systems or pursue residency training attend class more often than students who plan to practice in community pharmacy. A larger sample size of students and longitudinal data over the course of the Pharm.D. curriculum may lend more clarity to these results. Until that point, it appears that mandating student attendance in didactic courses does not influence semester GPA.

ABSTRACT NO. 46	
Name	Caitlin Carron
Category	Clinical Doctorate in Pharmacy
Title	Nephrotoxicity with Cefepime versus Piperacillin-tazobactam in Combination with Vancomycin Dosed by AUC
Authors	Caitlin Bolick Carron, MPH, PharmD Student; Sarah C.J. Jorgensen, PharmD, MPH, BCPS; Sara Alosaimy, PharmD, BCPS; Abdalhamid Lagnf, MBChB, MPH; Michael J. Rybak, PharmD, MPH, PhD
Abtract	Background: Broad-spectrum beta-lactam agents such as cefepime (FEP) and piperacillin/tazobactam (TZP) are frequently employed in combination with vancomycin (VAN) as empiric therapy for serious infections. Selection is based on susceptibility trends, hospital formularies, safety profile, and cost. The use of VAN has been associated with acute kidney injury (VAN-AKI) rates of 5 – 45%. In addition to increased VAN exposure and patient-related factors such as older age and baseline renal impairment, an important risk factor for VAN-AKI is concomitant nephrotoxins. Although penicillins are not typically regarded as nephrotoxic drugs, aside from rare reports of interstitial nephritis, several studies have shown increased VAN-AKI in patients treated concomitantly with TZP versus VAN monotherapy or VAN + FEP. In these studies, VAN was dosed and monitored to target a specific trough concentration (10 – 20 mg/L). However, recent data suggests that VAN AUC-guided dosing is associated with lower rates of VAN-AKI compared with trough-guided dosing. It remains unclear whether VAN + TZP is associated with increased VAN-AKI when AUC-guided VAN-dosing is used. Due to the morbidity, mortality, and healthcare resource utilization associated with AKI, coupled with limited options to treat resistant infections, it is important to evaluate the relative risk of VAN-AKI when VAN with AUC-guided dosing is used in combination with TZP versus FEP.

Objective: Compare VAN-AKI between VAN + FEP and VAN + TZP. We hypothesize that the risk of VAN-AKI with FEP is lower when compared to TZP. Methods: This will be a retrospective observational comparative cohort study of patients treated with VAN + FEP or TZP between 2015 to 2019. Adult patients (≥18 years) who received intravenous VAN plus FEP or TZP within 24 hours of VAN initiation for ≥ 48 hours were included. Patients with no documented patient-specific AUC-guided VAN dosing, acute kidney injury, end-stage renal disease or any renal replacement therapy (RRT) prior to initiation of VAN were excluded. Nephrotoxicity is defined as an increase in serum creatinine ≥ 50% and 0.5 mg/dL over two consecutive measurements. Once data collection is complete, multivariable analysis will be conducted to determine independent predictors of VAN-AKI. Assuming an absolute decrease of 15% from a baseline rate of 30% in the VAN + TZP group, the target sample size to achieve 80% power with a 95% confidence level is 213 [142 VAN+FEP: 71 VAN+TZP].

Results: To date, we have screened 166 patients who received VAN AUC-guided dosing. Of these patients, 44 met all inclusion/exclusion criteria (40 FEP and 4 TZP). Reasons for exclusion were: 74 had no concomitant FEP or TZP, 23 had AKI at baseline, 23 received combination therapy for < 48 hours, and 2 received FEP or TZP > 24 hours after VAN was initiated.

Conclusions: A large proportion of screened patients were ineligible for this study, predominantly due to AKI at baseline and combination given for too short a duration which may limit generalizability of results. Nonetheless, this study will provide valuable insight into VAN-AKI risk with TZP and FEP in the era of VAN AUC-guided dosing. |

ABSTRACT NO. 47	
Name	Wesley Chiu
Category	Clinical Doctorate in Pharmacy
Title	Microbiome Analysis of Household Biofilm Specimens in Flint, Michigan
Authors	Wesley Chiu, PharmD Candidate; Geehan Suleyman, MD; Shawn P. McElmurry, PHD, P.E.; Katherine Gurdziel; Mary B. Perri, MT (ASCP); Marcus J. Zervos, MD; Paul E. Kilgore, M.P.H., M.D.
Abtract	Background: In 2014--2015, the City of Flint, Michigan experienced a large Legionnaires' disease outbreak, following a switch in the source of drinking water. The change in water source for Flint and lack of corrosion controls resulted in changes to plumbing infrastructure. In water systems and household plumbing, the inner surfaces are often coated with biofilm. Biofilms have the capacity to support growth of a variety of bacterial species. Changes in water systems and associated premise plumbing can alter bacterial populations. The goal of this study was to evaluate the presence of opportunistic premise plumbing pathogens among households receiving water in the Flint water distribution system (WDS). Methods: Household sample collection was identified through convenience sampling approach. Biofilm samples were collected from water pipes in household showers and samples underwent DNA extraction using standard methods. DNA extracts were then provided to the Applied Genomic Technology Center at Wayne State University for metagenomic sequencing studies. Amplification and sequencing of the 16S ribosomal RNA gene was performed using the Illumina Demonstrated 16S Protocol. V3 and V4 regions of the 16S RNA gene was amplified using the S-D-Bact-0341-b-S-17/S-D-Bact-0785-a-A-21, making the amplicon size 464 base pairs. Sequence data was analyzed on the MiSeq using the Miseq Reporter software. Results: Multiple households demonstrated biofilms containing bacterial genetic sequences consistent with potentially pathogenic bacteria. Genetic sequences of potential pathogens found in varying levels across the sampled households included acid-fast (e.g., Mycobacterium ulcerans), gram-positive (e.g., Staphylococcus aureus) and gram-negative pathogens (e.g., Pseudomonas aeruginosa). Households from which potential pathogens were identified in systems with a range of chlorine residual levels, suggesting that human pathogens have the capacity to become established in households and survive exposure to free chlorine concentrations that exceed recommended levels. Conclusions: Biofilms in Flint homes sampled in January 2016 contained families of bacteria that could have been pathogenic. Additional research is needed to more fully understand risks at the time of sampling and, more broadly, the conditions that promote the growth of pathogenic bacteria in premise plumbing. Additional studies will help to understand the prevalence of potential human pathogens that may affect those with pre-existing medical conditions.

ABSTRACT NO. 48	
Name	Evan Cole
Category	Clinical Doctorate in Pharmacy
Title	#KnockOutHPV - A community-based, interdisciplinary approach to improving HPV vaccine uptake at a large urban public university
Authors	Evan Cole, B.H.S., Pharm.D. Candidate; Adalah Yahia, B.H.S., Pharm.D. Candidate; Ann Rayford, M.S.N, B.S., CHES; Karen Huyghe, MA; Joseph Fava, Pharm.D., BCACP
Abtract	Purpose Human Papillomavirus (HPV) is a cause of more than 32,000 cancers yearly in the United States. Despite the fact that the HPV vaccine is highly safe and effective, the Centers for Disease Control and Prevention (CDC) estimated that only 51% of U.S. adolescents had completed the 3-dose HPV vaccine series in 2018. Low rates of vaccine uptake can be attributed cultural, religious, financial, and social barriers. Targeted vaccination programs attempting to resolve this issue have largely showed mixed results. The purpose of this project was to use a unique, interdisciplinary approach to improve patient knowledge and understanding of HPV and the HPV vaccine (primary outcome), and to increase vaccine uptake among individuals in the Wayne State University (WSU) community (secondary outcome). Methodology This project was a pharmacy student-led, prospective, interdisciplinary campaign titled "#KnockOutHPV." The intervention consisted of five main components: promotion and outreach (print, digital materials, social media, immunization incentives), patient education (educational programming, health fairs, speaker engagements with immunization experts), provider education (strategies to increase vaccine uptake), improving access to the HPV vaccine, and documentation of vaccine receipt and series completion. The intervention period took place January 1 – June 30, 2019. The primary outcome was measured using a quantitative pre-post survey consisting of three demographic and four 10-point Likert-scale questions focused on HPV and HPV vaccine knowledge, and willingness to receive and recommend the HPV vaccine. The secondary outcome was measured by quantifying the number of HPV vaccines administered at the WSU Campus Health Center (CHC) in comparison to the number administered in the same time period during the previous year. The intervention and data collection/analysis was determined non-human participant research (Program Evaluation/Quality Improvement/Quality Assurance Activity) by the WSU Institutional Review Board (WSU IRB Number 201879). Results Surveys (n=248) were conducted immediately before and after each educational event conducted during the intervention. When asked how you would rate your current knowledge of HPV, mean responses increased from 5.09 pre-event to 7.96 post-event survey (p <0.001). When asked the same question regarding the HPV vaccine, responses increased from 5.19 to 8.09 (p<0.001). Significant increases in willingness to receive and recommend the HPV vaccine were also found. 83 HPV vaccine doses were administered at the CHC during the study period, compared to 47 administered during the same time period in 2018 (76.6% increase). 35 individuals initiated the HPV vaccine series in 2019 versus 14 in 2018 (250% increase). 21 individuals completed the HPV vaccine series in 2019 versus 21 in 2018 (no change). Conclusions A 6-month, pharmacy student-led interdisciplinary HPV education and vaccine update initiative resulted in significant improvements in individuals' knowledge and understanding of HPV and HPV vaccines and a 76.6% increase in HPV vaccines administered. This project may serve as a framework for other universities to improve public health education regarding HPV and the HPV vaccine, as well as vaccine uptake in campus communities, and/or may serve as pilot data to pursue larger initiatives for the WSU community, the city of Detroit, and/or the state of Michigan.

ABSTRACT NO. 49	
Name	Katherine Dada
Category	Clinical Doctorate in Pharmacy
Title	Update for Ebola in the Democratic Republic of the Congo 2018-2019
Authors	Katherine Dada, PharmD Candidate
Abtract	Background: On August 1, 2018 the Democratic Republic of the Congo (DRC) Ministry of Health declared an Ebola Virus Disease epidemic in the eastern province of North Kivu. The epidemic has grown from 26 cases on that date to more than 3000 cases as of August 28, 2019, with more than 2000 deaths. Several treatments and one vaccine are being used to help control the epidemic, as part of clinical trials and compassionate use protocols. The objective of this review is to provide an overview of the current epidemic and strategies for the response and control of the epidemic. Methods: The information on Ebola cases and deaths used in the paper were obtained from reports and data publications from the World Health Organization and DRC Ministry of Health. The information regarding current Ebola treatments and vaccines was found by searching Clinicaltrials.gov and PubMed. As no recent local population data was available, local population estimates were calculated based on available registered voter data and province population estimates from the DRC government. These population estimates were then used to calculate local incidence rates. Results: The number of Ebola cases has been steadily increasing since the epidemic was declared, but the regions in which these cases are occurring has not been consistent. In order to calculate incidence rates, and get a better understanding of the impact of the epidemic, population values had to be estimated from available registered voter information. The incidence rates are as high as 113 cases/100,000 residents. The response strategy has included four trial treatments and ring vaccination with an investigational vaccine. Conclusions: Although this outbreak faces some unique challenges, the response is equipped with some promising tools. The Ebola response faces challenges with regards to the ongoing conflict in the region, other simultaneous infectious disease outbreaks, and general lack of infrastructure. The response, however, is equipped with two promising treatments, REGN-EB3 and mAb114, that have lowered the case fatality rate, and the rVSV-ZEBOV vaccine, which has helped halt the spread of the virus.

ABSTRACT NO. 50	
Name	Alison Doane
Category	Clinical Doctorate in Pharmacy
Title	Pharmacist impact on smoking cessation and atherosclerotic cardiovascular disease risk in a transitional care clinic
Authors	Alison Doane, PharmD candidate; Aaron Brody, MD, MPH; Liying Zhang, PhD; Phillip Levy, MD, MPH; Brittany Stewart, RD, PharmD
Abtract	Introduction: There are 34 million smokers in the US, thus an increased rate of atherosclerotic cardiovascular disease (ASCVD). This study explores the impact of a pharmacist-led intervention on smoking cessation in an innovative outpatient transitional care clinic (TCC) that focuses on hypertension management for under-resourced patients discharged from the emergency department (ED). Research Question or Hypothesis: What impact does a TCC pharmacist have on smoking cessation and ASCVD risk over six months for patients discharged from the ED? Study Design: Prospective, interventional single arm pilot study. Methods: Patients presenting to the ED with elevated BP (>140/90mmHg), history of HTN, and no primary care visit within the past 6 months were recruited to follow up at the TCC for five visits. The pharmacist prescribed nicotine replacement therapy via a collaborative practice protocol and provided counseling. At each visit BP was measured and ASCVD risk was calculated at visits one and five. Descriptive statistics were used to analyze the data. Results: From May 2017 through August 2018, 116 patients were enrolled, 44 followed up for at least one visit, and 16 completed all five visits and are included in this analysis. The mean age was 48.6 years old (SD=7.65); 55% male; 93.8% African American, mean BMI 39.4 (SD=10.73), and 50% were smokers. Of the eight patients that smoke, six (75%) either quit smoking (n=3) or reduced their number of cigarettes per day. Mean baseline 10-year ASCVD decreased from 12.93 to 8.01% representing a relative reduction of 38%. Conclusion: This intervention achieved reduced smoking rates which leads to a reduction in ASCVD risk. These findings are relevant within a low income, urban population lacking primary care. These data provide a justification for larger scale, randomized control trial to generalize the findings.

ABSTRACT NO. 51	
Name	Sami Ftoini
Category	Clinical Doctorate in Pharmacy
Title	Ethanol and Marijuana Increase Crash Avoidance Reaction Time in a Driving Simulator via Changes in ATTENTION, but not REACTION TIME
Authors	Sami Ftouni; Jamie McQueen; Tailor Echols; Edison Nwobi; Doreen Head; Randall Commissaris
Abtract	We have previously reported that moderate marijuana or ethanol intoxication significantly increases crash avoidance reaction time in a driving simulator. The present study was designed to determine whether these effects are due to changes in ATTENTION versus changes in the actual REACTION TIME. The subject was a consenting adult with a history of moderate alcohol use (3-4 days/week for the past 6 months, but typically fewer than three drinks on any occasion) and very infrequent marijuana use (less than once/month for the past 6 months). For both tests, the subject had not used either alcohol or marijuana during the 24 hours prior to the test. On two test days separated by one week, driving performance was studied before and at various times after administration of (1) alcohol (consumption of 4 ounces of 80 proof vodka, mixed with orange soda), or (2) marijuana (approximately 12.5 mg of THC in an edible product). The test apparatus was a fixed base driving simulator. In the crash avoidance driving test, the subject was instructed to drive 55 mph on a straight roadway, and to swerve right or left to avoid a crash when one or more 'stalled cars' appeared ahead in the roadway. In previous studies, moderate alcohol or marijuana intoxication resulted in a dramatic increase in crash avoidance reaction times. The crash avoidance reaction test requires subjects to (1) recognize the stalled car in the roadway, then (2) determine what crash avoidance maneuver is needed and then finally (3) execute the crash avoidance maneuver using the steering wheel. To test the hypothesis that the crash avoidance impairments produced by moderate ethanol or marijuana intoxication were the result of changes in ATTENTION versus actual REACTION TIME per se, an Alerting Stimulus (three bell dings) was provided approximately 1 second before the appearance of the 'stalled car' for half of the trials (Alerted Trials). In the pre-treatment tests, there was no significant difference in crash avoidance reaction times for Alerted vs Not Alerted trials; thus, attempting to increase ATTENTION to the roadway did not improve crash avoidance reaction time in a sober driver. As reported previously, both alcohol (maximum BAC < 50 mg/dl) and marijuana (THC and metabolite concentrations not yet known) treatments significantly increased crash avoidance reaction times on the Not Alerted trials, with crash avoidance reaction times increasing from approximately 450 msec pre-treatment to 650 msec post-drug. In marked contrast, the effects alcohol and marijuana to increase crash avoidance reaction times were virtually eliminated when the subject was Alerted regarding the upcoming avoidance trial via use of the bell. These preliminary findings suggest that the debilitating effects of moderate alcohol or marijuana intoxication in this crash avoidance reaction test result from changes in ATTENTION to the road conditions while driving, and are not the result of changes in the actual REACTION TIME.

(This study was approved by the Wayne State University Internal Review Board (WSU IRB #066716B3E). |

ABSTRACT NO. 52	
Name	David Gutenschwager
Category	Clinical Doctorate in Pharmacy
Title	Community Pharmacy Implementation of a Medical and Medication History Form (P-MnM)
Authors	David Gutenschwager, Pharm.D. Candidate; Tara Orzechowski, Pharm.D. Candidate; Joseph Fava, Pharm.D.; Francine Salinitri, Pharm.D.; Richard Lucarotti, Pharm.D.
Abtract	Background & Objectives: Patient medical and medication history is key information for the pharmacist to have in conducting drug therapy review, monitoring and counselling. Currently that information is not readily available nor routinely obtained by the pharmacists in the community setting. To facilitate obtaining this information in this setting, we developed a process for patients to self-complete a form that queries for this information. Along with the development of this form in both electronic and paper formats, this project aims to study the time it takes a patient to complete the form, and their attitudes towards completing the form. Methods: The investigators conducted the study at Marinco pharmacy in Hazel Park, MI, an independently owned community pharmacy. Participants ages 18 and older were invited to complete a medical and medication history form using either a tablet or paper version. Participants were also asked to complete a short survey that assessed their attitudes towards the utilization of the form in a community pharmacy. A student pharmacist reviewed the medical and mediation history form with the patient for completeness and discussed any areas that were not addressed by the patient. During this process, investigators recorded the time for the participants to complete the form and the time for student pharmacist review. Results: Preliminary data for 10 study participants was assessed. The average time to complete the medical and medication history form was approximately 8 minutes and time for student pharmacist review with participants was approximately 11 minutes. Participants had generally favorable attitudes towards the layout of the form, providing all requested information, the importance of the pharmacist having all the information, and updating the form at future visits. Conclusion: The use of a self-completed medical and medication history form within a community pharmacy setting shows promise for being implemented into future pharmacy practice.

ABSTRACT NO. 53	
Name	Annelise Jongekrijg
Category	Clinical Doctorate in Pharmacy
Title	Effect of Treatment Duration on Outcomes in Septic Patients Admitted for Urinary Tract Infections from Extended Care Facilities
Authors	Annelise Jongekrijg, Pharm.D. Candidate; Jamie George, Pharm.D.; Pramodini B. Kale-Pradhan, Pharm.D.; Leonard B. Johnson, MD
Abtract	Background: Adults in extended care facilities (ECFs) are at an increased risk of urinary tract infections (UTIs) with sepsis, and there is little data on effective antibiotic duration. The purpose of this project was to assess the impact of inpatient antibiotic duration on clinical outcomes in these patients. Methods: A single-center, retrospective study of adult, ECF, septic UTI patients from 5/1/16 to 4/30/18 were included. In-hospital mortality, 30-day readmission rate, and length-of-stay (LOS) were compared based on effective antibiotic duration of short- and long-term therapies (≤5 and >5 days, respectively). Pregnant and asymptomatic bacteriuria patients were excluded. Demographics, Charlson Weighted Index of Comorbidity (CWIC), presence of indwelling catheter, SIRS criteria, and antibiotic regimen were collected. Continuous variables were analyzed using Student's t-test and categorical variables with Chi-square test. Results: 105 of 1,158 ECF patients met the inclusion criteria. 38 patients received ≤5 days of effective antibiotic therapy, and 67 received >5 days. Baseline demographics were similar, except the ≤5 days group were older and less likely to have fever (see table). In-hospital mortality was 18.4% in the short-term antibiotic group and 6.0% in the long-term group. Overall 30-day readmission was not significantly different in ≤ 5 days and > 5 days groups (31.6% vs. 25.4% p = 0.648). LOS was significantly greater in the >5 days overall (6.2 vs 9.2 days p = 0.009) and non-bacteremia group (5.3 in ≤5 days vs 9.8 days in > 5 days group p = 0.007). Conclusion: Duration of antibiotics (≤5 and >5 days) did not significantly affect 30-day readmission and in-hospital mortality; however, LOS was significantly longer in the >5 days group.

ABSTRACT NO. 54	
Name	Nicole Knoth
Category	Clinical Doctorate in Pharmacy
Title	Evaluation of Staphylococcus aureus bacteremia treatment at a community hospital
Authors	Nicole Knoth, PharmD Candidate; Vince Procopio, PharmD; Marilen Martinez, PharmD
Abtract	Purpose: In 2017, Staphylococcus aureus bloodstream infections resulted in 120,000 cases and 20,000 associated deaths in the United States. Each day blood cultures remain positive there is a 16% increase in death, highlighting the need for fast and appropriate antibiotic treatment. Several recent studies have demonstrated improved outcomes for patients who have an infectious disease (ID) consultation, repeat blood cultures to confirm bacteremia clearance, screening for source of infection and appropriate antibiotic selection. The purpose of this retrospective observational study is to evaluate the management and treatment of S. aureus bloodstream infections at Henry Ford Macomb Hospital (HFMH).

Methods: This was a retrospective chart review of patients admitted to HFMH between June 2017 and June 2019. Patients aged 18 years or older were included if they had a single positive blood culture for S. aureus and received antibiotic treatment at HFMH. Patients were excluded if pregnant at the time of treatment, had incomplete medical records or received treatment at a location other than HFMH. Patient specific variables that were recorded during the study included the source of infection, blood culture results, if an echocardiogram study was performed, length of bacteremia, length of stay and antibiotics administered during the hospital stay. The primary endpoint was to evaluate the percentage of patients whose antibiotic therapy was properly de-escalated following culture results. Secondary endpoints included the mean number of days to antibiotic de-escalation, percentage of patients who underwent an echocardiogram study, percentage of patients with an ID consult and number of patients who had repeat cultures drawn. Results/Conclusion Data analysis is currently in progress.

Results and conclusions will be presented on October 16th, 2019 at Wayne State Research Day. |

ABSTRACT NO. 55	
Name	Shelby Koppinger
Category	Clinical Doctorate in Pharmacy
Title	Infliximab use, adverse effects and discontinuation in subjects with sarcoidosis and rheumatoid arthritis at Henry Ford Health System
Authors	Shelby Koppinger, Student Pharmacist; Enrique Cavlo-Ayala, MD; Vince Procopio, PharmD; Amber Lanae Martirosov, PharmD, BCPS, BCACP.
Abtract	Background: Sarcoidosis and rheumatoid arthritis (RA) are inflammatory diseases that carry significant morbidity. The treatment for both conditions is similar and consists of modulating the immune system by decreasing chronic inflammation in order to prevent permanent end-organ damage. Tumor necrosis factor alpha (TNF-α) inhibition is usually indicated in both diseases as a second or third line therapy. Infliximab and adalimumab are some of many agents that block the TNF-α and are considered disease-modifying anti sarcoid agents (DMASD). Current expert opinion recommends the concomitant use of steroids or methotrexate to prevent the development of antibodies against infliximab or adalimumab, however this statement is not evidence-based in sarcoidosis patients, and many subjects have been on monotherapy for years. There is literature in RA patients to support the combination of methotrexate and biologic agents as this practice decreases the risk of antidrug antibody production. There is a theoretical increased risk of congestive heart failure and hematologic malignancies in subjects treated with infliximab or adalimumab, however, the frequency of these severe adverse effects has not been well established. The optimal duration of anti-TNF-α treatment is unknown, however, expert opinion guidelines recommend consideration of discontinuation after six months of therapy; however many patients stay in this treatment for many years and currently there is lack of published research describing if these subjects in long-term treatment develop any side effects. The objective of this study is to describe the duration of treatment with TNF-α inhibitors in subjects with sarcoidosis or RA, and to identify its side effects and reasons for discontinuation of treatment.

Methods: This was a single-center retrospective cohort study of adults (≥18 years old) with diagnoses of either sarcoidosis or RA treated with infliximab between the dates of 06/01/2015 to 06/01/2019. Data points collected included baseline characteristics, biopsy results for confirmation of sarcoidosis diagnosis, organ of biopsy, infliximab initiation and discontinuation dates, adverse effects (heart failure, leukemia, anaphylaxis, death, hospitalization, infusion reactions, and hepatotoxicity), serum levels of infliximab, antibodies to infliximab and initiation and discontinuation dates of immune modulating therapy during treatment with infliximab. Descriptive statistics will be used to summarize outcomes, time to discontinuation will be estimated using Kaplan-Meier analysis.

Results/Conclusion: Data collection and analysis are ongoing. An interim analysis will be presented at the WSU Research Day. |

ABSTRACT NO. 56	
Name	Jean Ashley Lava
Category	Clinical Doctorate in Pharmacy
Title	Evaluation of a Patient Intervention Capture Survey Process in an Interprofessional Student-Run Free Clinic
Authors	Jean Lava, Pharmacy Student; Eugenia Zeng, Medical Student; Justine Gortney, PharmD; Jennifer Mendez, PhD
Abtract	Purpose: In order to determine interventions made by students from different professional disciplines at a student-run free clinic, a patient intervention capture survey (PICS) was developed. The PICS generates data which showcases what kinds of education and services were provided to patients at the clinic. Patient records or student interview data were evaluated to ascertain the types of interventions made during the clinic, as well as determine any gaps in documentation of the patient's visit. This study evaluates how modifications over time made to a PICS has improved the collection of interventions. Methods: An initial PICS was developed, which captured medication and medication-related education, physical assessments, referrals to other providers, and other services provided by students during the clinic. Patient charts were reviewed retrospectively over an 11-month period. Results were evaluated and the survey was redesigned for easier data capture and better alignment with interventions with the intention of capturing prospectively. Results: The results of this study are from the original PICS and the modified PICS. While comparing the two versions, the values will be presented as data from original PICS then the modified PICS. The number of patients seen at the CHIP clinic was 101, from January 2016 to December 2016, and 161, from August 2017 to February 2019. Patients provided with medical and pharmacy education interventions increased from 58% to 94%, and an average of 5.4 patients per month to 8.3 per month. Medication counseling improved from 1.6 per month to 5.94 per month. A difference was also seen in social work interventions made, as the average monthly value went from 3.2 interventions and 3.8 referrals to 4.5 and 4.67 respectively. Conclusion: Modifications made to the PICS survey and clinic assessment forms have increased the quality of documentation. Students' awareness as to what is expected during clinic has also increased, which has enhanced their patient interaction skills. One of the modifications made to the original PICS, for example, was method of capture of medication-related education provided as well as developing more specific medical-related topics of education. Though there has been a general trend of an increase in the amount of interventions documented, there were still areas where some interventions were unclear. Students need to put an increased emphasis on counseling patients on medications, as some patients were given new medications but were not consistently counseled on it. Since the modified PICS was introduced, a fourth discipline has joined the clinic and further modifications will need to be made. Continued follow-up and evaluations of interventions captured during clinic will need to be made given these changes, and student education regarding potential shortcomings will be implemented.

ABSTRACT NO. 57	
Name	Andrew Mannino
Category	Clinical Doctorate in Pharmacy
Title	Efficacy and Safety of Ceftazidime/avibactam in Comparison to Polymyxin B and Colistin in Multidrug-resistant Gram-negative Organisms
Authors	Andrew Mannino Pharm. D Candidate; Sara Alosaimy, Pharm. D., BCPS; Sarah C.J. Jorgensen, Pharm.D., BCPS ;Abdalhamid M. Lagnf, M.P.H; Susan L. Davis, Pharm.D.; Michael J. Rybak, Pharm. D., MPH, Ph.D.
Abtract	Background: Multidrug-resistant (MDR) infections are associated with high mortality, morbidity and increased healthcare expenditure. Carbapenem-resistant Enterobacteriaceae (CRE) have been identified as an urgent threat according to the Center of Disease Control. Even with current treatment standards, the most common CRE pathogens; Klebsiella pneumonia, Acinetobacter baumannii, and Pseudomonas aeruginosa are associated with mortality as high as 50%. Current treatment standards for CRE infections include polymyxin B and colistin, however; they carry an acute kidney injury (AKI) risk of over 30%. Ceftazidime/avibactam (CZA) is a new beta lactam beta lactamase inhibitor combination that has been approved for multi-drug resistant gram-negative infections including CRE. CZA has been associated with low incidence of side effects including nephrotoxicity. Previous data on Klebsiella pneumoniae being treated with colistin vs ceftazidime avibactam showed superiority for the newer agent. We aim to assess the efficacy and safety of ceftazidime/avibactam in comparison to polymyxin B and colistin in the treatment of CRE infections.

Methods: This is a retrospective analysis of efficacy and safety of CRE agents in treating MDR organism infections ranging from January 2010 to August 2019. We included patients in Detroit Medical Center and Henry Ford Hospital treated for ≥72 hours with ceftazidime/avibactam, polymyxin B, or colistin as definitive therapy after culture differentiation. MDR organism was defined according to the CDC definition (i.e. an isolate that is resistant to one antibiotic in ≥3 drug classes). Patients were excluded if they left against medical advice, being under palliative care, had end stage renal disease, were pregnant, or incarcerated. Patients were screened and analyzed based on these primary outcomes: resolution of infection, adverse drug reactions, survival at 30 days, and reoccurrence of infection within 60 days. We will also be focusing on renal safety outcomes based on RIFLE criteria for grading nephrotoxicity. Secondary outcomes include: length of hospital stay, 60-day infection related readmission, development of resistance during treatment, eradication of the organism based on a negative follow up culture, discontinuation of therapy due to adverse drug effects, appropriateness of therapy, and time to onset of AKI. Patients will be matched 2:1 using inverse probability of treatment weighting. Categorical data will be analyzed using and continuous data will using Chi squared or Fischer exact test. Kaplan Meier estimation and Cox Proportional Hazards Regression will be used to analyze time to events such as mortality and adverse reactions to medications

Results: Upon screening for 623 Cases, we have identified 33 with Klebsiella pneumoniae, 58 with Pseudomonas aeruginosa and 110 with Acinetobacter baumannii. We excluded N=283 (45%) cases for treatment being less than 72 hours and N=92(15%) for being same patient readmissions. The remainder of the results are in progress.

Conclusion: In progress |

ABSTRACT NO. 58	
Name	Rylie Martin
Category	Clinical Doctorate in Pharmacy
Title	The impact on systolic blood pressure and atherosclerotic cardiovascular disease risk in a pharmacist-led transitional care clinic for patients discharged from the emergency department
Authors	Rylie Martin, PharmD Candidate; Shivan Patel, PharmD Candidate; Aaron Brody, MD, MPH; Liying Zhang, PhD; Phillip Levy, MD, MPH; Brittany Stewart, RD, PharmD
Abtract	Purpose: Uncontrolled blood pressure (BP) is the most modifiable risk factor related to atherosclerotic cardiovascular disease (ASCVD). Several studies have shown that pharmacist-led hypertension (HTN) management is effective and improves patient outcomes in multiple settings. This study explores an innovative outpatient transitional care clinic (TCC) that focuses on HTN management for under-resourced patients discharged from the emergency department (ED). Methods: This is a prospective, interventional single-arm pilot study of a unique health care delivery system. Patients presenting to the ED with elevated BP (>140/90 mmHG), history of HTN, and no primary care visit within six months were recruited to follow up at an outpatient pharmacy clinic for five visits. The pharmacist initiated and titrated antihypertensive therapy via a collaborative practice protocol and provided lifestyle counseling. BP was measured at each visit and ASCVD risk score was calculated at visits one and five. Descriptive statistics were used to analyze the data. Results: From May 2017 through August 2018, 116 patients were enrolled, 44 followed up for at least one visit, and 16 completed all five visits and are included in this analysis. The mean age was 48.6 years old (SD=7.65); 50% male; 93.8% African American; mean BMI 39.4 (SD=10.73) and 50% were smokers. Average systolic BP decreased from 162 mmHG (SD=27.5) to 139 mmHG (SD=19.3) and the ASCVD 10-year risk score decreased from 12.93% to 8.01% (SD= 5.11) which represents a relative reduction of 38%. Conclusions: This intervention achieved an average BP reduction of 23 mmHg and remained controlled throughout the study. The 10-year ASCVD risk showed a meaningful decrease of 4.92%. These results are encouraging in this high risk, under-resourced population. These data provide justification for a larger scale randomized controlled trial in order to generalize the findings.

ABSTRACT NO. 59	
Name	Hannah Moore
Category	Clinical Doctorate in Pharmacy
Title	Evaluation of the Appropriateness of Acid Supprressive Therapies at Hospital Admission
Authors	Hannah Moore, Pharm.D. Candidate; Derek Volgyi, Pharm.D. Candidate; Sean McConachie, Pharm.D., BCPS
Abtract	Purpose: Acid suppressive therapies (AST), such as proton pump inhibitors (PPI) and histamine-2 receptor antagonists (H2RA), have been linked to serious adverse events; however, over-prescribing of these therapies in hospital and community settings remains common. The purpose of this project is to determine the appropriateness and prescribing origin of inappropriate AST among newly admitted internal medicine patients. Methodology: This is a retrospective, observational analysis of patients who received admission medication reconciliation and acid suppressive therapy during their stay at Beaumont Dearborn. Information was gathered from electronic medical records on medication administration and patient interview data. Appropriateness was determined using indication and duration criteria. Appropriate indications for AST included: gastroesophageal reflux disease, erosive esophagitis, prophylactic therapy for patients on concomitant high-risk medications, and other FDA-approved indications. Appropriate duration was determined using clinical guidelines and varied based on indication. Patients who tried to discontinue therapy but were unable to due to adverse effects were considered appropriate. Data was collected on PPI/H2RA use, dose, duration of therapy, and initial prescriber. Data was also collected regarding if the patient had ever seen a gastroenterologist, had gotten an esophagogastroduodenoscopy (EGD), or if the patient had ever attempted to stop their acid suppressive therapy. Results: Of the 89 patients evaluated, 62 (69.7%) patients had appropriate indications for PPI/H2RA therapy, 12 (13.5%) patients had inappropriate indications, and 15 (16.8%) patients had no PPI/H2RA previously prescribed. Of these 15 patients who were prescribed a PPI or H2RA in the hospital, only 8 (53.3%) had appropriate indications for prescription. Of the 62 patients who had appropriate indications, only 21 (33.9%) had been seen by a gastroenterologist, only 33 (53.2%) had ever had an EGD done, and only 27 (43.5%) had ever attempted to discontinue therapy. Of the 62 appropriate patients, 15 (24.1%) had inappropriate duration of therapy. Of the 12 patients who had inappropriate indications, only 2 (16.7%) had been seen by a gastroenterologist, only 4 (33.3%) had ever had an EGD done, and only 5 (41.6%) had ever attempted to discontinue therapy. Conclusions: A substantial portion of AST prescriptions identified in our study were inappropriate and used without proper diagnosis, follow up, or monitoring. Our results show that many patients are prescribed acid suppressive therapy and stay on this therapy for decades without gastroenterological follow up. This can increase the risk of adverse drug effects caused by these medications. Assessing and deprescribing AST medications in the outpatient setting may be a valuable role for ambulatory and community pharmacists.

ABSTRACT NO. 60	
Name	Pia-Allison Roa
Category	Clinical Doctorate in Pharmacy
Title	Evaluation of adverse effects associated with the use of high dose steroids in intensive care unit patients
Authors	Pia-Allison Roa, PharmD Candidate; Allison Bouwma, PharmD, Zachary Smith, PharmD, BCPS, BCCCP, Mark Mlynarek, RPh, BCPS
Abtract	Purpose: High dose steroids are commonly prescribed in Intensive Care Unit (ICU) patients for their anti-inflammatory and immune-modulating properties.1 Common indications for high dose steroids include immunosuppression for transplant patients, hypersensitivity drug reactions, sarcoidosis, neurologic disorders, and interstitial pulmonary fibrosis. The long-term side effects of steroids such as weight gain, hypertension, hyperglycemia, mood disorders, osteoporosis, and higher risk of infection are well-known and well-documented in literature.2,3 The acute side effects of high dose steroids in ICU patients, however, are not as prominent in current literature, making monitoring parameters difficult to predict. Studies focusing on inpatient steroid use have shown corticosteroid-induced bradycardia and other arrhythmia's such as atrial fibrillation and ventricular tachycardia.4,5 This medication use evaluation (MUE) will evaluate the safety of high dose steroid use, specifically in the ICU for acute disorders.

Methods: This MUE was a retrospective, observational cohort study approved by the study center's investigational review board. Patients were included if they were 18 years of age or older, admitted to the ICU at Henry Ford Hospital from August 2016 to June 2019, and received at least one dose of a high dose steroid. High dose steroid was defined as a dose greater than 500 mg of methylprednisolone equivalent. Patients who received a high dose steroid for a new solid-organ transplant were excluded. The primary endpoint was occurrence of an adverse effect occurring during the course of high dose steroids. Adverse effects assessed were hyperglycemia defined as a glucose greater than 200 mg/dL or greater than 400 mg/dL, documented infection 48 hours after the start of the steroid, hypertension defined as greater than 160 mmHg systolic blood pressure, bradycardia defined as less than 60 beats per minute, tachycardia defined as greater than 150 beats per minute, hypernatremia defined as greater than 150 mEq/L, and hypokalemia defined as less than 3.5 mEq/L. Secondary outcomes include dosing, duration of high dose steroids, and characteristics of the patient population receiving treatment. Descriptive statistics will be used to summarize outcomes.

Results/Conclusion: Data analysis is ongoing. Results and conclusion will be presented at the WSU Research Day. |

ABSTRACT NO. 61	
Name	Ashley Semma
Category	Clinical Doctorate in Pharmacy
Title	Evaluation of anticoagulation prescribing patterns in patients with suspected or confirmed heparin-induced thrombocytopenia
Authors	Ashley Semma, B.S, PharmD Candidate; Mya Tran, B.S, PharmD Candidate; Jona Lekura PharmD, BCPS; Ahlam AlMansoub PharmD; Klarita Seitllari PharmD, BCPS
Abtract	Background: Heparin-induced thrombocytopenia (HIT) is a serious complication that occurs in approximately 0.2% of patients who are exposed to heparin. Although rare, it is a serious disease which if not treated appropriately can lead to thrombosis or limb ischemia. National guidelines give recommendations on which anticoagulant to select based on patient and clinical characteristics. However, there is a lack of a singular preferred anticoagulant medication for treatment of HIT in clinical practice and heterogeneity exists in the prescribing patterns of the available options among different health care systems. At our institution, argatroban or fondaparinux are agents of choice for suspected or confirmed HIT with eventual transition to warfarin. The purpose of this study is to evaluate anticoagulation prescribing patterns of non-heparin anticoagulation medications, as well as short and long term outcomes in patients with suspected or confirmed HIT at Henry Ford Hospital (HFH).

Methods: This retrospective cohort medication use evaluation focuses on patients with suspected or confirmed HIT from August 2017 to July 2019 who were initially managed with at least one of the following: argatroban, bivalirudin, fondaparinux, or direct oral anticoagulants during their admission at HFH. Data was extracted from electronic medical records using a standardized case report form. Patients were excluded if they were: <18 years old, pregnant at the time of admission, transferred from outside facility, or used anticoagulants other than the ones described. The primary aim was to describe the characteristics of patients with suspected or confirmed HIT. The second aim was to assess the anticoagulation prescribing patterns in patients with suspected or confirmed HIT. The third aim was to evaluate short and long term outcomes in patients with suspected or confirmed HIT.

Results: Data analysis is currently in progress and final results will be presented at Wayne State research day.

Conclusion: Data analysis is currently in progress and final results will be presented at Wayne State research day. |

ABSTRACT NO. 62	
Name	Gaurangi Trivedi
Category	Clinical Doctorate in Pharmacy
Title	Integration of the Wayne State Pharmacy Program into the Jamaica Dental Mission: Pharmacy Student Experiences and Clinical Outcomes
Authors	Gaurangi Trivedi, Pharm.D Candidate; James Christopher Lynch, Pharm.D; Opal Bacon, Pharm.D; Helen Berlie, Pharm.D, BCACP
Abtract	Dental and pharmacy professionals from various universities have been providing dental care to underserved populations in Montego Bay, Jamaica. This year one third year pharmacy student from Wayne State University joined this experience. The purpose of pharmacy participation in the Jamaica Dental Mission (JDM) is to promote oral health literacy, access to dental care, and interprofessional education through the collaborative efforts with the dental team. Each July since the year 2000, a group of dentists, dental students, dental hygienists, pharmacists, pharmacy students and aspiring medical professionals spend one week providing free dental and pharmaceutical care in western Jamaica. Three different dental clinics run simultaneously: Kew Park Elementary School in Westmoreland, Flankers Health Center in St. James, and Cambridge Health Center in Saint James Parish. Each clinic houses an onsite pharmacy, staffed with two pharmacists and four pharmacy students. Pharmacy students conduct patient intake by taking medical histories, documenting allergies, measuring blood pressure (BP), and assessing blood glucose (BG) levels in patients with a history of diabetes. Patients with elevated BP (>180/110 mmHg) or uncontrolled BG (>200mg/dL) are referred to a local clinic for an expedited consultation with a physician. Each dental care clinic provides patients with necessary dental procedures, and the clinic's onsite pharmacies distributes free oral care products. The pharmacists adopted a collaborative practice with the clinic dentists to determine dosing for patients that were prescribed antibiotics and/or analgesics. The pharmacy team also provides counseling to patients on their respective medications, as well as any necessary post-operation instructions. The 2019 Jamaica Dental Mission brought a total of 77 volunteer participants to underserved areas of Western Jamaica. A total of 1,018 patients were cared for over 4 clinic days (332 juveniles and 686 adults). During this period, the dental services provided include the following: 539 cleanings, 258 fluoride applications, 26 sealants, 16 quadrants of scaling and root planing, 617 routine extraction and 46 surgical extractions, 84 glass ionomer restorations, 2 amalgam restorations, 297 composites, and 31 partial dentures. The pharmacies dispensed 344 prescriptions, which included: 4669 ibuprofen tablets, 1003 acetaminophen tablets, 326 amoxicillin capsules, 21 clindamycin tablets, and 6 azithromycin. The pharmacy team performed a total of 690 BP measurements of those a total of 14 patients were referred for immediate medical care for elevated BP and 38 patients were referred to their primary care physician for potential undiagnosed hypertension. Additionally, the pharmacy performed 162 point-of-care BG measurements, and 15 patients were referred to their primary care physician for potential undiagnosed diabetes or follow up of uncontrolled diabetes. Free dental and pharmaceutical care continue to be provided to underserved patients in Jamaica through the JDM. The pharmacy program at Wayne State University has recently established a partnership with the JDM, thereby fostering collaborations and participation in future trips. Furthermore, interprofessional collaboration between dental and pharmacy student teams offers a unique platform for experiential learning and professional development.

ABSTRACT NO. 63	
Name	Gaurangi Trivedi
Category	Clinical Doctorate in Pharmacy
Title	Institutional antibiograms are insufficient to guide clindamycin use in pediatric skin and soft tissue infections
Authors	Gaurangi Trivedi, Pharm.D. Candidate; Sarah Firmani, Pharm.D; Leah Molloy, Pharm.D; Nahed Abdel-Haq, M.D.
Abtract	Clindamycin (CLN) is a common empiric treatment for pediatric skin and soft tissue infections (SSTI) and musculoskeletal infections (MSKI) despite decreasing susceptibility of Staphylococcus aureus (SA) to CLN on institutional antibiograms. The objective of this study was to describe rates of CLN susceptibility in different types of SA infections among patients most likely to receive empiric treatment with CLN. A cohort of patients aged < 18 years that presented to Children's Hospital of Michigan (CHM) in 2016 or 2017 with community-acquired SA infections were evaluated for CLN susceptibility. The following infections were included: abscess, bullous impetigo, non-bullous impetigo, eczema superinfection, lymph node, osteomyelitis, and staphylococcal scalded skin syndrome (SSSS). Patients that had cultures on or after the 4th day of hospitalization, during an outpatient visit, or admitted to the hematology/oncology service were excluded. CLN susceptibility was compared between each infection type and with the overall CHM 2016-2017 antibiogram. The CHM 2016-2017 antibiogram included 1384 patients with SA infections and 1095 (79%) were Clindamycin-susceptible (CLN-S). 113 patients were included in this study, 90 (80%) of whom had CLN-S infections. The most common infection type was abscess (n= 64), and 89% of these were CLN-S ($p = 0.054$) compared to the antibiogram. Other infections included osteomyelitis (n = 29, 72% CLN-S, $p = 0.380$), eczema superinfection (n = 9, 55% CLN-S, $p = 0.083$), non-bullous impetigo (n = 3, 67% CLN-S, $p = 0.596$), bullous impetigo (n = 3, 33% CLN-S, $p = 0.051$), SSSS (n = 3, 67% CLN-S, $p = 0.596$), and lymph node (n = 2, 100% CLN-S, $p = 0.468$). No statistically significant difference was observed between the study population or any specific infection type and the antibiogram. However, the 10% greater susceptibility SA isolated from community acquired skin abscesses compared to all SA infections factored in to the antibiogram provides some reassurance for continued empiric treatment. Therefore, empiric therapy recommendations for specific infections should not solely rely on the institutional antibiogram.

ABSTRACT NO. 64	
Name	Derek Volgyi
Category	Clinical Doctorate in Pharmacy
Title	Evaluation of Adverse Drug Reaction Formatting in Common Drug Information Databases
Authors	Derek Volgyi, Pharm.D. Candidate; Hannah Moore, Pharm.D. Candidate; Sean McConachie, Pharm.D., BCPS; Christopher Giuliano, Pharm.D., MPH
Abtract	Purpose: Formatting of drug information impacts risk-benefit interpretation of medications by both patients and healthcare providers. A previous research study found that the formatting of adverse drug reaction (ADR) information significantly influenced how likely pharmacists and pharmacy students were to attribute a potential ADR to a corresponding medication, even if the likelihood of medication-induced ADR was very low. The purpose of this project is to determine the current formatting variations of basic ADR information in commonly used drug information databases. Methodology: This is a cross-sectional analysis of ADR formatting among seven commonly-used drug information databases including Micromedex, Micromedex In-depth answers, Epocrates, Lexicomp, Clinical Pharmacology, RxList.com, and Physicians Desk Reference (pdr.net). Databases will be assessed for the following ADR information: presence of placebo comparisons, severity assessment, onset information, qualitative vs. quantitative frequency information, word count, and formatting style (bullets vs. paragraphs vs. tiered hierarchies). Twenty commonly-used oral medications will be assessed in each database to obtain a representative sample. Data will be collected independently by two investigators and discrepancies will be resolved via consensus. Descriptive statistics will be used to describe and categorize ADR formatting results among the different databases. Results: Results currently pending. Conclusions: Variations in formatting for adverse drug reactions have the potential to influence clinical decision-making. Knowledge of formatting differences can be used to optimize drug information practices among pharmacists and other healthcare providers.

ABSTRACT NO. 65	
Name	Sharon Yousif-Dickow
Category	Clinical Doctorate in Pharmacy
Title	Association between melatonin and antipsychotic use in non-critically ill patients
Authors	Sharon Yousif-Dickow; Shutian Ju; Opal Bacon
Abtract	Purpose: Acute or subacute fluctuating disturbances of consciousness including disorientation, inattention, disordered thinking, cognitive impairment, emotional liability, hallucinations, delusions, and sleep-wake cycle disturbances define delirium. Additionally, the mortality rates among hospitalized patients with delirium range from 22-76%. Pharmacologic management and prophylaxis of delirium typically involve antipsychotics, subjecting patients to the adverse effects associated with this class. As sleep-wake cycle disturbance is a factor associated with delirium, there is conflicting evidence suggesting that melatonin can prevent hospital-associated delirium. Moreover, data is limited regarding non-ICU patients. The purpose of this study is to evaluate the use of melatonin versus the use of benzodiazepines (BZD) or zolpidem in non-critically ill adult patients to examine how the use of these agents may impact the use of antipsychotics for delirium. Methodology: This study is a multi-center retrospective cohort analysis of non-critically ill patient encounters between August 2012 to September 2016 with an order for pro re nata (PRN) antipsychotic agents. The primary endpoint will be examining whether a PRN antipsychotic is administered within 5 days after the subject receives their first dose of melatonin, BZD, or zolpidem. Admission characteristics, past medical history, comorbidities, and home medications related to the primary and secondary outcomes will be collected. Results: Research is still in progress. All results will be available and presented at the 2019 EACPHS Research Forum.

ABSTRACT NO. 66	
Name	Humayoun Ahmed
Category	Clinical Doctorate in Pharmacy
Title	Impact of a Pharmacy-Led Transitions of care program on internal medicine readmission rates
Authors	Sean McConachie Pharm.D., BCPS; Humayoun Ahmed, Pharm.D. Candidate; Mohammad Chahrour, Pharm.D. Candidate
Abtract	Background: Hospital readmissions are common, costly, and often preventable; however, the overall impact of pharmacist-led transitions of care programs to reduce readmissions remains controversial. A meta-analysis from the Cochrane Collaboration concluded that the impact of pharmacist-led transitions of care on medication discrepancies was uncertain based on low quality of current evidence, contrary to other published meta-analyses. These analyses demonstrate that further studies are needed to clarify the impact of pharmacist-provided-transitions of care on 30-day readmission rates. Additionally, current studies have primarily analyzed pharmacist interventions and have not explored layered-learning models with pharmacy interns and residents. The aim of the study is to determine the effect of pharmacist-led transitions of care services on 30-day readmission rates for internal medicine patients compared to standard of care practice using a layered-learning model. Purpose: The primary objective of this study is to assess 30-day readmission rates among internal medicine patients who are targeted by a pharmacist-led-transitions of care team compared to patients who receive standard of care at Beaumont Hospital Dearborn. The secondary objective is to assess the financial impact of a pharmacy-led transitions of care program on hospital costs. Methodology: This is a retrospective cohort study assessing 30-day all-cause readmission rates between patients who received intervention from the pharmacy transitions of care team (PTOC) and those who received standard of care treatment (SOC) at Beaumont Hospital, Dearborn. The PTOC team (pharmacy specialist, students, and resident) performed admission/discharge medication reconciliation, medication education, and followed up patients that were "high-risk for readmission" after discharge. SOC patients received routine care from nurses and physicians, where nurses conducted admission/discharge medication reconciliation. The EMR was used to identify internal medicine (IM) patients admitted to the IM resident teaching service between January 1, 2019 and May 31, 2019. Charts were reviewed to determine if patients were managed by the PTOC team or SOC group. Afterwards, patient charts were evaluated to identify 30-day readmissions after the initial encounter during the study period. Chi-square analysis will be used to compare the 30-day hospital readmission rates in PTOC and SOC teams. Multivariable logistic regression will be performed to determine the impact of pharmacy intervention (of any type) on 30-day readmission rates. All variables which are significantly different between the two groups will be added to the regression model to ensure analysis of potential confounding. A cost-analysis will be performed using a pharmacist base salary of $130,000 dollars per year and an estimated cost of readmission of $14,400 per year (based on 2019 estimates from the Healthcare Cost and Utilization Project, or HCUP). Results/Conclusions: Pending

ABSTRACT NO. 67	
Name	Wasem Altwil
Category	Clinical Doctorate in Pharmacy
Title	A retrospective evaluation of the impact of interprofessional efforts with an ambulatory pharmacy team on hemoglobin A1c in an internal medicine clinic
Authors	Insaf Mohammad, Pharm.D., BCACP; Wasem M Altwil, Pharm.D. Candidate; Heba Chahrour, Pharm.D. Candidate
Abtract	Background: Diabetes mellitus is a clinical disorder that is characterized by hyperglycemia as a result of insulin resistance, reduced insulin secretion, or both. Subpar management of this chronic condition can lead to worsening health outcomes, such as the development of microvascular and macrovascular complications and excessive healthcare costs. Among the reasons for the worsening health outcomes are poor medication adherence, increasing cost of medications, poor dietary considerations, health literacy issues, and lack of patient motivation. Positive clinical, humanistic, and economic outcomes highlight the value of multidisciplinary collaborative diabetes care with a pharmacy team in the literature. The Beaumont Schaefer Internal Medicine Clinic is an academic training clinic for medical residents, pharmacy residents, and pharmacy students. The ambulatory pharmacist joined the clinic in August 2017, at which time an interprofessional approach to the management of diabetes began. In this model, the pharmacist manages patients with uncontrolled diabetes via shared medical appointments, independent pharmacist visits, and telephonic encounters in between visits.

Primary objective: To evaluate the change in hemoglobin A1c in the two years pre- and two years post-intervention (pharmacist introduction to clinic) Secondary objectives: • To evaluate the proportion of hemoglobin A1c values at designated goal for each patient in the two years pre- and post-intervention • To evaluate the average hemoglobin A1c for each patient in the pre- and post-intervention periods

Methodology: This is a retrospective observational study that will include diabetic patients who have had ≥1 encounter with the ambulatory pharmacy team since August 2017. Hemoglobin A1c values will be evaluated in the two years pre- and two years post- introduction of the clinic pharmacist in August 2017, and each patient will serve as his/her own control. For the primary outcome, we will use the most recent HgbA1c values surrounding August 2017 as points of reference (evaluate change from oldest A1c to August 2017, then reading immediately following August 2017 compared to most recent value in present time). The proportion of hemoglobin A1c values at each patient's individualized hemoglobin A1c goal pre-intervention and post-intervention will also be compared. Lastly, an average of all hemoglobin A1c values for patients who have at least two values in each time period will be obtained. We will capture baseline demographics, the number of encounters the patient had with the pharmacy team, and hospitalizations related to hypoglycemia. Descriptive statistics will be used to summarize the baseline characteristics of the study population. Change in hemoglobin A1c in the two years pre- and two years post-intervention will be analyzed using a paired t-test and generalized linear model to adjust for covariates. Generalized linear models will also be used to evaluate the proportion of hemoglobin A1c values at designated goal for each patient in the two years pre- and post-intervention. A paired t-test and generalized linear model to adjust for covariates will be used to analyze average HgbA1c for each patient in the pre- and post-intervention periods. A sample size of 30 patients is estimated to detect an average of 1% change of A1c.

Results/Conclusions: Pending |

ABSTRACT NO. 68	
Name	Amina Ammar
Category	Clinical Doctorate in Pharmacy
Title	Pharmacist Impact on Physician Practices in Diabetes Management
Authors	Amina Ammar; Lindsay M. Darghali; Hannah Ferrari; Dena Berri; Hassan Nasser; Daniel Varghese; Iman Bazzi; Helen Berlie, Pharm.D.; Linda Jaber Pharm.D.
Abtract	Background: The American Diabetes Association (ADA) recommends patients achieve the following composite goal: A1c <7%, blood pressure (BP) <140/90 mmHg, and low-density lipoprotein (LDL) <100 mg/dL to reduce the risk of diabetes-related morbidities.

Objectives: The specific aims were to: (1) Examine the impact of the physical presence of a pharmacist on physician practice for diabetes management and (2) examine the pharmacist's impact on physician adherence to ADA standards of care in an outpatient primary care clinic. The central hypothesis was that DM patients managed in a clinic with a pharmacist present (Group A - Intervention) would achieve more optimal care than those managed in a clinic without a pharmacist present (Group B - Control).

Methods: This was a retrospective, randomized, quantitative study of patients seen within Health Centers Detroit Medical Group. Patients with diabetes >18-years-old seen by their physician at least twice between June 1, 2018-June 30, 2019 were eligible for inclusion; those seen by the pharmacist were excluded. A sample size of 177 patients was estimated with the G* Power Statistical Analysis software. Statistical significance was defined by a 95% power (1-Beta) and a one-tailed t-test at a 5% significance level (alpha= 0.05). Main Outcomes and Measures The primary outcome was to examine group differences in the composite targets: A1c, BP, and LDL. The secondary outcomes were to analyze group differences in individual A1c, BP, and LDL targets and to compare physician adherence to ADA standards of care.

Results: Two-hundred and four patients were included (Group A: 104; Group B: 100). Participants were 57% female with a mean age of 61 years. The mean ± SD A1c was 7.4 ± 2.2% for Group A and 7.7 ± 2.1% for Group B. For Group A, 57% achieved an A1c of <7.0% versus 50% of Group B (p=0.346). The mean ± SD BP was 139/76 ± 21/12 mmHg for Group A and 135/81 ± 21/13 mmHg for Group B. In both groups, 54% achieved BP <140/90 mmHg. The mean ± SD LDL was 92.3 ± 38.7 mg/dL for Group A and 102.3 ± 39.6 mg/dL for Group B. For Group A , 64% achieved LDL <100 mg/dL compared to 54% for Group B. Only 16.4% of participants achieved the three ADA goals. However, significantly more patients in Group A (22.2%) compared to Group B (10.4%) achieved this goal (p = 0.026, OR = 2.18). When comparing individual physicians, those working directly with pharmacists were more adherent to ADA standards.

Conclusion and Relevance: This study demonstrated a trend toward improvement in diabetes management as a result of pharmacist presence. A significant reduction in the composite goal was achieved in patients managed in a clinic with pharmacist presence. Data is limited by a small sample size, lack of baseline A1c data, and inconsistent documentation. Future studies are needed to further characterize the impact of pharmacist presence on physician practices. |

ABSTRACT NO. 69	
Name	Lindsay Darghali
Category	Clinical Doctorate in Pharmacy
Title	Barriers to Pharmacist Managed Diabetes Clinic Visits: A Performance-Improvement Process
Authors	Hannah Griffin; Amina Ammar; Lindsay M. Darghali; Hannah Ferrari; Iman Bazzi; Dena Berri; Hassan Nasser; Daniel Varghese; Michelle McGarrity, MA, LLP, PhD; Linda Jaber Pharm.D.; Helen Berlie Pharm.D.
Abtract	Background/Importance: A recent study conducted by Pharm.D. students at Health Center Detroit Medical Group (HCMDG) demonstrated consistent lowering of A1c in patients with diabetes seen in the Pharmacist Managed Diabetes Clinic (PMDC). However, this study also revealed that 54% of patients stopped returning for their follow-up appointments. Objectives: The specific aims of this study were to: (1) identify barriers that prevented patients from consistently following-up at the clinic and (2) utilize these barriers to reconnect patients to the PMDC. Methods This was a prospective, qualitative, performance-improvement measure. A previously constructed survey was used to identify barriers preventing patients from returning to the PMDC. Over 600 patients were screened for inclusion in this study. Patients were eligible if they had been seen by the PMDC team at least once, but had not returned for follow-up care within the last 12 months (inactive patients). Patients were excluded if they had never been seen by the PMDC team or if they had been seen within the past 12 months (active patients). Using the barriers survey, inactive patients were contacted via telephone. Research is currently in progress. Results: Of the 250 patients called, barrier information has been collected for 92 patients. Preliminary examination of the data indicates identified barriers were diverse. The most common barrier was misconception of the need for follow-up with PMDC (23%). Other important barriers included: physical barriers (6.5%), issues with facility (7.6%), financial barriers (5.3%) beliefs and attitudes (5.4%), perception of disease (8.4%), and dissatisfaction with care received (6.5%). Phone call interventions resulted in 43.5% of patients scheduling a follow-up appointment with the PMDC. Conclusion and Relevance: Preliminary results indicate that many patients were unaware that their PCPs wanted them to continue following up with the PDMC, and were interested in seeing the pharmacist after clarification. Data was limited by patient recall and a small sample size. However, this research is ongoing and upon completion will have a larger sample size. Current and future results are clinically significant to the HCDMG to increase patient visits and more importantly to improve patient outcomes.

ABSTRACT NO. 70	
Name	Samantha Langell
Category	Clinical Doctorate in Pharmacy
Title	Evaluation of Point of Care Testing in Community Pharmacies
Authors	Samantha M. Langell; Frass Ahmed; Mahfuz Haque; Mohammed Adbi; Harris Khan; Navreen Cheema; Apala Vaishnav; Paul E. Kilgore, M.D.
Abtract	In the United States, pharmacists are often the first healthcare provider that patients turn to even before visiting their primary care physician or emergency department. Over the past few years, community pharmacists are offering an increasing array of services including medication therapy management and immunizations. This places pharmacists in a unique position to offer additional services such as point-of-care testing (POCT). The use of POCT in community pharmacies represents a practical approach that brings diagnostic testing closer to the patient where testing is most urgently needed. In urban settings such as those in Detroit, patients have limited access to healthcare facilities and diagnostic testing for acute and chronic disease states. Such limited access may delay diagnosis and treatment of common health conditions. At the same time, there are few studies that have evaluated the practical implementation and effectiveness of POCT in communities. The study hypothesis is that pharmacists do not have an extensive knowledge about POCT. The study group believes that the survey and video may change the pharmacist's opinions of POCT and some of the post-survey questions. The study group created a standardized survey that determines the baseline knowledge, attitudes, beliefs and practices (KABP) of community pharmacists. In addition to the survey, the study team devised an educational video and a list of pharmacies in Detroit. The study team divided the list of pharmacies. The students called that pharmacies and used a pre-written script to determine the pharmacist's interest in participating in the research. If the pharmacist elected to participate in the research then students set an appointment to visit the pharmacist at the pharmacy. The students administered the pre-survey, played the educational video and then administered the post-survey. After all the surveys are complete, analysis will be conducted to evaluate changes in KABP with respect to point of care test usage in the community pharmacy. Study variables collected include: pharmacist name, study address, email, phone number, age group, educational degree and years in practice. Other variables include questions related to POCT usage and performance in a community setting. The expected outcomes of the project are to determine the POCT-related KABP among community pharmacists. The study team also plans to determine the helpfulness of the educational video. Moreover, the study group would like to identify a group of motivated pharmacists who will integrate POCTs into their community pharmacy. Finally, the study team will determine the feasibly of POCT in community pharmacies.

ABSTRACT NO. 71	
Name	Christopher Miller
Category	Clinical Doctorate in Pharmacy
Title	Distinct Subpopulations of Intravalvular Methicillin-Resistant Staphylococcus aureus With Variable Susceptibility to Daptomycin in Tricuspid Valve Endocarditis
Authors	Christopher R. Miller; Somrita Dey; Paula D. Smolenski; Pushkar S. Kulkarni; Jonathan M. Monk; Richard Szubin; George Sakoulas; Andrew D. Berti
Abtract	Background: Daptomycin resistance, although rare, is often associated with the presence of sequestered infection including osteomyelitis or infective endocarditis. Anatomical site susceptibilities are not routinely performed and the susceptibility of blood cultures is used as a surrogate. Development of two bacterial populations with different susceptibilities at a single anatomical site is not necessarily surprising; however, the exclusive recovery of only daptomycin-resistant populations from one leaflet and exclusive recovery of only daptomycin-susceptible populations from another leaflet of the same valve is surprising and to our knowledge has not been reported elsewhere.

Patient case: A 46 year old female with a history of IV drug abuse presented to hospital July 2018 with MRSA bacteremia susceptible to both vancomycin and daptomycin. Tricuspid valve infective endocarditis was diagnosed by transesophageal echocardiogram. The patient initially refused valve replacement surgery and was managed medically with vancomycin for 6 days before leaving against medical advice. Prior to leaving, blood cultures had cleared and the patient was switched to daptomycin as an outpatient treatment. The patient was readmitted to hospital in August 2018 claiming she was perceptive to heart valve surgery. Blood cultures on readmission were positive for MRSA, again susceptible to both vancomycin and daptomycin. Intra-operative cultures were taken from each leaflet of the removed tricuspid valve. The septal leaflet was sterile, the anterior leaflet contained daptomycin-susceptible S. aureus (B308), and the posterior leaflet contained exclusively daptomycin-resistant S. aureus (B309, MIC=4).

Methods: Both isolates were subjected to comparative whole genome sequencing. In-vitro one-compartment PK modeling was performed on both isolates to assess comparative fitness in the presence of various antibiotics. Regimens modeled included DAP 10mg/kg every 24 hours (fCmax 12 mg/L, t½ 8h), VAN 2g every 12 hours (fCmax, 36 mg/L, t½ 6h) and CFZ 2g every 8 hours (fCmax 26 mg/L, t½ 2.8h). Hemolysis assays comparing both isolates were performed using traditional blood agar plating.

Results: Vancomycin monotherapy, while initially efficacious against both MRSA strains, supported regrowth at 12 hrs for BSN9R and at 24 hr for BSN9S. Additional doses of vancomycin were ineffective in bacterial killing. DAP monotherapy likewise displayed early efficacy, but allowed for significant regrowth of both strains by 72 hrs. VAN+CFZ was efficient at reducing cell counts early, but allowed for regrowth starting at 24 hours. In contrast to other simulated regimens, DAP+CFZ combination was superior in the eradication of both BSN9S and BSN9R, bringing cell concentrations below the limit of detection within 2 hours and maintaining durable activity for the entirety of the 72 hour simulation. Several mutations were also present in the resistant strain including an agr mutation.

Conclusions: Peripheral blood cultures may not always accurately represent antimicrobial susceptibilities in deep-seated infections. DAP-CFZ combination therapy appears to be effective in the treatment of deep-seated S. aureus infections and the data presented supports it's use empirically in similar clinical scenarios. Agr dysfunction may be associated with increased bacterial persistence due to its function in the regulation of virulence factors. |

ABSTRACT NO. 72	
Name	Christopher Miller
Category	Clinical Doctorate in Pharmacy
Title	Suppression of daptomycin resistance development in Staphylococcus aureus is a class effect of beta lactams and is independent of daptomycin-beta lactam synergy
Authors	Miller CR; Dey S; Smolenski PD; Kulkarni PS; Baines SL; Berti AD
Abtract	Background: Previous studies demonstrate that adding oxacillin during daptomycin (DAP) exposure can prevent DAP resistance development in community-acquired (ST8/USA300) MRSA, presumably by preventing mprF mutation. Hospital-acquired strains, such as MRSA sequence types 5 and 239, typically have higher beta lactam (BL) minimum inhibitory concentrations (MICs) than their community-acquired counterparts and are often less toxigenic, more multidrug-resistant and more refractory to primary antistaphylococcal therapies. It is unknown if DAP resistance prevention occurs in hospital-acquired MRSA lineages or if augmenting DAP therapy with BL antibiotics other than oxacillin would prevent DAP resistance development.

Methods: MRSA ST5/USA100 (D592) and ST239 (JKD6004) differ in the degree to which BL enhances DAP activity. D592 and JKD6004 were passaged in escalating concentrations of DAP in a stepwise fashion in vitro as described previously. Following 28 days of serial passage all replicates were passaged twice on mannitol-salt agar and tested for DAP MIC by Etest. Parallel passages were performed in media supplemented with BL antibiotics. Between-group differences in DAP MIC suppression effectiveness among individual BLs compared to nafcillin was evaluated using Kruskal-Wallis rank sum testing with Holm-adjusted post-hoc Dunn testing. Eleven additional sequence types were passaged to demonstrate the broad applicability of findings.

Results: Passage of D592 or JKD6004 in DAP resulted in highly DAP-resistant isolates (median ≥ 256 mg/L, IQR [96,256]). In contrast, when passages were performed in the presence of DAP+BL, DAP resistance development was suppressed. This effect was consistent regardless of sequence type. No between-group differences in DAP MIC suppression effectiveness was observed among individual BLs compared to nafcillin. Highly DAP-resistant isolates demonstrated variable collateral susceptibility to BL monotherapy but were frequently susceptible to combination antibiotic exposure.

Conclusion: Addition of beta lactams to DAP can prevent DAP resistance development in vitro in thirteen distinct MRSA sequence types, consistent with findings in ST8/USA300 lineages. Furthermore, this ability appears to be a class effect of beta lactam antibiotics and is independent of the extent of DAP-BL synergy. This provides evidence to support use of BL combination therapy without regard of staphylococcal lineage or specific BL used. |

ABSTRACT NO. 73	
Name	Leah Samman
Category	Clinical Doctorate in Pharmacy
Title	Pharmacists Prescribing a Birth Control in a Community Pharmacy - College Student Opinions
Authors	Leah Samman, PharmD Candidate; Mary Beth O' Connell, Pharm D; Theresa Bailey, PharmD; Greg Wellman PhD, RPh; Larissa King, Pharm D Candidate
Abtract	Introduction: In the United States the unintended pregnancy rate is about 50% and has an annual healthcare associated cost of $21 billion. Ten states and Washington DC allow pharmacists to prescribe birth control. Past data states 68% of women would access birth control from a pharmacy. The study purpose was to evaluate female college students' opinions about pharmacists prescribing birth control in a state without this service. Methods: Online anonymous quantitative survey distributed by two colleges geographically distant to capture urban and rural cities. Survey piloted first in 10 students. Survey had 48 items - 3 healthcare experience values, 3 pharmacy services and evaluation, 22 pharmacist prescribing birth control advantages and barriers, sexual and reproductive history, and 20 demographics items, which were investigator developed. Students entered a raffle for $250 gift cards. Survey link sent via emails, social media, and snowballing recruitment strategies. SPSS vs. 25 used including descriptive, Chi square, and paired T-tests with $p < 0.05$ significant. IRB approved. Results: Respondents (N=182) were 24.5 + 5.5 years old, predominantly white (82%), 71% in a health curriculum (36% student pharmacists), 76% were sexually active, 58% having at least one unprotected intercourse within a year, and 46% never using condoms. There were several significant differences with healthcare experiences between providers. Students stated primary care providers are more trustworthy and have greater privacy. While students believed pharmacists provide better birth control education, offer easier appointment scheduling, and would take less time and cost less to get birth control. Concerns were Pap smear availability and wrong birth control prescribed. 41% of students surveyed were extremely likely and 30% moderately likely to get birth control from a pharmacist because they believed it would be more convenient, take less time, easier, and they would be less likely to run out of medication (in order of frequency). Conclusions: Most students attending Michigan colleges would use a pharmacist for birth control. Based on opinions, sexual activity and unprotected intercourse, this service is needed.

ABSTRACT NO. 74	
Name	Zied Shammout
Category	Clinical Doctorate in Pharmacy
Title	Biofilm Susceptibility Tests to Assess the Bactericidal Activity of Daptomycin Combinations against Biofilm-Producing VRE faecium (Efm) and faecalis (Efc)
Authors	Zied Shammout, BS; Razie Kebriaei; Katherine Lev; Katie Barber; J Smith; Michael Rybak
Abtract	Purpose: E. faecium (Efm) and E. faecalis (Efc) are responsible for 13.9% of hospital-acquired infections with frequent resistance to vancomycin (82.6% of Efm, 9.5% of Efc). Medical device infections secondary to enterococci often require combination therapy due to impaired activity against biofilm embedded cells. In vitro data demonstrate synergistic activity of daptomycin combinations. Using a novel, biofilm time-kill approach, we evaluated whether daptomycin combinations maintained synergy against Vancomycin Resistant Enterococcus (VRE) biofilm-producing Efm and Efc. Methods: Minimum inhibitory concentration (MIC) and minimum biofilm eradication concentration (MBEC) values for daptomycin, ampicillin, ceftriaxone, fosfomycin, and rifampin were determined using broth micro-dilution method (BMD) against biofilm-producing Efm and Efc. Daptomycin combination MBEC values were determined in presence of MIC biologic peak concentrations of the adjunct antimicrobials (whichever is lower). Synergy was evaluated against two Efc (R6981, R7808) and two Efm (5938 and 8019) using a previously described biofilm time-kill method. Synergy was defined as >2 log10 CFU/ml reduction comparing to the most active agent alone. Results: Daptomycin MBECs were 4-16 fold higher than BMD. In the presence of adjunct antimicrobials, daptomycin MBECs were reduced 8-128 fold (Table 1). Ceftriaxone and ampicillin demonstrated the most potent combinations with daptomycin, yielding synergy against 3 of 4 strains. Daptomycin plus rifampin was synergistic against Efm 5938 and Efc 6981 and produced bactericidal kill. The combination of daptomycin plus fosfomycin displayed synergy solely against Efc 6981. [Tables not included] Conclusions: Daptomycin combinations with beta-lactams demonstrated promising synergistic activity against biofilm embedded Efm and Efc. While daptomycin plus rifampin yielded bactericidal results in some strains, the effect was not seen across all organisms. These combinations warrant more detailed investigation with more strains and antibiotics.

ABSTRACT NO. 75	
Name	Nicole Zabik
Category	Clinical Doctorate in Pharmacy
Title	Detla-9-Tetrahydrocannabinol Moderates the Effects of Avoidance Symptom Severity During Fear Extinction in Trauma-Exposed Individuals
Authors	Nicole L. Zabik, B.S.; Allesandra Iadipaolo, B.A.; Farrah Elrahal, B.A.; Craig Peters, B.S.; Hilary A. Marusak, Ph.D.; Christine A. Rabinak, Ph.D.
Abtract	Purpose: Avoidance of stimuli associated with a traumatic event can lead to the development of trauma-based disorders and perpetuate the severity of symptoms. Indeed, avoidance can interfere with the ability to extinguish conditioned fear responses, one of the hallmarks of trauma-based disorders. Recent data from our lab suggests that an acute dose of Δ9-tetrahydrocannabinol (THC), prior to fear extinction, facilitates recall of extinction learning by increasing activation in corticolimbic brain regions. However, it is unknown if THC can facilitate fear extinction in individuals with high avoidance symptoms. The present study examines the effect of avoidance symptoms on fear-related neural activation during extinction memory recall and how THC moderates that relationship.

Methods: 60 trauma-exposed adults (ages 18 – 60) participated in a randomized, double-blind, placebo-controlled, between-subjects design and completed a novel Pavlovian fear-extinction paradigm using virtual reality coupled with FMRI. During fear acquisition, two conditioned stimuli (CSs) were presented: two CS+s paired with an aversive unconditioned stimulus (US) and one CS- never paired with the US (safety cue). Before fear extinction, participants were administered an oral capsule containing either 7.5 mg of THC or sugar (PBO). During fear extinction, one CS+ was extinguished (CS+E), while the other was not (CS+U). 24 hours later, all CSs were presented during recall of extinction learning. Avoidance symptom severity scores were measured with the Clinical Administered PTSD Scale-5.

Results: Participants given THC had higher medial prefrontal cortex (mPFC) activation during recall of extinction learning (CS+E, $t(32.59) = 2.093$, $p < .05$) compared to those given PBO. Moreover, THC was a significant moderator in the relationship between avoidance symptom severity and vmPFC activation during recall of extinction learning ($\Delta R2 = .17$, $\Delta F(1,56) = 11.58$, $p < .005$; $b = .45$, $t(56) = 3.35$, $p < .005$). Specifically, when participants were given THC, vmPFC activation increased with increasing avoidance symptom severity scores. However, vmPFC activation decreased with increasing avoidance symptom scores in participants given PBO.

Conclusions: This data suggests THC modulates fear-related neural activation during extinction memory recall and may be most beneficial to trauma-exposed individuals with high avoidance symptom severity. |

ABSTRACT NO. 76	
Name	Aida Hijazi
Category	Clinical Doctorate in Pharmacy
Title	Effects of Ethanol versus Marijuana on Crash Avoidance in a Driving Simulator: Both Bad, But in Different Ways? A Preliminary Report.
Authors	Aida Hijazi; Kawthar Alali; Edison Nwobi; Tailor Echolsl; Ki-Jana Malone; Jamie McQueen; Doreen Head; Randall Commissaris.
Abtract	The present study tested the hypothesis that driving scenarios geared toward sedation versus assessment/analysis might be used to differentiate the effects of ethanol versus marijuana, respectively. Two consenting adults served as the subjects; one was a regular marijuana user and the other was a regular alcohol user. After training sessions, both subjects were tested on two occasions: (1) no recent drug use (>12 hours abstinent), and (2) one hour after alcohol or marijuana use. The test apparatus was a driving simulator. In a crash avoidance driving test, the subject was instructed to drive 55 mph on a straight roadway, and to swerve right or left to avoid a crash when one or more 'stalled cars' appeared ahead in the roadway. There were two kinds of crash avoidance trials. For MONO trials ('see => do'), the subject was presented with a single 'stalled car' and the decision to swerve right or left depended upon the lateral position of the 'stalled car', i.e., swerve right if the car ahead is on the left side, and vice versa. For TRIO trials ('see => assess => do'), the subject was presented with three cars simultaneously, and the relative position served to guide the driver, i.e., swerve to the right if the front two cars are on the left and the third car is further behind on the right, and vice versa. In both situations, the front 'stalled car' appeared only 40 meters ahead of the driver, requiring an immediate assessment and steering avoidance maneuver. The primary dependent variable was the time (15 msec epochs) required to initiate an appropriate steering avoidance reaction, i.e., a turn of >10 degrees. Our hypothesis was that drug changes in both MONO and TRIO trial reaction times would be reflective of sedation, whereas changes in only TRIO trial reaction time would reflect impairment in executive decision-making. On control days, the two subjects had similar mean reaction times (approx. 450 msec) on the MONO trials; mean reaction times for TRIO trials were slightly greater (approx. 475 msec), and this was largely due to occasional TRIO trials (approximately 10%) in which the driver initially would turn in the wrong direction for approximately 45-75 msec, but would then 'double-take' and make a rapid correction to turn in the proper avoidance direction. There were no 'double-takes' observed on the MONO trials. The 'buzzed' driver (BAC approximately 50 mg/dl ethanol) exhibited a significant increase in reaction time for both MONO and TRIO trials and did not exhibit an increase in 'double-takes'. In contrast, recent marijuana use had no effect on the reaction time for the MONO trials, but significantly increased reaction time for the TRIO trials; this was due to 'double takes' on more than half of the individual TRIO trials. These data suggest that low dose alcohol exhibits its effects on crash avoidance primarily via sedative effects, whereas marijuana exerts less sedative effects and more effects on driving scenarios requiring evaluation and assessment of the situation. (This study was approved by the Wayne State University Internal Review Board (WSU IRB #066716B3E).

ABSTRACT NO. 77	
Name	Corey Rowe
Category	Clinical Doctorate in Pharmacy
Title	Virtual Screening for Inhibitors Targeting N5-CAIR Mutase and AIR Carboxylase
Authors	Corey J. Rowe, PharmD Candidate; Steven M. Firestine, PhD
Abtract	The enzymes AIR carboxylase and N5-CAIR mutase play a key role in the de novo purine biosynthetic pathway. These two enzymes, while evolutionarily related, are found in different organisms. N5-CAIR mutase is found in bacteria, yeast, and fungi, whereas AIR carboxylase is found in humans. Inhibitors of N5-CAIR mutase have potential as new antimicrobial agents, while inhibitors of AIR carboxylase in humans may hold promise as new anticancer agents. Unfortunately, despite high-throughput screening efforts, no potent, drug-like, small molecule inhibitors of these enzymes have been discovered. To address this problem, preliminary in-silico computational docking studies were conducted to identify potential inhibitors from large databases of commercially available compounds. Docking was performed using the Grid, Wayne State University's high-performance computing cluster, and AutoDock, a free software package developed by the Scripps Research Institute. Computational representations of FDA approved agents and compounds from the National Cancer Institute Diversity III subset were downloaded from the ZINC15 database. Docking was conducted using the E. coli N5-CAIR mutase structure (2ate) from the Protein Data Bank. The results for 4011 docked compounds were analyzed by Raccoon2, which reported an estimated range of binding energies from -2.3 to -8.9 kcal/mol. Selecting only the most potent inhibitors (-7.5 to -8.9 kcal/mol) gave 137 compounds with a wide range of ligand efficiencies. Narrowing the ligand efficiencies to those between 0.3 to 0.45 gave 12 compounds. The binding orientations and interactions with the protein were manually inspected using the Molecular Operating Environment (MOE) program. The calculated binding energies using MOE agreed with those determined by AutoDock, and the docking poses for the 12 compounds were chemically sound. Future studies will focus on evaluating compounds for binding and inhibition of N5-CAIR mutase, conducting a larger docking study with a library containing over 100,000 compounds, and performing docking studies on AIR carboxylase.

Master's Students

ABSTRACT NO. 78	
Name	Jennifer Reish
Category	Master's Students
Title	Dual-plasmid technology for genetic manipulation in methicillin-resistant Staphylococcus aureus
Authors	Jennifer Reish, BS; Somrita Dey, PhD; Andrew Berti, PharmD, PhD
Abtract	Methicillin-resistant Staphylococcus aureus (MRSA) produces an array of virulence factors allowing it to cause a wide range of infections and diseases. Many genes are suspected to contribute to the virulence, however, associating genetic variation to a specific virulence trait has been limited by the overall difficulty of genetic manipulation of staphylococci. Specific challenges include poor transformation efficiency, limited endogenous DNA repair activity, strain-specific methylation patterns and intrinsic resistance to common selectable markers. The goal of this work is to create a robust methodology that enables any mutation to be made in S. aureus. We adapted a dual-plasmid system that incorporates the CRISPR cas9 enzyme into an efficient and reliable technology. Modifications to the plasmids include an expanded selection of antibiotic resistance markers, tight control of the cas9 enzyme allowing for simultaneous maintenance of both plasmids and continued expression of both repressor elements and the foreign DNA recombinase. Improvements in competent cell preparation and electroporation protocols have facilitated efficient DNA transfer. Using this dual plasmid system along with the improved transformation method we have successfully made several mutations in MRSA in as little as 12 days. This robust platform to specifically alter the genetic material of staphylococci will allow us to study the contributions of specific genetic polymorphisms to the virulence of MRSA.

ABSTRACT NO. 79	
Name	Rachel Jimenez
Category	Master's Students
Title	Follicular Ameloblastoma of the Jaw: A Case Study
Authors	Rachel Jimenez, BSN, RN
Abtract	

Background: Ameloblastomas are typically benign neoplasms originating from the odontogenic epithelium. They make up 1% of all oral tumors and 18% of odontogenic tumors. The presented case study follows a 60-year-old female patient who presented to the emergency room with a chief complaint of lower lip edema. Radiographic imaging confirmed a mixed solid and cystic lesion with bony remodeling of the alveolar ridge to the left of the mental protuberance of the mandible. Biopsy of the lesion showed ameloblastoma of the follicular type, and the patient underwent a marginal mandibulectomy following diagnosis.

Method: The marginal mandibulectomy specimen consisted of the anterior left mandible with teeth numbers 18, 22, 23, 24, and 25. The specimen was sectioned to reveal a soft, gray-white mass measuring 2.0 x 1.5 x 1.2 cm. Adjacent to the mass was a 1.8 x 1.3 x 0.7 cm cavity devoid of contents. Representative sections were submitted to include the mass, cavity, soft tissue margin, underlying bone, and bone margin.

Results: Follicular ameloblastoma was confirmed histologically by recognition of islands of epithelium within a fibrous stroma. The epithelium was composed of columnar, pre-ameloblast-like, palisaded cells with peripheral reverse polarization. Centrally, there were loosely arranged cells resembling the stellate reticulum. Ancillary studies that may be helpful in the diagnosis of ameloblastoma include immunohistochemistry of several cell markers including osteonectin, matrix metalloproteinases, and Ki-67. Molecular testing for FGFR2, RAS, and BRAF mutations may also aid in diagnosis as they have been identified in the majority of ameloblastoma cases. Lastly, frozen sections are of interest. They are highly recommended for potential ameloblastomas because they ensure that a wide resection margin is achieved.

Conclusion: The rare occurrence and benign nature of ameloblastoma has made it a low priority for research. More studies must be conducted to solidify proposed ideas of pathogenesis, molecular involvement, and treatment outcomes. Radiography and histology are the most useful diagnostic techniques, and with early diagnosis and wide local incision, there is a good prognosis. Other treatment options such as chemotherapy and radiotherapy have not proved to be reliable at this time.

ABSTRACT NO. 80	
Name	Hannah Mulcahy
Category	Master's Students
Title	Adenocarcinoma of the Bladder Presenting in a 37-Year-Old Caucasian Female with a History of Recurrent Bladder Cancer
Authors	Hannah Mulcahy, BA
Abtract	Introduction: Adenocarcinoma of the bladder is extremely rare, accounting for approximately 0.5-2% of all bladder neoplasms. These tumors are more commonly secondary metastases from other organs, such as the colon, prostate, and breast, however primary tumors occur as well. The pathogenesis of primary bladder adenocarcinoma remains largely unknown, but potential risk factors include exstrophy of the bladder and endemic schistosomiasis. These tumors are often associated with poor prognosis due to late detection.

Materials and Methods: The patient presented with recurrent, poorly differentiated primary adenocarcinoma of the bladder and was treated via cystectomy with anterior exenteration and bilateral pelvic lymph node dissection with excision of the right pelvic wall to remove the mass. Upon opening, the right anterior, superior bladder dome mucosa was remarkable for an endophytic, tan-gray, solid, hemorrhagic, and partially necrotic mass.

Results: H&E staining revealed purely glandular differentiation that was inconsistent with enteric or mucinous morphology, and the tumor was classified as not otherwise specified (NOS) primary adenocarcinoma. Muscular and perivesical fat invasion was present, and the right pelvic wall margins were found to be positive. The tumor was subsequently staged as pT4b N2 with poor differentiation.

Discussion: Adenocarcinoma of the bladder is a diagnostically challenging neoplasm due to the breadth of the differential diagnosis and similarities to other bladder pathologies. Primary lesions must be differentiated from secondary lesions, which can be difficult due to their morphologic, immunohistochemical, and molecular similarities. Clinical correlation plays a large role in diagnosis, which often occurs at a late stage. Accurate AJCC TNM staging is integral in the determination of the prognosis of these rare bladder neoplasms. |

ABSTRACT NO. 81	
Name	Lindsay Gburek
Category	Master's Students
Title	The Relationship Between Stress and Depression Among Student Registered Nurse Anesthetists During Three Stages of Curriculum
Authors	Lindsay Gburek, BSN, RN; Rachel Mastay, BSN, RN; Kristen Warnick, BSN, RN; Javier Zarate, BSN, RN
Abtract	The prevalence and severity of mental health disorders has been on the rise among graduate university students (Macauley et al., 2018). Although several studies have examined the types of stressors nurse anesthesia students experience, little literature exists on the relationship between stress and depression. The purpose of the study was to discover the relationship between stress and depression in Michigan Student Registered Nurse Anesthetists (SRNAs) during three critical time periods of the curriculum, transitioning in, finding their way, and transitioning out. A quantitative cross-sectional design was utilized and an anonymous Qualtrics survey was administered via email. All students enrolled in a Michigan Nurse Anesthesia school as of fall 2018 were eligible for participation. The survey contained demographic data, a modified version of The Modified Stress Scale and the PHQ-9 depression screening tool. 64 responses were included in statistical analysis. The majority of subjects were between the ages of 24-32 years of age (range of 56% - 82.7% by time period in the program) and female (58.6% - 71.4% by time period). Most of the subjects (55.2% - 84%) had financial assistance to attend school other than student loans, such as household income, family assistance, or government programs. Finally, between 10.3% – 20% of all subjects had a history of depression which had been diagnosed by a medical professional. All data was analyzed using SPSS v. 25.0 (IBM, 2018). An alpha level of .05 was selected for analyses apriori. Demographic information was analyzed using frequency and descriptive statistics. The findings indicated that depression levels were not statistically significant between groups. However, the incidence of moderate to severe depression was nearly doubled in students enrolled from 0-9 months with a rate of 17.2% compared to students enrolled to 18+ months at a rate of 35.7%. A statistically significant trend of higher median feedback stress, student-faculty interaction stress, and environmental stress was observed the longer a student was enrolled in the program. Additional research on stress and depression in this vulnerable population is required for a more complete understanding of the relationship between stress and depression among Michigan SRNA's.

ABSTRACT NO. 82	
Name	Andrea Davidson
Category	Master's Students
Title	Severity Illness Clinical Key "SICK": A Scoring System to Predict Bariatric Patient Perioperative Factors Affecting Length of Stay
Authors	Rakshika Rajakaruna, M.D.; Wael Saasouh, M.D.; Vinay Pallekonda, M.D.; Michael Wood, M.D.; Ariana Bennett, C.R.N.A.; Andrea Davidson, C.R.N.A.; Jordan Judge, C.R.N.A.; Johnathan Kirupakaran ,M.D.; John Yousef, M.D.; George M. McKelvey, Ph.D.
Abtract	Clinical scoring systems can be invaluable in diagnostic and predictive aspects of clinical treatment. There are numerous systems for predicting surgical risk using explicit variables in many specific populations and treatment groups. Many of the scoring calculators include common comorbidities, yet do not categorize the severity of disease status. Many of these scoring systems also do not take into account metrics that may quantify the quality of disease management or the severity of disease. The Severity Illness Clinical Key "SICK" scoring system is designed to assess the varying degrees of optimization of commonly encountered medical comorbidities present in the bariatric population. The SICK score also aims to stratify how the quality of disease optimization in addition to factors external to medicine such as education and health insurance status. The purpose of this study is to develop a predictive scoring system to identify bariatric patients at risk of intraoperative complications and specifically identifying risk factors that may increase prolonged length of stay, re-operations and emergency room visits. The scoring system known as the Severity Illness Clinical Key "SICK" currently assigns weighted scores based on the worsening scales of morbidities (rather than statistical validation) to different categories of illness, socioeconomic status, and functional status. Using the scores collected from the studied surgical population, the aim is to validate statistically which are the major factors which correlate between higher perioperative score and poor patient outcomes.

ABSTRACT NO. 83	
Name	Sri Aneesha Chundru
Category	Master's Students
Title	Regulatory roles of IQGAPs in Glucose-stimulated Insulin secretion
Authors	Sri Aneesha Chundru; Vijayalakshmi Thamilselvan,Ph.D; Anjaneyulu Kowluru,Ph.D
Abtract	Background: Type-2 Diabetes Mellitus is a chronic metabolic disease characterized by insulin resistance and pancreatic beta-cell dysfunction, the latter is caused due to the defects in glucose metabolism and insulin secretion in beta-cells. Evidence from several laboratories, including our own established novel roles for small G proteins (e.g., Rac1) in glucose-stimulated insulin secretion (GSIS). Recent studies demonstrated roles for scaffolding proteins, such as IQ motif-containing GTPase-activating protein (IQGAPs) in a variety of cellular functions including cytoskeletal organization, cell adhesion and the control of intracellular signaling pathways involving small G proteins, such a Cdc42 and Rac1. Three isoforms of IQGAPs (i.e., IQGAP1, IQGAP2 and IQGAP3) have been identified in the human genome. Despite this evidence in other cells, modulatory roles of IQGAPs in islet beta-cell function have not been examined to date. Herein, we investigated the potential regulatory roles of IQGAP proteins in GSIS from pancreatic islet beta-cell. Methods: INS-1 832/13 cells, rat islets and human islets were used in these studies. Total lysates and subcellular fractions are isolated using a commercially available kit, and were used to determine expression of IQGAPs by Western blot. siRNA knockdown technology was used to suppress the expression of endogenous IQGAPs. Enzyme-linked immune sorbent assay (ELISA) technique was used to measure the amount of insulin secreted under glucose stimulus. Results: Western blot analysis indicated that IQGAP1 and IQGAP2, but not IQGAP3 are expressed in INS-1 832/13 cells, human and rat islets. Sub-cellular fractionation studies revealed that these proteins are present predominantly in the cytosolic fraction. siRNA-mediated knockdown of endogenous IQGAPs showed significant decrease in glucose-stimulated insulin secretion in INS-1 832/13 cells. Conclusion: These findings provide preliminary evidence for a regulatory role of IQGAPs in glucose-stimulated insulin secretion. Studies are underway to assess the roles of IQGAP proteins in G protein (Rac1 and Cdc42) activation in pancreatic beta-cells.

ABSTRACT NO. 84	
Name	Noah Gleason
Category	Master's Students
Title	Acyl Carrier Protein as a Potential Driver for the ISC Mitochondrial Fe-S Cluster Bioassembly Machinery
Authors	Noah Gleason; Ronnie Frederick, PhD; John Markley, PhD; Timothy Stemmler, PhD
Abtract	Iron-sulfur (Fe-S) clusters are a crucial cofactor for many proteins that make up the cellular machinery that is shared across all living organisms. As a result, these are essential for a wide array of biochemical pathways. The unique redox and coordination chemistry of the Fe-S clusters allow proteins partners to participate in and regulate diverse cellular processes, including DNA synthesis, electron transfer, and signaling. This makes the assembly pathway essential for cell viability and a breakdown or failure in this pathway can prove fatal. One such instance, of a breakdown in this pathway is characteristic of a hereditary neurodegenerative disorder called Fredrich's ataxia (FRDA). FRDA is the most common ataxia affecting 1 in every 30,000 people and it involves a point mutation in the gene coding for a protein called frataxin. This protein plays a role in the iron sulfur cluster (ISC) assembly pathway. In eukaryotes, the mitochondrial ISC pathway generates most of the Fe-S clusters used ubiquitously within cells. In yeast, ISC activity is accomplished through coordinated efforts of the multiprotein complex constructed of: the Fe- scaffold protein (Isu1) on which Fe-S clusters are assembled, the cysteine desulfurase (Nfs1) that provides sulfur, the accessory protein (Isd11) and acyl carrier protein (Acp) both essential for Nfs1 activity, the adrenodoxin (Yah1) that provides reducing equivalents for cluster stability and frataxin (Yfh1) which is essential for assembly but with an unclear function. The focus of my work is the aforementioned acyl carrier protein (Acp). Our working hypothesis is that Acp binds metals and the metal loaded protein helps drive activation of the ISC machinery. In this study a comparison of three orthologs of this protein will be looked at; Yeast, Bacterial, and Human. Characterization of these three orthologs and their structural and chemical similarities will further our understanding of the complex system that we call the ISC pathway and the possible role Acp has to play in it. Our studies show that Acp has an affinity for several divalent metals prevalent within the mitochondria. Our initial focus in this report is to characterize the interaction of human Acp with Zn(II). The biophysical characteristics of this interaction have been looked into using different techniques within our lab including Circular Dichroism, which gives us the ability to view any secondary structural changes within the Acp:Zn compound, Differential Scanning Calorimetry (DSC), which helps determine its thermal stability and also if the protein will refold back to its original form after each thermal cycle, Metal Binding Competition Assay using UV-vis, which gives us the binding affinity of Zn to the protein, and X-Ray Absorption Spectroscopy (XAS), which informs us about the oxidation state of the metal and the ligand environment surrounding it. Combined, these studies describe the metal binding characteristics of the protein which set the foundation for understanding the physiological relevance of metal loaded protein towards Fe-S cluster biosynthesis.

ABSTRACT NO. 85	
Name	Hainan Li
Category	Master's Students
Title	Blood pressure elevation induced by deoxycorticosterone acetate (DOCA)-salt model is blunted by deletion of G Protein-coupled Receptor 35 Gene in mice.
Authors	Hainan Li, MS, Megan O'Meara, BS, Sai Pranathi Meda Venkata, MS, Jie-Mei Wang, MD, PhD.
Abtract	Introduction: G protein-coupled receptor 35 (GPR35) is a poorly characterized receptor with controversial endogenous ligands and unclear intracellular signaling pathways. The connection between GPR35 and hypertension have been suggested in recent studies. It has been reported that GPR35 knockout mice showed resistance to the development of hypertension induced by angiotensin II but the mechanism was unclear. We hypothesized that deletion of GPR35 protects blood pressure through augmenting endothelial cell function.

Methods and Results: Human aortic endothelial cells (HAECs) at passaged 5-7 were cultured in vitro. Real-time PCRs confirmed that GPR35 had descent expression levels in HAECs. HAECs with knocking-down of GPR35 by infection of adenovirus carrying shRNA against GPR35 showed improved cell functions including angiogenesis (3D tube formation in collagen culture) and migration (modified Boyden Chamber assay) (n=6, p<0.05 vs. control). Mouse aortic endothelial cells (MAECs) were isolated from adult male GPR35 global knockout (GPR35-/-) mice and their wild type control (GPR35+/+) litters. GPR35-/- MAECs showed improved angiogenesis, migration and proliferation compared with GPR35+/+ MAECs (n=5, p<0.05), with enhanced eNOS protein expression and its phosphorylated form (p-eNOS) (Western Blot, n=5, p<0.05). In the in vivo study, GPR35-/- mice had 22 mmHg of decrease in mean blood pressure (MBP) compared to GPR35+/+ mice as measured by implanted telemetry (n=2-3, p<0.05 vs. GPR35+/+). The plasma levels of angiotensin II were comparable between GPR35-/- and GPR35+/+ mice (n=6-10, p>0.05). In a deoxycorticosterone acetate (DOCA)-salt induced low-renin hypertensive mouse model, GPR35 deletion lowered MBP by 11 mmHg as measured by tail-cuff method (n= 5-6, p <0.05 vs. DOCA-GPR35+/+).

Conclusion: Our data suggest that deletion of GPR35 can prevent blood pressure elevation induced by DOCA-Salt model in mice, possibly through improving endothelial cell function. This is related to the enhanced angiogenesis through higher expression of eNOS and its activated phosphorylated form in endothelial cells. Our study has provided evidence for highlighting GPR35 as a novel potential therapeutic target in anti-hypertensive treatments. |

ABSTRACT NO. 86	
Name	Kushall Vanamala
Category	Master's Students
Title	Targeted Nanostructures for delivering maximum drug payload of Vancomycin at MRSA-infected tissue
Authors	Kushal Vanamala; Samaresh Sau Ph.D; Ketki Bhise MS; Miao Zhao MS; Hiram Sanchez MS; Anthony Bally[1], David Andes Ph.D[3], Michael J. Rybak Ph.D[2], Arun K. Iyer Ph.D[1]
Abtract	Purpose: Infections caused by Methicillin Resistant Staphylococcus aureus (MRSA) in humans are difficult to treat and are resistant to most of the β-lactam antibiotics like cefazolin. The infection is associated with inflammation which triggers and accumulate pro-inflammatory macrophages. These macrophages are characterized by the folate receptor overexpression which can be used as a biomarker to selectively target the infected site. Vancomycin is the first-choice drug used in the treatment of MRSA infections but gave poor clinical outcome due to high dose which led to nephrotoxicity. The current study is to develop folate-targeted liposomal formulation to deliver vancomycin with high drug payload at the infected site for a sustained release action and thereby reduced MIC.

Methods: i. Folate receptor expression: Immunohistochemistry (IHC) was performed for Control vs MRSA infected mouse eye tissue to check the folate receptor expression on the macrophages at the infected site. ii. Preparation of liposomes: Vancomycin liposomes were prepared by reverse phase evaporation method with a mixture of lipids – HSPC, Cholesterol, DSPE-mPEG2000, and DSPE-PEG2000-FA. iii. Optimization: Empirical optimization was done by varying parameters like lipid concentration. 5 liposome batches of different lipid concentrations were prepared. The best batch was selected in terms of particle size, %drug loading and serum stability. iv. Drug payload at infected site: The selected formulation was used to perform in vivo study with Rhodamine labelled vancomycin liposomes (LVAR) vs free vancomycin (VAR) administered through intraperitoneal injection in MRSA infected mouse (infected thigh tissue). After treatment for specified time, mice were euthanized, and thigh tissues were collected. Harvested tissues were embedded in paraffin glass slides and fluorescence imaging was done to evaluate the sustained release of the drug.

Results: The IHC study inferred that compared to the control, MRSA infected eye tissue had higher expression of the folate receptor. This led to the development of folate targeted vancomycin liposomes. % Drug loading and serum stability showed a comparative trend with respect to cholesterol composition of the 5 batches. The liposome formulations have followed a pattern (i) increase of vancomycin loading with a decrease of cholesterol amount, (ii) increase of serum stability with an increase of cholesterol in liposomes. The batch of liposome with optimum %drug loading and serum stability was selected for in vivo to check the sustained release of the drug. The higher accumulation of LVAR with higher fluorescence intensity compared to VAR indicate the active MRSA targeting of vancomycin in liposome formulation, correlating profound therapeutic benefit in MRSA.

Conclusion: The preliminary results of initial optimization direct towards developing a robust liposomal Vancomycin formulation that may show high potential for clinical translation on extensive optimization by Quality by Design (QbD) approach. The fluorescence imaging showed high drug payload at the infected site for liposomal vancomycin vs free vancomycin which infers that targeted liposomes are more efficient in giving sustained release of vancomycin which reduces the MIC and reduces nephrotoxicity of the drug. Reference: Materials 2018, 11(7), 1245; https://doi.org/10.3390/ma11071245. |

Undergraduate Students

ABSTRACT NO. 87	
Name	Amanpreet Bhogal
Category	Undergraduate Students
Title	Martial arts-based meditative intervention for improving attention among high-risk elementary students
Authors	Amanpreet Bhogal; Manasi Desai; Sean Minton; Charis Wiltshire; Sterling Winters; Cassandra Wanna; Anais Stenson; Tanja Jovanovic; Christine A. Rabinak; Shelley Paulisin; Autumm Heeter; Cindy Cohen; Jamila Carrington Smith; Marc Cohen; Peter Davenport; Michael Hunt; Richard Plowden; Naami Kosofsky; Martin H. Bluth; Elimelech Goldberg; Hilary A. Marusak
Abtract	Purpose: Relative to their more affluent counterparts, lower income, minority schoolchildren are at higher risk of attentional problems and associated negative outcomes (e.g., educational underperformance, truancy). We are conducting a study to test whether a martial arts-based meditative intervention can reduce attentional problems in elementary students from an at-risk school district (i.e., poor state test scores, predominantly lower income and minority). The present study tests whether individual variation in mindfulness (i.e., trait mindfulness) is associated with attention-related problems among students. We also tested whether a novel school martial arts-based meditative curriculum is associated with better attentional control, as measured using a validated behavioral task.

Methodology: Sixty-eight 3rd and 4th grade students from the Oak Park School District (8-10 years, 83% African American) completed an in-classroom survey which assessed their trait mindfulness, attention-related problems, and anxiety. Students from one of the schools in the district (Pepper Elementary) completed a ±12-week curriculum at their school that involved teaching martial arts-based therapy (MAT) techniques ('Heroes Circle'). A subset of students participated in a pilot behavioral study that involved two study visits – one before and one after the implementation of the curriculum. During the study visits, students completed a validated, age-appropriate behavioral task to assess emotional control – Attention Network Task. The Task involved identifying the direction (i.e., left or right) of a central target fish that is surrounded by four flanker fish. Of note, the direction of the target fish was either congruent or incongruent with the flanker fish. Attentional control was calculated by examining reaction time to incongruent trials.

Results The survey demonstrated that overall, more mindful students reported fewer attention-related problems at school (r = -0.51, p < 0.001). Fewer attention problems, in turn, was associated with lower anxiety (r = 0.41, p < 0.001). Overall, during the Attention Network Task, reaction time was slower for incongruent relative to congruent trials. Compared to before the curriculum, there was a significant reduction in reaction time to incongruent trials after the curriculum; however, this effect did not reach significance (p = 0.1).

Conclusions: Results of the present study demonstrate that mindfulness is associated with fewer attention-related problems, which in turn, is associated with lower anxiety among high-risk schoolchildren. Although results of our pilot behavioral study did not reach significance, previous studies indicate that meditative interventions are associated with improved behavioral performance (e.g., faster reaction times) on attention-related tasks. Taken together, meditative interventions – such as the 'Heroes Circle' – may be beneficial for strengthening attentional control among high-risk schoolchildren. Higher attentional may reduce negative outcomes that are more common among high-risk schoolchildren (e.g., educational underperformance, truancy). |

ABSTRACT NO. 88	
Name	Manasi Desai
Category	Undergraduate Students
Title	Martial Arts Therapy Based Mindfulness is Associated With Fewer Emotional Problems and Lower Subjective Emotional Distress Among High-Risk Elementary Schoolchildren
Authors	Manasi Desai; Amanpreet Bhogal; Sean Minton; Charis Wiltshire; Sterling Winters; Cassandra Wanna; Anais Stenson; Tanja Jovanovic; Christine A. Rabinak; Shelley Paulisin; Autumm Heeter; Cindy Cohen; Jamila Carrington Smith; Marc Cohen; Peter Davenport; Michael Hunt; Richard Plowden; Naami Kosofsky; Martin H. Bluth; Elimelech Goldberg; Hilary A. Marusak
Abtract	Purpose: Mindfulness is defined as the nonjudgmental awareness of the present moment. Individuals who are more mindful (i.e., higher trait mindfulness) frequently report lower stress and emotion-related problems (e.g., anxiety) as compared to their less mindful counterparts. In addition, mindfulness-based approaches, including simple meditative techniques (e.g., focused attention to breath), can be easily taught to children and have been consistently shown to reduce stress and emotional problems. Thus, mindfulness may be particularly beneficial for lower income, minority children, who are at increased risk of emotional problems and related negative outcomes (e.g., poor school engagement, educational underperformance). The present study tests for associations between mindfulness and emotional problems among elementary students from an at-risk school district (i.e., poor state test grades, predominantly lower income and minority), and whether active engagement in mindfulness techniques can alleviate subjective emotional distress.

Methodology: Sixty-nine 3rd and 4th grade students from the Oak Park School District (8-10 years, 83% African American) completed an online survey that included standardized, age appropriate measures of trait mindfulness, emotional problems, and school engagement. A subset of students participated in a pilot behavioral study. During the pilot study, students completed an emotion regulation task that involved viewing negative, distress-inducing video clips (e.g., child fighting with a parent, child being bullied), and subsequently rating their current emotional distress. Prior to each video clip, students were given one of three instructions: (1) attention to breath (mindfulness) using a mindfulness technique used in an established martial art therapy (MAT) program, (2) count backwards from ten (non-mindfulness distraction condition), or (3) passive viewing (non-mindfulness control condition). Results The survey demonstrated that overall, more mindful students reported fewer emotional problems (r = -0.438, p < 0.001) and anxiety, in particular (r = -0.425, p < 0.001). Fewer emotional problems, in turn, was associated with higher school engagement. During the emotion regulation task, students reported lower emotional distress during the MAT-based mindfulness (i.e., attention to breath) condition as compared to passive viewing. A similar reduction in emotional distress was reported during the non-mindful distraction (i.e., count backwards from ten) condition relative to passive viewing.

Conclusions Results of the present study demonstrate that mindfulness is associated with fewer emotional problems, which in turn, is associated with higher school engagement among high-risk schoolchildren.

Results of the pilot behavioral study, in alignment with previous MAT-based studies, indicate that active engagement in MAT-based mindfulness techniques (e.g., attention to breath) can attenuate subjective emotional distress. Although a similar attenuation was observed during the non-mindful distraction condition (i.e., count backwards from ten), previous research suggests that distraction-based techniques may be effective for reducing anxiety in the short term but maladaptive in the longer term. Taken together, these results support the integration of MAT-based mindfulness techniques into standard school programs. |

ABSTRACT NO. 89	
Name	Lauren Harven
Category	Undergraduate Students
Title	Effectiveness of antibiotics against tolerance-induced Staphylococcus aureus
Authors	LT Harven; PS Kulkarni; SM Khaire; VL Bingley; S Dey; PD Smolenski; CR Miller, AD Berti
Abtract	Background: Within a sufficiently large bacterial population, some of the members will naturally adopt an alternate, metabolically-active state that favors small molecule synthesis over cell division. In Staphylococcus aureus this process is induced by multiple factors present during infection including nutrient limitation, host cationic peptide exposure and polymorphonuclear neutrophil internalization. These isogenic "tolerant" subpopulations have variable responses during antibiotic exposure and can remain viable in the presence of typically bactericidal concentrations. Survivors of the antibiotic exposure can restart cell division upon cessation of antibiotics and cause relapse or recurrent infection. In this study we determine the ability of typical and atypical antistaphylococcal therapies to reduce the viability of tolerant Staphylococcus aureus bacteria. Methods: Overnight cultures were diluted in pre-warmed Mueller Hinton broth to approximately 1×10^6 cfu/mL. Guanosine-3',5'-bisdiphosphate-mediated tolerance was induced by exposure to mupirocin (0.032 – 3.2 µg/mL) for 30 min. Tolerant cultures were exposed to vancomycin (20 µg/mL), cefazolin (25 µg/mL), ertapenem (7 µg/mL), dalbavancin (40 µg/mL) or oritavancin (14 µg/mL) and viability was assessed by dilution plating at pre-defined time points (0, 2, 6, 24, 48 h). The minimum duration until 2- and 3-log viability reduction from baseline (MDK99/MDK99.9) was calculated independently for three biological replicates. Results: The viability of cultures synchronized to a tolerant state was more resilient to change when exposed to typical antistaphylococcal antibiotics as compared to their exponentially-growing counterparts. In contrast, killing of tolerance-induced bacteria by lipoglycopeptides was indistinguishable from killing of exponentially-growing bacteria. Conclusion: S. aureus that has become tolerant to typical antistaphylococcal therapies may respond favorably to lipoglycopeptide-based therapies. Lipoglycopeptides should be considered in cases of recurrent or relapse staphylococcal infections.

ABSTRACT NO. 90	
Name	Shelley Paulisin
Category	Undergraduate Students
Title	The effects of genetic variability and the cannabinoid receptor 1 gene on fear extinction neural circuitry in healthy adults
Authors	Shelley M. Paulisin[1], Hilary A. Marusak[1] (PhD) , Allesandra S. Iadipaolo[1], Craig Peters[1], Christine A. Rabinak[1] (PhD)
Abtract	Background: Recent studies in humans have shown that genetic variants of CNR1, the gene that encodes for cannabinoid type 1 receptor, has been linked to fear extinction success and anxiety symptoms. Individuals with the A/A genotype show impaired extinction of fear potentiated startle compared to G-allele homozygotes, suggesting a potential mechanism that may increase risk for anxiety disorders. However, it is unknown whether the CNR1 variant effects the underlying neural mechanisms of fear extinction (e.g., amygdala (AMYG), hippocampus (HPC), and medial prefrontal cortex (mPFC)). The present study examines the effect of CNR1 on fear extinction neural circuitry. Methods: Twenty-nine healthy adults (ages 19-33, 16 female) underwent a novel two-day fear extinction paradigm during functional magnetic resonance imaging (fMRI). Participants were genotyped for a polymorphism located within the promotor region of CNR1 (rs2180619). Skin conductance responses (SCRs) and fMRI response in extinction-related neural circuitry was compared between gene groups (A-allele carriers vs. GG homozygotes). Results: Overall, participants showed intact fear extinction learning and recall, evidenced by sustained low SCRs at the end of extinction to the beginning of recall. Surprisingly, there were no differences in SCRs between A-carriers and GG-carriers during fear extinction learning or recall. However, there was an effect of CNR1 on neural activation during recall, such that A/A carriers showed higher activity in the AMYG and mPFC during extinction recall, as compared to GG homozygotes. Conclusion: These results link variation in endocannabinoid signaling to disruptions in fear extinction neural circuitry, which has been postulated as an important mechanism in the pathogenesis of anxiety disorders

ABSTRACT NO. 91	
Name	Xhenis Brahimi
Category	Undergraduate Students
Title	Abnormal Structure of Fear Circuitry in Children with Cancer-Related Posttraumatic Stress
Authors	Xhenis Brahimi; Hilary Marusak, Ph.D; Christine Rabinak, Ph.D
Abtract	Pediatric cancer is a stressful event that can have life-altering effects on children and their families. It has long been recognized that some children will experience post-traumatic stress symptoms (PTSS) related to cancer or its treatment. Research has identified fear neural circuitry, particularly in the amygdala, as central to the expression of PTSS/PTSD in adults and in children. Although research on noncancer related PTSS in children has been linked to altered morphology of limbic brain regions, including the amygdala, no studies have examined the effect of cancer or cancer-related PTSS on amygdala volume. In this study, we examined PTSS in association to volumetric changes in the amygdala in a set of 24 children with a previous cancer diagnosis (11 female, ages 5-17 years) and 24 healthy controls (15 female, ages 6-17). There were no group differences between cancer and controls when looking at corrected right and left amygdala volumes. However, higher cancer-rated PTSS was associated with increased volume of the left amygdala, which appeared to be driven by specific PTSS dimensions, including hyperarousal and avoidance, but not re-experiencing. A positive association was also found between PTSS and number of noncancer related adverse events. This study demonstrated that childhood cancer increases subjective PTSS and affects proper future development of limbic control, while increasing symptoms of hyperarousal, avoidance, and intrusion.

ABSTRACT NO. 92	
Name	Zachary Mason
Category	Undergraduate Students
Title	Unique roles of iron and zinc binding to the yeast Fe-S cluster scaffold assembly protein "Isu1"
Authors	Zachary Mason; Brianne E. Lewis; Andria V. Rodrigues; Manunya Nuth; Eric Dizin; J. A. Cowan; Timothy L. Stemmler
Abtract	Mitochondrial Fe-S cluster biosynthesis is accomplished within yeast utilizing the biophysical attributes of the "Isu1" scaffold assembly protein. As a member of a highly homologous protein family, Isu1 has a sequence conservation between orthologs and a conserved ability to assemble [2Fe-2S] clusters. Regardless of species, scaffold orthologs have been shown to exist in both "disordered" and "structured" conformations, a structural architecture is directly related to conformations utilized during Fe-S cluster assembly. During assembly, the scaffold helps direct the delivery and utilization of Fe(II) and persulfide substrates to produce [2Fe-2S] clusters, however Zn(II) binding alters the activity of the scaffold while at the same time stabilizing the protein in its structured state. Our working hypothesis is that Isu1 binds iron at a site distinct from the protein's active site, iron binding does not alter the protein's structured state and that this iron can be used for Fe-S cluster assembly. Understanding the interplay between Fe(II) and Zn(II) binding in vitro may help clarify metal loading events that occur during Fe-S cluster assembly in vivo. Here we determine the metal:protein stoichiometry for Isu1 Zn and Fe binding to be 1:1 and 2:1, respectively. As expected, while Zn binding shifts the Isu1 to its structured state, however folding is not influenced by Fe(II) binding. X-ray absorption spectroscopy (XAS) confirms Zn(II) binds to the scaffold's cysteine rich active site but Fe(II) binds at a location distinct from the active site. XAS results show Isu1 binding initially of either Fe(II) or Zn(II) does not perturb the metal site structure of alternate metal. XAS confirmed that four scaffold orthologs bind iron as high-spin Fe(II) at a site composed of ca. 6 oxygen and nitrogen nearest neighbor ligands. Finally, in our report Zn binding dramatically reduces the Fe-S cluster assembly activity of Isu1 even in the presence of frataxin. Given the Fe-binding activity we report for Isu1 and its orthologs here, a possible mechanism involving Fe(II) transport to the scaffold's active site during cluster assembly have been considered. This work was supported in part by NIGMS/NIH grant R25 GM 058905 - 21.

ABSTRACT NO. 93	
Name	Edison Nwobi
Category	Undergraduate Students
Title	Edison Nwobi; Brandon Buchanon; Brianna Murdock; Ki-Jana Malone; Kawthar Alali; Jamie McQueen; Doreen Head; Randall L Commissaris
Authors	Marijuana Effects on Driving Performance: Driving Simulator Studies in Medical Marijuana Patients
Abtract	In 2012, Washington and Colorado were the first states to legalize recreational marijuana, with eight states (including Michigan) following their lead. As a consequence of this legalization, the concern for driving safety following marijuana use has become an increasingly important area for research. To study this issue, our research group has developed a reliable way to measure the effects of marijuana, alcohol and other drugs on driving performance using a fixed base driving simulator. In these experiments, we measure the reaction time (in msec) for subjects to initiate a crash avoidance steering response. In a pilot study (Experiment I; n=1 subject), we found that treatment with either alcohol (6 beers) or marijuana (10-15 mg orally, in an 'edible') significantly increased crash avoidance reaction time. In Experiment II we found that this crash avoidance response was not significantly impaired by marijuana use in Medical Marijuana patients, even though all of the Medical Marijuana patients had measurable concentrations of tetrahydrocannabinol (THC) in their blood. This surprising finding suggests that the Medical Marijuana patients had developed tolerance because of their chronic marijuana use. Consistent with this hypothesis, preliminary studies (Experiment III) have shown that Recreational Marijuana users are more affected than Medical Marijuana subjects. These studies are ongoing. (This study was approved by the Wayne State University Internal Review Board (WSU IRB #066716B3E).