School of Pharmacy

2025

RESEARCH RECOGNITION DAY

Friday, April 25, 2025

School of Pharmacy
3307 N. Broad Street
Philadelphia, PA 19140

MESSAGE FROM THE DEAN

Greetings,

It's my pleasure to welcome you to our 2025 Research Recognition Day here at Temple University School of Pharmacy. This day has become a proud tradition – a celebration of the vibrant research culture that continues to thrive in our school. That culture is shaped by the curiosity, determination, and forward-thinking spirit of our students and faculty.

But today is about more than just sharing research. It's a time to reflect on how our academic community contributes to meaningful, lasting change in healthcare – from groundbreaking discoveries to tangible impact in patients' lives. The posters and presentations you'll see today highlight how pharmacy, pharmaceutical sciences, and regulatory affairs and quality assurance connect with public health, policy, and innovation in ways that truly matter.

We're especially honored this year to welcome Dr. Don Siegel, PhD, MD, Professor of Pathology and Laboratory Medicine and Director of several key programs at the Hospital of the University of Pennsylvania. His keynote address, "*Innovations in Cellular Therapies for Cancer, Autoimmune Disease and Other Maladies*," will shine a light on the exciting intersection between basic science and clinical application – an area where pharmacy research plays a crucial and growing role.

Of course, this event would not be possible without the generosity and support of our valued sponsors. I want to sincerely thank the Philadelphia Pharmaceutical Forum through the support of Dr. Ani Railkar, Dr. Jan Kitzen (Pharmacy Class of 1972), and Gregory Papa, RPh (Pharmacy Class of 1975), for their continued commitment to our students, our research mission, and the future of our profession. Their partnership is both meaningful and inspiring.

A heartfelt thank you also goes to our presenters, evaluators, and the outstanding 2025 planning committee – Drs. Carlos Barrero, Patrick Glassman, Van Hellerslia, Tina Tran, Ho-Lun Wong, and Vasyl Zbyrak, along with our pharmacy and graduate students Swak Sarpong and Lauren Morelli. Your efforts and attention to detail have made this day possible.

Thank you for being part of this celebration of scholarship, collaboration, and discovery. I look forward to the conversations and inspiration that today's program will surely spark – and to seeing many of you throughout the day.

Warm regards,

S. Suresh Madhavan, MBA, PhD, FAPhA
Dean

TEMPLE UNIVERSITY SCHOOL OF PHARMACY GRATEFULLY ACKNOWLEDGES

Philadelphia Pharmaceutical Forum (Dr. Ani Railkar, PhD)

Jan Kitzen, PhD, BSPharm '72, RPh

Gregory Papa, BSPharm '75, RPh

AGENDA

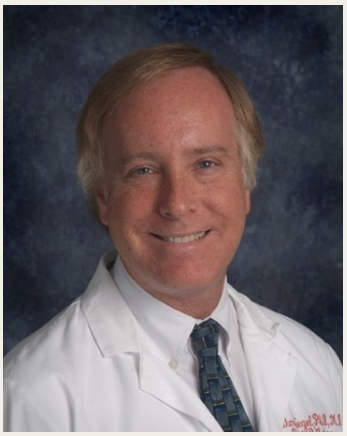
Temple University School of Pharmacy
Research Recognition Day

Friday, April 25, 2025, 11:30 AM-4:15 PM
School of Pharmacy at 3307 N. Broad Street, Philadelphia, PA 19140

11:30 AM - 12:45 PM	**Evaluator Registration and Lunch (TUSP 260)** For student presenters and poster evaluators
12:45 - 1:00 PM	**Welcome Remarks (TUSP 230)** S. Suresh Madhavan, MBA, PhD, FAPhA, Dean, Temple University School of Pharmacy
1:00 - 2:00 PM	**Keynote Lecture (TUSP 230)** Don Siegel, PhD, MD Professor of Pathology and Laboratory Medicine at University of Pennsylvania Perelman School of Medicine "*Innovations in Cellular Therapies for Cancer, Autoimmune Disease and Other Maladies*"
2:00 - 3:15 PM	**Poster Presentations/Judging (4th floor hallway)**
3:15 - 4:00 PM	**Select Oral Research Presentations (TUSP 230)**
4:00 - 4:15 PM	**Awards Presentation (TUSP 230)**
4:15 PM	**Closing Remarks and Networking Opportunities (TUSP 230)**

KEYNOTE SPEAKER

Don L Siegel, PhD, MD



Dr. Don Siegel is a Professor of Pathology and Laboratory Medicine at the University of Pennsylvania Perelman School of Medicine and the Founding Director of the Division of Transfusion Medicine and Therapeutic Pathology, Director of the Clinical Cell and Vaccine Production Facility, and Director of the Fellowship Program in Blood Banking/Transfusion Medicine. He has authored more than 100 scientific papers, and holds over 40 patents.

Dr. Siegel's research focuses on understanding human auto- and alloimmune responses in both health and disease. His lab uses phage and yeast display technologies to clone antibody repertoires and generate monoclonal antibodies for applications in transfusion medicine, hematology, infectious diseases, and oncology.

Dr. Siegel will present on “Innovations in Cellular Therapies for Cancer, Autoimmune Disease and Other Maladies”.

RESEARCH DAY EVALUATORS

Gautam Baheti, PhD, Scientific Director, Biogen

Chris Bode, VP of Scientific Affairs, Pharmaron (Exton) Lab Services LLC

Edward W Casey, BSPharm '88, RPh, MBA '96, National Account Payer Medical Lead, Pfizer, Inc.

Sarah Davis, PhD, Postdoctoral Fellow, Temple University Center for Substance Abuse Research (CSAR)

John C. Gordon, PhD, Screening Manager for the Moulder Center for Drug Discovery at the Temple University School of Pharmacy

Scott Greene, RPh, MS, PhD, Assistant Dean of Experiential Programs, Philadelphia College of Pharmacy at St. Joseph's University

Marc A. Ilies, Faculty, Professor, Temple University School of Pharmacy

Jan M. Kitzen, PhD, BSPharm '72, RPh, Former Laboratory Scientist and Medical/Scientific Writer (Wyeth-Ayerst; Wyeth, Rhone-Poulenc Rorer)

Edwin Lam, PharmD, Associate Scientific Director, Biogen

David Lebo, PhD, RPh, Professor and Director of CGMP Services, Temple University School of Pharmacy

Melissa Potts, PharmD '03, Clinical Associate Professor, Temple University School of Pharmacy

Talitha Pulvino, PharmD '01, BCPS, Clinical Associate Professor, Director of Diversity, Equity and Inclusion, Temple University School of Pharmacy

Aniruddha Railkar, PhD, Associate Director, CMC Regulatory Affairs, Relay Therapeutics

Mario Rico, MD, Associate Scientist, Lewis Katz School of Medicine at Temple University

Natalie Rodriguez, PharmD, BCACP, Clinical Assistant Professor, Temple University School of Pharmacy

Mahmut Safak, PhD, Associate Professor, Department of Microbiology, Immunology & Inflammation, Lewis Katz School of Medicine at Temple University

Divita Singh, PharmD, BCPS, BCACP, Clinical Assistant Professor and Director of Continuing Education, Temple University School of Pharmacy

Louis Speizer, PhD, Managing Partner at Griffing Speizer and Partners

Nina Tachikawa, PharmD, BCPS, BCACP, BC-ADM, Director, Internal Medicine Medical Outcomes & Analytics, Pfizer, Inc.

Ellen Unterwald, PhD, Professor, Lewis Katz School of Medicine at Temple University

Craig Whitman, PharmD, BCCCP, FCCM, Clinical Professor and Assistant Dean of Academic Affairs, Temple University School of Pharmacy

Johnny Zapata, PharmD '19, RPh, Medical Science Liason, Bristol Myers Squibb

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Graduate Platform – Abstract Winner

Poster 17

Mathias Sanchez Machado* and Dr. Marc Ilies[1]

Establishing a Recombinant Protein Expression System: Optimization of Human Carbonic Anhydrase II Expression, Isolation, Purification and Folding for Drug Testing and Delivery Applications

*Graduate Student

[1]Department of Pharmaceutical Sciences, School of Pharmacy, Temple University

Purpose: Carbonic anhydrase II (CAII) is a zinc metalloenzyme widely expressed in erythrocytes, kidneys, and other tissues. It catalyzes the reaction $CO2+H2O \rightleftharpoons HCO_3^- + H^+$ and is utilized in pharmaceutical delivery, diagnostic, and biotechnological applications. Successful expression, folding, and purification are essential for CAII's effective use in research and large-scale industry. Therefore, this work aimed to maximize CAII production in Escherichia coli (E. coli) in terms of yield, solubility, and enzymatic activity with scalable purification.

Methods: Plasmid was designed on the pET100/D-TOPO vector and employed to transform BL21(DE3) E. coli cells to express rhCAII (rh= recombinant human). Induction was carried out with 0.25 mM IPTG at 34°C and supplemented with 60 μM $ZnSO_4$ to ensure enzymatic activity. Purification was achieved through Ni^{2+} affinity chromatography (HisTrap FF column) followed by sulfonamide-based affinity purification to reach high purity. An enterokinase digestion approach was also used to remove the His-tag and produce the free protein. Structural integrity and concentration were assessed using SDS-PAGE, BCA assays, and dynamic light scattering (DLS). Enzymatic activity was evaluated utilizing the CO_2 hydration method with phenol red as a pH indicator to measure catalytic efficiency and proton transfer dynamics.

Results: Optimal conditions were achieved to obtain a yield of approximately 20 mg/L (commercial value: USD 512000) of rhCAII with good stability and solubility. SDS-PAGE and BCA assays confirmed high concentration and purity, while DLS showed no aggregation for up to 2 weeks at 4°C in an optimized storage buffer. Enzymatic assays demonstrated 100% retention of activity both with and without the His-tag, confirming that purification and cleavage methods preserved functionality.

Conclusion: We established a high-yield and fully active CAII production system by optimizing expression and purification conditions. Such improvements render CAII more accessible for biomedical uses such as targeted drug delivery and screening, paving the way for future pharmaceutical advancements.

PharmD Platform – Abstract Winner

Poster 6

Manali Patel* and Dr. Patrick Glassman[1]

Pharmacologic Characterization of Novel Fatty Acid-Bivalirudin Conjugates

*Pharmacy Student

[1]Department of Pharmaceutical Sciences, School of Pharmacy, Temple University

Purpose: Bivalirudin can only be administered as an infusion due to its short half-life (25 minutes). This affects its clinical utility since it can only be used in acute, inpatient settings compared to enoxaparin, which can be dispensed to patients and dosed subcutaneously. We hypothesized that conjugation to fatty acids, analogous to Ozempic®, would confer albumin affinity and prolong pharmacokinetics. This study explores whether fatty acid conjugation affects Bivalirudin's potency, albumin affinity, and pharmacokinetic properties.

Methods: In vitro effects of fatty acid chain length on bivalirudin were assessed using clotting assays and high-performance liquid chromatography (HPLC). Bivalirudin was conjugated with either palmitic or myristic acid at a 2:1 molar ratio for one hour at room temperature. The presence of conjugated bivalirudin was confirmed through SEC-HPLC analysis. To evaluate the potency of the conjugates on clot formation, clotting assays were performed in a 96-well plate using thrombin, calcium chloride, fibrinogen, and bovine serum albumin. Additionally, tail clip studies were performed in mice to evaluate in vivo pharmacology.

Results: Conjugation of bivalirudin to each fatty acid was confirmed via SEC-HPLC. In vitro clotting assays were used to assess if conjugation affects potency with the following mean IC50 values estimated: bivalirudin (0.677 μM), bivalirudin-myristate (0.432 μM), and bivalirudin-palmitate (4.89 μM). Physiological albumin concentrations had stronger effects on bivalirudin-myristate (21.7 μM) versus bivalirudin-palmitate (5.61 μM). IV injection of 8.5 mg/kg bivalirudin revealed a trend towards increased bleeding risk with conjugates (blood volume loss, % of control: bivalirudin-myristate: 372%, bivalirudin-palmitate: 430%, $p>0.05$ vs. control).

Conclusion: The data suggest that acyl chain length influences bivalirudin potency. The trend towards increased bleeding risk indicates that acyl chain length is critical in balancing the activity and safety of fatty acid-conjugated bivalirudin. Future studies will aim to identify an optimal chain length that maintains efficacy while minimizing safety risks.

Poster 1

Carmelina Branca* and Dr. Dr. Craig Whitman[1]

Student and Faculty Perceptions of Inclusion of Death, Dying and End-of-Life Care in a Doctor of Pharmacy Program

*Pharmacy Student

[1]Department of Pharmacy Practice, School of Pharmacy, Temple University

Purpose: End-of-life (EOL) care is a crucial aspect of pharmacy education. Pharmacists are vital in managing complex medication regimens and providing compassionate support to patients and families. Ensuring pharmacy students are adequately trained in these topics enhances their ability to collaborate within interdisciplinary teams and deliver patient-centered care. This study aimed to assess student and faculty perceptions of EOL education in the Doctor of Pharmacy (PharmD) curriculum at Temple University School of Pharmacy (TUSP).

Methods: Surveys were distributed to TUSP students and faculty to evaluate perceptions of EOL topics in the curriculum and assess whether the coverage was sufficient. Demographics such as age, gender, race, religious beliefs, country of origin, and academic year were collected. Informed consent was obtained, and institutional review board approval was secured before survey distribution. Descriptive statistics were used to analyze responses.

Results: A total of 55 students and 9 faculty members completed the survey. Among the students, 54.5% had personal experience with EOL care, while only 16.4% had professional exposure. In terms of preparedness, 63.7% of students felt unprepared or neutral about discussing EOL care with patients, and only 29.6% felt confident in explaining the medications used in palliative and hospice care. Furthermore, 49.1% believed the curriculum did not adequately prepare them for EOL care, and 67.3% advocated for more dedicated time in therapeutics courses. Faculty responses reflected these concerns, with 75% believing students were unprepared to care for terminally ill patients and 62.5% agreeing that more curriculum time should be dedicated to EOL topics.

Conclusion: The findings indicate that the current TUSP curriculum inadequately prepares students for EOL care. Both students and faculty advocate for the integration of more comprehensive EOL education into the program.

Poster 4

Katie Fabbri*, Drs. Divita Singh[1] and Nicholas Ferraro[2]

Clearing the Air: Identifying Errors in Smoking Cessation Treatment Among Hospitalized Patients with COPD

*Pharmacy Student

[1]Department of Pharmacy Practice, School of Pharmacy, Temple University

[2]Department of Pharmacy, Temple University Hospital

Purpose: To quantify smoking cessation treatment errors among hospitalized patients with chronic obstructive pulmonary disease (COPD) as per the 2018 ACC Expert Consensus Decision Pathway on Tobacco Cessation Treatment and evaluate correlations in patient characteristics among those who were inaccurately treated.

Methods: A retrospective chart review was conducted on patients 18 years and older admitted to Temple University Hospital from April 1, 2023 to July 1, 2023 with a diagnosis of COPD upon discharge. Data collection included demographic information such as age, gender and ethnicity, preferred language, past social history including duration of smoking history, packs smoked per day, time to first cigarette, previous quit attempts, and other medical history such as supplemental oxygen use, asthma comorbidity, and insurance status. Upon discharge, it was recorded whether or not a patient was offered smoking cessation counseling, smoking cessation pharmacotherapy, if the pharmacotherapy was administered during hospitalization and/or prescribed at discharge.

Results: Of 70 total current smokers, 25 (35.7%) were offered smoking cessation counseling, 29 (41.4%) were offered pharmacotherapy while inpatient, and 22 (31.4%) were administered pharmacotherapy while inpatient (7 patients rejected pharmacotherapy). Consequently, 16 (22.9%) were offered pharmacotherapy at discharge. 24 current smokers received the patch while inpatient, of which 10 (41.7%) were dosed correctly based on smoking history. Patients on Medicaid were less likely to be offered smoking cessation counseling and pharmacotherapy (30%) during the hospitalization compared to those not on Medicaid (50%). Patients on Medicaid were also less likely to be administered smoking pharmacotherapy while inpatient (28%) compared to those not on Medicaid (35%).

Conclusion: Results indicate an opportunity to educate healthcare professionals on the need for additional smoking cessation counseling and pharmacotherapy for current smokers with COPD in order to optimize patient care.

Poster 7

Elias Nowroozi*, Ramneek Kaur*, Sammy Liang* and Dr. Nicole Sifontis[1]

Prescribing Practices Associated with Diuretics Use in Hospitalized Patients with Acute Heart Failure Exacerbation: A Single Center Experience

*Pharmacy Student

[1]Department of Pharmacy Practice, School of Pharmacy, Temple University

Purpose: The 2022 AHA/ACC/HFSA guidelines for the management of heart failure (HF) emphasized the use of intravenous loop diuretics to alleviate symptoms and reduce morbidity in patients with acute exacerbation of HF. If diuresis is inadequate, increasing the loop diuretic dose or adding a second diuretic is recommended. This retrospective observational cohort study aimed to assess our center's adherence to these guidelines.

Methods: We analyzed patients admitted to Temple University Hospital with acute HF exacerbation between July 2022 to June 2023. Data retrieved from electronic medical records included patient demographics, comorbidities, outpatient HF regimens, diuretic use pre- and post-admission, 30-day readmission rates, hospitalization duration, and one-year mortality. Primary outcomes consisted of type, mean dose and frequency of combination diuretic used as first line treatment options for acute HF exacerbation. Secondary outcomes included 30-day readmission rates, length of hospitalization, and one-year mortality.

Results: 200 patients were screened and 194 met inclusion criteria. Mean age 63±13 years. A majority were Black females. Common comorbidities included hypertension, diabetes, and hyperlipidemia. All patients received loop diuretics within 24 hours of admission, with mineralocorticoid receptor antagonists (MRAs) and thiazide diuretics used in 12% and 6% of cases, respectively. The mean furosemide dose at admission was 124.2 mg, with a maximum average dose of 156.9 mg. Among loop diuretic users, 78% received furosemide, and 22% received bumetanide. Multiple diuretic classes were used in 66% of cases, most commonly furosemide plus spironolactone. The 30-day readmission rate was 17%, Mean length of hospitalization was 7.2 days. One year mortality was 13.4%.

Conclusion: Our data suggests that clinical management of patients admitted with an acute heart failure exacerbation during the study period met standard AHA/ACC/HFSA guidelines. Future long-term analyses are warranted to understand the impact of these interventions on morbidity and mortality in this patient population.

Poster 9

Sammy Liang*, Michelle Ros*, Jessica Lessard*, Ramneek Kaur*, Drs. Christina Rose[1] and Jason Gallagher[1]

Drug Use Evaluation of Pharmacist-Initiated IV-to-Oral Antibiotic Conversion at Temple University Hospital

*Pharmacy Student

[1]Department of Pharmacy Practice, School of Pharmacy, Temple University

Purpose: To assess Temple University Hospital's (TUH) pharmacist-driven IV to PO program, particularly focusing on the conversion of certain IV to PO antimicrobial agents. The evaluation aims to determine if patients were appropriately switched from intravenous (IV) to oral (PO) administration and if the conversion was pharmacist-driven and dosed correctly.

Methods: This was a retrospective chart review of patients receiving azithromycin, metronidazole, ciprofloxacin, or levofloxacin in 2023. Data collected from medical records included age, gender, duration of IV antibiotic therapy, if PO order was placed, duration of PO therapy, pharmacist led conversions to PO, day the conversion could have occurred and the day on which the conversion actually occurred. The primary outcome was to determine the number of IV therapy days suitable for PO conversion. The secondary outcome was aimed to determine the number of patients eligible for IV to PO conversion, assess pharmacist-led IV to PO conversion and evaluate the appropriateness of the conversions.

Results: 590 patients were screened and 52 (8.8%) were included. 40/52 (77%) were eligible to be converted from IV to PO on day 3. 12/52 (23%) successfully converted to PO therapy. 0/12 (0%) patients were converted by a pharmacist. 10/12 (83%) patients were correctly converted from IV to PO dosing using the policy conversion chart.

Conclusion: Our data showed that TUH's IV-to-PO pharmacist-driven conversion protocol was rarely used, if not at all, as the inclusion criteria may be too restrictive, suggesting that there needs to be a reevaluation of the protocol. Many patients were eligible to be converted from IV to PO, however, the actual conversion rarely occurred. Most of the conversions done were due to patients being discharged to home.

Poster 11

Erin Torrance*, Daniel Ghattas*, Lydia Eskinder Tirfe*, Drs. Corinne Whiteman[1] and Christina Rose[1]

Impact of a Mechanical Ventilation Sedation and Analgesia Order Set on Continuous Sedation Utilization Rates in Medical ICU Patients

*Pharmacy Student

[1]Department of Pharmacy Practice, School of Pharmacy, Temple University

Purpose: Deep sedation and prolonged time on mechanical ventilation has been shown to negatively impact intensive care (ICU) patients as well as the use of continuous intravenous sedation may result in patient instability and increased delirium. Standardizing sedation practices may help reduce adverse outcomes such as increased mortality, prolonged mechanical ventilation, and ICU-associated delirium. This retrospective chart review aimed to assess whether the implementation of a sedation and analgesia order set for mechanically ventilated patients would affect time on mechanical ventilation, length of stay in ICU, length of stay in hospital, number of days with ICU associated delirium and average amount of benzodiazepines and opioids used.

Methods: The institutional review board approved this retrospective, single-center, pre- and post- intervention quality assurance study. Adults (>18 years old) were included if they were intubated between 02/14/2023- 05/15/2023 (pre-implementation) and 02/14/2024-05/14/2024 (post-implementation). Patients who were pregnant, on continuous neuromuscular blockage, on targeted temperature management, had a documented critical airway, traumatic brain injury, status epilepticus, substance use disorder, acute liver injury, or hypertriglyceridemia were excluded. A chart review was completed for 315 participants admitted to the MICU at Temple University Hospital, and 116 of those were included. The primary outcome was the rate of continuous sedation selected as the first sedative for mechanically ventilated patients. Secondary outcomes included time on mechanical ventilation, length of stay in the hospital, length of ICU stay, ICU associated delirium, average intravenous lorazepam equivalent use while intubated and fentanyl equivalent total while intubated. Data was compared between the two groups, before and after an order set was implemented.

Results: Before the order set was implemented, the mean length of ICU stay was 9.11 days and after it was 5.47 days. The average time to extubation was 7.37 days before the order set versus 3.89 days. The mean length of total duration of hospital stay was 18.63 days before the order set and 9.36 days after implementing the order set. The mean ICU associated delirium days before and after the order set was 1.74 for both. The average IV lorazepam equivalent total while intubated before and after the order set was 27.28 mg and 10.69 mg, respectively. The average fentanyl equivalent total while intubated before the order set was 1326.69 mcg and 1999.45 mcg after the order set.

Conclusion: The implementation of the order set led to improvements in ICU outcomes, including reductions in the mean length of ICU stay, time to extubation, and total hospital stay. There was a decrease in the use of IV lorazepam equivalents while intubated, though the fentanyl equivalent total increased post-implementation. Because the order set was only used in 8 patient cases, there is a need for increased use and a larger population to determine significant changes.

Poster 13

Lara Srour*, and Dr. Patrick M. Glassman[1]

Formation and Characterization of Site-Specific Bivalirudin-Albumin Conjugates

*Pharmacy Student

[1]Department of Pharmaceutical Practice, School of Pharmacy, Temple University

Background: Bivalirudin, a direct thrombin inhibitor, has a half-life of only 25 minutes in patients with normal renal function. Extension of its half-life is of interest and could enhance its therapeutic potential outside of the acute setting. Albumin, the most abundant plasma protein, has a prolonged half-life (19 days) due to neonatal Fc receptor-mediated recycling and may offer a solution for short-lived biotherapeutics like bivalirudin. This study explores site specific conjugation of bivalirudin to albumin's single unpaired cysteine residue (Cys34) using a PEGylated linker molecule. The objective is to assess the antithrombotic activity and impact of conjugation on bivalirudin's in vitro activity and pharmacokinetics and efficacy.

Methods: Bivalirudin was site-specifically conjugated to albumin at Cys34 via click chemistry, and conjugation was confirmed by high-performance liquid chromatography (HPLC). A thrombin activity assay (Chromozym TH) was conducted to evaluate the ability of the conjugate to inhibit thrombin, while clotting assays assessed anticoagulant efficacy. Data analysis was performed using spectrophotometric (SpectraMax), and HPLC methods.

Results: The Chromozym TH assay revealed that while the albumin-bivalirudin conjugate retained some inhibitory activity (IC50 =1.52 μM), potency was markedly reduced compared to unmodified bivalirudin (IC50 = 0.381 μM), possibly due to steric hindrance. However, clotting assays indicated that the conjugate had no effect on clot formation across all tested concentrations. In contrast, free Bivalirudin showed a dose-dependent decrease in clotting activity (IC50 = 1.49 μM), confirming its anticoagulant function.

Conclusion: These results suggest that conjugation at the Cys34 residue of albumin significantly reduces or eliminates bivalirudin's ability to inhibit clot formation. Lack of activity suggests that conjugated bivalirudin may be sterically hindered or unable to interact effectively with thrombin. These findings emphasize the need to explore a wider design space in future experiments, such as extending the PEG spacer to provide additional steric freedom.

Poster 15

Komal Kumar*, Hala Easmael* and Dr. Tina Tran[1]

FRAME-IS in Action: A Framework to Document Adaptations of a Cardiovascular Disease Medication Supply Chain Model from Kenya to Vietnam

*Pharmacy Student

[1]Department of Pharmacy Practice, School of Pharmacy, Temple University

Purpose: Cardiovascular disease (CVD) is a global health concern, especially in low- and middle- income countries (LMICs), where access to essential medications in rural areas remains limited. The Revolving Fund Pharmacy (RFP) model has previously been proven effective in improving the availability of essential medicines in western Kenya. Leveraging lessons learned there, the RFP model was adapted and implemented in Ba Vi District, Vietnam. Here, we used the Framework for Reporting Adaptations and Modifications to Evidence-based Implementation Strategies (FRAME-IS) to report the adaptations made within the RFP model in Vietnam.

Methods: This is a retrospective study utilizing administrative data collected during the routine operation of the RFPs in Vietnam between January 2020 and June 2022. Guided by the FRAME-IS framework, we qualitatively described (1) the implementation of the RFP model in Vietnam, including strategies used and modifications made, (2) the core elements of the model that were modified, and (3) the rationale behind these modifications.

Results: Multiple key adaptations were introduced. First, the RFP program was implemented within a comprehensive rollout that included community screening, linkage, and management of CVD. Second, the drug formulary was smaller due to insurance policies specific to Vietnam, consisting of only 13 CVD medications. Finally, the rationale for the modifications was to increase reach, effectiveness, and adoption, with the level of modification occurring at the sociopolitical level to comply with existing national mandates. This adaptation successfully established nine RFPs, serving 20% of Ba Vi District's population.

Conclusion: The RFP model showed successful adaptation from Kenya to Vietnam, effectively addressing medication access barriers in rural settings. These findings support further expansion and integration of RFPs into primary healthcare to improve CVD medication access in LMICs.

Funding: The implementation of the RFPs in Vietnam was funded by LINKS Community Awards and Resolve To Save Lives (RTSL).

Poster 19

Marena Martinez* and Dr. Patrick M. Glassman[1]

Development of Anti-Thrombotic Antibody Drug Conjugates

*Pharmacy Student

[1]Department of Pharmaceutical Practice, School of Pharmacy, Temple University

Background: Thrombosis and inflammation are inextricably linked processes, which has led to the term 'thromboinflammation' being coined. Inflammatory mediators promote a thrombotic state in part through endothelial activation, which is also associated with upregulation of adhesion molecules such as vascular cell adhesion molecule 1 (ABP-VCAMelid). Previous work has proven the worth of nanobodies in drug delivery with the development of an antibody fragment with dual affinity to VCAM-1 and albumin (ABP-VCAMelid) that strongly targets inflamed lymphoid tissues and prolongs circulation time. We propose to couple ABP-VCAMelid to the potent anti-thrombotic peptide bivalirudin to achieve localized thromboprophylaxis.

Methods: ABP-VCAMelid was selectively modifed at the C-terminus using the bacterial transpeptidase Sortase A5 at its recognition motif (LPETG) to attach a peptide containing an N-terminal tri-glycine, fluorescein, and C-terminal dibenzocylcooctyne (DBCO). Bivalirudin was modified at its N-terminus with azide to allow conjugation to ABP-VCAMelid-DBCO. Two reaction ratios were tested (5:1, 10:1; bivalirudin:ABP-VCAMelid-DBCO). Conjugation was confirmed using HPLC and activity was measured using an in vitro clotting assay.

Results: Sortase-based modification of ABP-VCAMelid resulted in 28.9% modification of the protein. HLPC demonstrated conjugation of bivalirudin to ABP-VCAMelid. Conjugates effectively inhibited clot formation at both reaction ratios (IC50 5:1 1.22 μM; 10:1 0.622 μM).

Conclusion: HPLC and clot formation assays suggested that the 10:1 reaction ratio provided more complete conjugation of bivalirudin to ABP-VCAMelid. The formation of homogeneous conjugates may be advantageous for drug development. Following in vitro characterization, we will pursue in vivo studies to evaluate the safety, pharmacokinetics, and thromboprophylactic efficacy of conjugates in mice.

Poster 21

Benjamin Arias* and Dr. Van Hellerslia[1]

Developing A Culturally Tailored Stroke Education Toolkit For Hispanic American Communities: Impact Esparanza

*Pharmacy Student

[1]Department of Pharmacy Practice, School of Pharmacy, Temple University

Background: Stroke is a leading cause of death and disability, affecting millions of Americans each year. Optimal treatment of stroke is time sensitive, making awareness and recognition of the signs and symptoms, as well as immediate activation of emergency medical services paramount. Research indicates that stroke symptom recognition is lower among both Spanish speaking and English-speaking Hispanics than non-Hispanic whites. A culturally tailored toolkit would be beneficial in addressing the need for community-based health education interventions.

Purpose: The purpose of this research project is to build a toolkit tailored to the cultural experience of Hispanic Americans, to be evaluated for its effectiveness in improving stroke awareness and prevention within the Hispanic American community.

Methods: The first phase of research consists of conducting an extensive literature search to identify Culturally tailored educational materials aimed at stroke education for Hispanic Americans, After collecting and assimilating this data, it will be used to create a toolkit to be used for a community-based stroke education intervention in the Hispanic American population.

Results: To be determined

Poster 23

James Fang*, Thomas Pham*, Muhibatu Osumanu*, Chisom Achinivu*, Drs. Jason Gallagher[1] and Christina Rose[1]

Evaluation of Proper Use Of Tenecteplase within Temple University Hospital

*Pharmacy Student

[1]Department of Pharmacy Practice, School of Pharmacy, Temple University

Purpose: Tenecteplase (TNK) is a tissue plasminogen activator FDA-approved to treat ST-elevation myocardial infarction (STEMI) with off-label indications for stroke, pulmonary embolism, and PE-caused cardiac arrest. We assessed the appropriateness of the use of TNK in accordance with the Temple University Hospital (TUH) protocol and incidence of stroke according to the National Institute of Health Stroke Scale (NIHSS).

Methods: We examined patients who were ≥18 years old. Data was collected from June 2023 to December 2023 of patients admitted at Temple University Hospital and ordered a dose of TNK. The primary objective was to measure whether the use of TNK in patients for stroke, STEMI, or pulmonary embolism was appropriate. Appropriate use was definedvas evidence of stroke as assessed via the NIHSS score, dose not exceeding 25 mg, and absence of absolute contraindications regardless of actual presence of stroke. Secondary objectives evaluated the occurrence of any type of bleeding and antiplatelet/antithrombotic administration within 24 hour of TNK.

Results: The study consisted of 42 patients :19 males (45.2%) and 23 females (54.8%). Following exclusion, 38 patients remained in the study. Most patients fell under the NIHSS score of ≤15, ranging from no stroke to moderate stroke. One patient had a relative contraindication due to prior seizure (2.6%) and one had an absolute contraindication (BP of 184/98 (2.6%)). 8 of the total 38 patients showed signs of bleeding (21%), with 7 minor bleeding events (18.4%) and 1 bleeding event in a major organ area 2 days after TNK administration (2.6%) . 5 patients (13.2%) received antithrombotics within a 24 hour period after TNK administration.

Conclusion: TNK use was deemed appropriate in most cases based on stroke evidence, dosage, and contraindications. Bleeding incidence was low, with only one case of major bleeding. Additionally, most patients adhered to TUH guidelines regarding delayed antithrombotic administration.

Poster 26

Rachel Huynh*, Mi Tran*, Julianne Le*, Bryanna Phung* and Dr. Van Hellerslia[1]

Bridging the Gap: Enhancing Stroke Awareness and Education in the Vietnamese Population

*Pharmacy Student

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Purpose: This project describes the design, implementation, and evaluation of a culturally tailored stroke education program guided by the PRECEDE-PROCEED framework.

Methods: Application of PRECEDE-PROCEED Implementation Science Framework.

Results: This project describes the development, implementation, and evaluation of a culturally tailored stroke education program for the Vietnamese community, utilizing the PRECEDE-PROCEED implementation science framework. Four Vietnamese-speaking pharmacy students (Years 1–3), supported by three Vietnamese-speaking pharmacists, applied the framework to identify significant community barriers, including language barriers, low health literacy, and cultural misconceptions about stroke. These insights informed the creation of customized educational materials emphasizing accessibility, cultural relevance, and emergency preparedness. The event was delivered at a Vietnamese Baptist Church and engaged more than 20 community members. Key components included a bilingual presentation covering critical stroke facts, symptom recognition, and instructions on calling 911 in Vietnamese. Exploratory pre-post tests suggest increased stroke knowledge and confidence in calling 911, with participants expressing a greater willingness to act despite language barriers.

Conclusion: The PRECEDE-PROCEED framework effectively guided the design, planning, and implementation of a culturally responsive stroke education program. This structured, theory-based approach successfully aligned educational interventions with community-specific needs, underscoring its utility in enhancing public health outreach initiatives.

Poster 27

Sarah Uddin*, Daniel Ghattas*, Katie Fabbri*, Victoria Guinto*, Drs. Jason Gallagher[1] and Christina Rose[1]

Drug Use Evaluation of Sodium Ferric Gluconate (FERRLECIT)

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Purpose: Sodium ferric gluconate (FERRLECIT) is an intravenous iron product approved off-label for iron deficiency anemia (IDA) in non-hemodialysis patients who are not responding to or cannot tolerate oral therapy, usually given in 8 doses. We aimed to identify areas for improvement by directly assessing the indication, dosing schedule, and continuation of therapy at discharge with FERRLECIT use at Temple University Hospital (TUH).

Methods: This was a retrospective chart review of all patients 18 years and older admitted into TUH from January 2023 to December 2023 who received at least one dose of FERRLECIT. The primary outcome was a composite of patients being administered sodium ferric gluconate (FERRLECIT) for iron deficiency anemia, received an iron panel within 30 days of IV iron administration, and planned to continue iron supplementation upon discharge if all 8 doses were not given inpatient. The secondary outcome included the percentage of patients that did not have an iron panel collected at any time before IV iron administration.

Results: 93 patients were screened and 79 were included. The primary composite outcome was met by 28 patients (35.4%). For the secondary outcome, seven patients (8.9%) did not have an iron panel ordered before IV iron administration.

Conclusion: Data showed that sodium ferric gluconate (FERRLECIT) is being used 35% of the time for the correct indication of IDA, with an iron panel collected within 30 days before administration and given iron upon discharge if all 8 doses of iron were not received inpatient. Results indicate a need for a greater emphasis and priority on proper transitions of care and appropriate use based on correct indication for FERRLECIT at TUH.

Poster 29

Clarissa Abella* and Dr. Tina Tran[1]

A retrospective analysis of baseline atherosclerotic cardiovascular disease (ASCVD risks among an East African Cohort of Persons Living with HIV

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Purpose: Persons living with HIV (PLWH) in sub-Saharan Africa (SSA) face an increased cardiovascular disease (CVD) risk. The global Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) demonstrated that giving statins to PLWH with low-to-moderate CVD risk is highly effective for reducing the risk of developing major cardiovascular events. However, barriers to establishing baseline ASCVD risks exist in SSA due to structural, access, and cost limitations. This study aims to establish baseline ASCVD risks among an East African Cohort of PLWH.

Methods: We analyzed baseline demographic and clinical data collected from the International epidemiology Database to Evaluate AIDS Sentinel Research Network (IeDEA_EA SRN), a prospective cohort to study the epidemiology of non-communicable diseases and aging among PLWH in Uganda, Tanzania, and Kenya. Baseline ASCVD risk scores were estimated using the AHA/ACC 2013 Pooled Cohort Equation, and categorized to low, borderline, moderate, and high risk. A two-sample t-test of equality of mean ASCVD risk scores between the IeDEA_EA SRN and REPRIEVE African Cohorts was calculated.

Results: The cohort (N=398) had a median age of 49 years and a median time since HIV diagnosis of 12.9 years. Mean systolic/diastolic blood pressure was 125/82 mmHg. ASCVD risk scores were: 149 (37.4%) had low risk (ASCVD risk score of <5%), 41(10.3%) had borderline risk (5 to <7.5%), 35 (8.8%) had moderate risk (7.5 to <20%), 0 (0%) had high risk (> 20%), and 173 (43.5%) had missing data. Difference between the ASCVD risk score means was not statistically significant t=0.98 (p=0.33).

Conclusion: PLWH with calculated ASCVD risk scores from the IeDEA_EA SRN had low-to moderate ASCVD risk. This risk is comparable to PLWH from the REPRIEVE African region. An opportunity exists to implement recommendation for the use of statin as primary prevention of ASCVD in PLWH in SSA.

Funding: TUSP Small Grants Program

Poster 2

Yifan Gong*, Drs. Ken Korzekwa[1] and Swati Nagar[1]

Development of a Novel Physiologically Based Pharmacokinetic (PBPK) Model in Rats for Enhanced Drug Concentration-Time Predictions

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Purpose: The purpose of this study is to develop a rat PermQ model to evaluate mechanisms of distribution kinetics of drugs.

Methods: This permeability- and perfusion-limited model was developed using the human PermQ framework. Drugs can reversibly distribute between capillaries and interstitial fluid by discontinuities in capillaries or transcellular diffusion through endothelial cells. Passive membrane permeability and transporters are considered. Drugs also can partition into intracellular phospholipids and neutral lipids. For midazolam and glyburide, in vitro data were collected in-house. Pharmacokinetic (PK) profiles were modeled for 7 drugs using the same experimental inputs for three different models: Rodgers and Rowland (RR), a perfusion-limited membrane-based model (MemPBPK), and rat PermQ. Models were built and evaluated using Mathematica 13.1.

Results: For atorvastatin and glyburide (acids), all models predicted atorvastatin PK profiles well, and rat PermQ predicted glyburide PK profiles better compared to the other 2 models. For the neutral drug digoxin, all 3 models predicted digoxin PK equally well, with the RR model resulting in a slightly better compared to rat PermQ. The MemPBPK model predicted midazolam well, followed by rat PermQ. Rat PermQ resulted in the best prediction of C-t profiles for all three bases tested compared to RR and MemPBPK.

Conclusion: Overall, for the 7 drugs tested, PK predictions with rat PermQ were the best for 4 of 7 drugs, with MemPBPK performing better for 2 of 7 drugs. Rat PermQ model improved the prediction of rat C-t profiles for basic drugs.

Funding: Grants NIGMS 2R01GM104178 and 3R01GM114369.

Poster 3

Lauren Morelli*, Drs. Mirza Feroz Baig[1], Daniel J. Canney[1] and Benjamin E. Blass[1]

Design and synthesis of 5-HT7 antagonists for the treatment of Cocaine Use Disorder

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Cocaine Use Disorder (CUD) is one of the biggest epidemics to impact the US in the 21st century. Not only does this disorder affect an individual's brain and behavior, inducing an inability to control their substance use, this disorder also affects families, communities, and healthcare systems. Importantly, cocaine use carries a significant risk of neurotoxicity, heart attacks, strokes, and overdose related death. As the number of patients impacted by CUD continues to rise, novel CUD therapies have the potential to improve the lives of millions. Cocaine produces euphoria via the mesocorticolimbic dopamine (MCL-DA) system, also known as the reward system. It has been previously demonstrated that there is substantial interplay between MCL-DA activity and serotonergic 5-HT receptors. Specifically, the 5-HT7 receptor, has been found to have the ability to regulate dopaminergic activity in the reward system, has been linked to alcohol dependance, and can improve attention set shifting, reversal learning, and extinction in preclinical assays. There are no FDA approved treatments for CUD. Temple University has developed highly potent and efficacious 5-HT7 antagonists (Ki < 100nM, Kb < 100 nM) that are selective, orally bioavailable compounds capable of producing statistically significant improvements in mouse models of CUD. Here, we focus on the expansion of this previously developed 5-HT7 antagonist technology by exploring the chemical space and biological activity of a closely related series by modifying four regions of a substituted lactone: the aryl region, lactone β-substituents, bioisosteric piperazine replacement, and linker size changes for future in vivo pharmacokinetic studies.

Poster 5

Brandon Shepherd*, Kerim Cakir† and Dr. Ellen Walker[1]

Modeling withdrawal from xylazine-adulterated fentanyl in a conditioned-place aversion assay

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Purpose: Opioid withdrawal is a key driver to continued drug-taking and relapse. Understanding withdrawal is critical to developing treatments to lower the risk of relapse and increase patient compliance. The α2-adrenoreceptor agonist xylazine is becoming an increasingly common adulterant in illicit opioid supplies throughout the United States. Some people report that fentanyl adulterated with xylazine precipitates heightened withdrawal symptoms.

Methods: To investigate these self-reports, we developed a conditioned-place aversion protocol in mice. We hypothesized that the aversion to fentanyl withdrawal would be increased when xylazine was also administered. Mice were conditioned to associate one of two chambers with a state of withdrawal, allowing us to measure the aversive nature of that state. This allows us to model fentanyl withdrawal and characterize xylazine's modulation of it.

Results: We established that naloxone produces a dose-dependent increase in place aversion when administered alone. When fentanyl was given followed by a low dose of naloxone that was not aversive on its own, there was a significant increase in place aversion. Under these conditions, withdrawal from xylazine failed to produce place aversion. Xylazine also had no effect on fentanyl withdrawal place aversion when it was co-administered with fentanyl. Place aversion of withdrawal from xylazine was not observed under conditions of increased xylazine dosing or increased time between xylazine and idazoxan administration. Idazoxan, unlike naloxone, was not aversive on its own. However, xylazine did produce a place-preference on its own when mice were conditioned to the chamber 4 hrs after injection.

Conclusions: Our work suggests that xylazine's role in fentanyl reward and withdrawal is time-dependent. This work is valuable to the understanding of xylazine's impact in the illicit drug supply and can be used to guide further research into treatment methods for the simultaneous use of fentanyl and xylazine.

Supported by the Peter F. McManus Charitable Trust, P30 DA013429, 5T32 DA7237-35.

Poster 8

Bayan Alshahrouri*, Drs. Benjamin E. Blass[1], Thomas Dürig[†] and Reza Fassihi[1]

Investigation of release kinetics from thermo-responsive in situ gel-forming PLGA-based hydrogels for intravitreal drug delivery: A novel "Mesh-in-Basket" method

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Biodegradable thermo-responsive poly(lactic-co-glycolic acid) (PLGA)-based in situ gel-forming hydrogels are extensively studied for intravitreal drug delivery to the posterior segment of the eye (1) due to their ability to prolong drug release, decrease injection frequency, and enhance patient compliance.

In vitro sustained release studies for in situ gel-forming hydrogels typically use membraneless (ML) or dialysis-based methods. The ML approach exposes a limited surface of the gel depot to the dissolution medium, while the dialysis-based method introduces an artificial barrier. Both methods poorly simulate in vivo conditions, which allows for full contact of depot to vitreous humor in the eye. The lack of standard USP dissolution methodology for such studies further complicates accurate drug release evaluation. Consequently, there is a need for in vitro release methods that better mimic the vitreous humor microenvironment.

Objective: investigate the release kinetics of in situ gel-forming PLGA-depot using ML, basket-in-tube (mesh #40), and a proposed mesh (#140) in-basket methods.

Methods: A 30% w/w PLGA-PEG-PLGA thermoresponsive triblock copolymer was used to develop a highly water-soluble pirfenidone (PRF)-loaded formulation. Optical clarity and rheological characterization of the gel were studied. In vitro release kinetics were evaluated using the proposed three methods. Pirfenidone quantification was performed via High-performance Liquid Chromatography (HPLC).

Results: The PRF formulation gelled within 1 minute at 37°C. It exhibited excellent optical clarity with spectral transmittance greater than 85 % at 490 nm. Rheologically, the hydrogel showed a storage modulus of 756.2 Pa, with a gelation temperature (Tgel) of 31.23 °C and maximum strength near 37 °C (body temperature). In vitro release kinetics varied significantly across methods. The ML approach provided sustained release over 14 days with less than 60% cumulative release in the first 24 hours. In contrast, the basket-in-tube method resulted in accelerated release, achieving 85% within 24 hours and complete release in 3 days. It was observed that gel leaked through the mesh of the standard basket (mesh #40). In contrast, the proposed new method, where mesh# 140 was inserted into the basket, prevented gel leakage and resulted in release lasting 7 days with approximately 80% cumulative release at 24 hours.

Conclusions: The standard ML method tends to underestimate cumulative initial drug release. The initial release was rapid with the basket-in-tube method, and the total release took 3 days. In contrast, the mesh-in-basket, release lasted for 7 days with comparable initial release to the basket-in-tube method and the absence of gel leakage from the basket. The proposed mesh-in-basket method appears to mimic the actual in-vivo conditions for release more closely.

Poster 10

Lisa Petersohn* and Dr. Marc A. Ilies[1]

Targeting of Carbonic Anhydrase IX with PEGylated Sulfonamide Inhibitors with Restricted Cell Penetration

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Background: Carbonic anhydrase is a zinc-metalloenzyme that catalyzes the reversible hydration of carbon dioxide, producing bicarbonate and a proton. Due to their various functions, carbonic anhydrases are targeted for several diseases. Classic, non-selective carbonic anhydrase inhibitors (CAIstreat various conditions but cause side effects from unspecific inhibition. CA IX is a major target because of its role in solid tumor progression. Inhibiting CA IX slows tumor growth and induces tumor cell death. The highly conserved structure across isoforms has limited the success in designing subtype-selective CAIs. However, selectivity for CA IX over intracellular isoforms can be improved with membrane-impermeable inhibitors. A promising delivery platform are water-soluble, bioavailable polymers like PEG. Since CA IX and CA XII are dimeric in vivo, PEG bi-functionalization can further enhance binding affinity and selectivity.

Methods: The conjugates are linked to the PEG backbone via succinyl linkage. This is achieved by reacting a primary amino group on the warhead with succinic anhydride, which results in a carboxylic acid functionalized CAI. The free amine is either already present on the warhead or will be added by reducing nitro-functionalized inhibitors using mild and selective conditions. Once attached, the free acid group on the succinyl inhibitor is activated using 2-chloro-4,6-dimethoxy-1,3,5-triazine (CDMTas the coupling agent. The respective molecular weight PEG is then added to the reaction mixture, yielding the final bi-functionalized polymeric CA inhibitor.

Outcomes and Conclusions: Previous works have demonstrated the viability of PEGylated bis-sulfonamides as a mode of selectively targeting CA IX, thus improving both selectivity and physicochemical properties of existing inhibitors. The synthetic route has been validated and allows the attachment of potent CAIs onto the PEG backbone. We will present our recent results towards testing different warheads and PEG linker lengths to establish the most effective CA IX inhibitors.

Poster 12

Mohammed Yousuf*, Drs. Swati Nagar[1] and Ken Korzekwa[1]

Predicting impact of the Pgp transporter on drug distribution and disposition from in vitro drug transport assays with modeling and simulation

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Purpose: Transporters have a significant role in drug permeation, distribution, and disposition. We can evaluate potential drug candidates for transporter activity prior to preclinical and clinical studies. Our research aims to determine transporter efflux clearance from in vitro drug permeation studies with MDCK cell monolayers.

Methods: MDCK cells are cultured as a monolayer on the insert filter of a transwell device. Upon plating, the Pgp transporters are expressed on the apical side of the cells. Using the net clearance concept, we developed equations for measuring the efflux clearance (CLeffand clearance into the membrane (CLifrom the apparent permeability from the apical side to the basolateral side and the basolateral side to the apical side. Drug transport assays provide the time course of drug concentrations in the donor and receiver chambers after dosing in the apical or basolateral chamber with or without a Pgp inhibitor. These data optimize model parameters. The unbound fraction in microsomes (fum, measured by equilibrium dialysis, represents the membrane partition coefficient (Kp, mem. The apical-to-basolateral membrane surface area ratio is determined via a transwell diffusion assay after loading the MDCK monolayer with a probe compound.

Results: The measured fum value for Loperamide is 0.38 at 1mg/ml microsomal protein concentration after 6 hours of incubation in an equilibrium dialysis device. The non-steady state transport model, incorporating surface area ratio and non-specific binding, is parameterized using concentration-time data of four drugs (loperamide, quinidine, verapamil, and propranolol. This mathematical model for the MDCK cell monolayer accurately simulates drug permeation over time.

Conclusions: Efflux clearance (CLeffand clearance into the membrane (CLican be used in pharmacokinetic models to predict the impact of Pgp for drug candidates early in drug discovery. This approach will help predict the distribution and disposition profiles of Pgp substrate molecules.

Funding: NIGMS R01GM104178 and 2R01GM114369

Poster 14

Xinyue You*, Drs. Ken Korzekwa[1] and Swati Nagar[1]

Modeling kinetic data from in vitro propranolol metabolism assays

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Purpose: Enterohepatic recirculation of beta-blockers like propranolol raises concerns, necessitating a comprehensive understanding of its metabolism. Various enzyme kinetic models were evaluated to fit in vitro kinetic datasets for propranolol 4-hydroxylation, propranolol glucuronidation, and 4-hydroxypropranolol glucuronidation in rat liver and intestinal microsomes. Propranolol incubation with enzyme co-factors was studied to assess the contribution of different metabolic pathways.

Methods: Hydroxylation reactions were initiated by adding the NADPH regeneration system and incubated at 37°C before termination with acetonitrile (with internal standard, IS). For glucuronidation assays, substrates were incubated in alamethicin-activated microsomes at 37°C, with UDPGA initiating and acetonitrile (with IS) terminating the reactions. Incubation time varied from 5 to 30 minutes, depending on the enzyme source. Equilibrium dialysis was performed at 37°C with 5% CO_2 for 6 hours to determine the unbound fraction in microsomes. Samples were then analyzed by LC-MS/MS. Different enzyme kinetics models were evaluated using explicit equations and fitted by nonlinear regression analysis, with the best fit determined by Eadie-Hofstee plots and corrected Akaike Information Criteria.

Results: In rat liver and intestinal microsomes, propranolol metabolism exhibited atypical kinetics for both hydroxylation and glucuronidation. Co-incubation in rat liver microsomes (RLM) confirmed 4-hydroxypropranolol as the dominant metabolite, while the relative abundance of propranolol glucuronide and 4-hydroxypropranolol glucuronide varied with substrate concentration. Detailed kinetic data will be presented. The unbound fraction of propranolol (0.91) and 4-hydroxypropranolol (0.87) in 0.23 mg/mL RLM was determined. Unbound fractions in rat intestinal microsomes will be analyzed and presented.

Funding: Grants NIGMS 2R01GM104178 and 3R01GM114369.

Poster 16

Tashnuva Rifat* and Dr. Marc A. Ilies[1]

Determination of enzyme activity and potency of standard inhibitors for different carbonic anhydrase isozymes

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Purpose: Carbonic anhydrase (CA) enzymes are Zn containing metalloproteins that efficiently catalyze the reversible conversion of CO2 and bicarbonate as well as other hydrolytic reactions such as 4-nitrophenyl acetate hydrolysis. CAs have been therapeutic targets for many diseases. Different clinically used carbonic anhydrase inhibitors (CAIs) are being used as diuretics, antiglaucoma, anti-epileptic agents. In this study, we have developed and optimized methods to determine the kinetic parameters of different CA isozymes and the potency of their inhibitors. We also validated these assays using different clinically used CAIs.

Methods: The CO2 hydration method and the 96-well plate based 4-NPA assay method have been developed and optimized. The kinetic parameters of bCAII, hCAII and hCAVB were determined using these assays. The potency of different clinically used CAIs were determined against hCAII to validate these assays.

Results: The Km values for bCAII, hCAII and hCAVB were determined from these assays and were found to be 14.5 mM, 7.2 mM and 5 mM respectively, in good agreement with literature data. The assays were validated by determining the Ki value of the clinically used inhibitors within a wide range of potencies (nM to μM.

Conclusion: The kinetic parameters of different CA isozymes and the potency of clinically used inhibitors were successfully determined using both the CO2 hydration and 96 well plate-based esterase activity assays. These validated assays can be used to determine the potency of novel CAIs.

Poster 18

Mst Jasmin Akter* and Dr. Patrick M. Glassman[1]

Evaluation of Evans Blue as a Marker of Endogenous Albumin Distribution

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Purpose: Evans blue (EB) is a dye that binds tightly to serum albumin and is often used to assess vascular permeability. The tissue distribution of EB is often used semi-quantitatively as a surrogate for albumin distribution. We hypothesize that quantification of EB can be used to determine the absolute concentration of albumin in tissues

Method: First, a commercial ELISA kit was used to measure albumin concentrations in mouse plasma (standard range: 62.5 – 2,000 ng/mL). Mice were injected intravenously with 50 mg/kg EB, which was allowed to circulate for 20 minutes, based on a published protocol. Blood was collected and mice were perfused with 20 mL of ice-cold PBS to remove residual blood from tissues. Organs (intestine, liver, muscle, bone, stomach, brain, lung, heart, kidney, spleen, skin). EB was extracted from organs for 4 days in formamide and 50 µL of the extract was analyzed spectrophotometrically at 620 nm wavelength to quantify EB.

Results: Plasma albumin concentrations were measured in mice by ELISA to be 9.73 ± 4.80 mg/mL. EB was quantified in the following tissues: plasma: 575.12 ± 315.15 µg/g, liver: 21.3 ± 7.9 µg/g, and lungs: 16.7 ± 13.32 µg/g.

Conclusion: The high affinity of EB for albumin may allow for quantification of albumin distribution in tissues. However, these results should be confirmed with complementary methods. Future studies will complete the quantification of EB in the remaining collected organs. We anticipate using these results to set endogenous albumin concentrations in tissues in a pharmacokinetic model of albumin-coupled drugs.

Poster 20

Shibbir Ahmed Khan*, Md Abu Sufian*, Drs. John C. Gordon[1] and Marc A. Ilies[1]

Design and optimization of loading of a lipophilic carbonic anhydrase inhibitor into PLGA nanoparticles and its detection using LC/MS-MS method

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Background and purpose: Carbonic anhydrase (CA) is a zinc metalloenzyme that catalyzes the reversible conversion of CO2 and water into carbonic acid and H+ (proton). One of the isozymes, carbonic anhydrase IX (CAIX), is overexpressed in various solid tumors, where it plays essential roles in maintaining the pH of the tumor microenvironment, ensuring cancer cell survival, growth and metastasis. Our lab has developed a series of ureido sulfonamides as carbonic anhydrase IX inhibitors (CAIs) as a potential treatment for tumors expressing CA IX. They have good activity against CA IX; however, they have reduced solubility in water. Thus, the goal of this study is to encapsulate CAI drugs in PLGA-based formulations, optimize different parameters and analyze them by developing LC/MS-based method for their detection and quantification.

Method: PLGA nanoparticles were formulated using the nanoprecipitation technique. Parameters such as rotation speed, flow rate, order of addition of aqueous and organic phase, and different additives as stabilizers were optimized to formulate the nanoparticles and then load them with CAI-29 (5-adamantaneureido-1,3,4-thiadiazole-2sulfonamide), one of the CAIs we found to be very efficient in tumor killing. An LC/MS-MS method was developed using Acquity (Waters) UPLC/Xevo TQ MS system and was used to detect and quantify the concentration of CAI-29 into the PLGA nanoparticles.

Results: The PLGA nanoparticles formulated using the nanoprecipitation technique were optimized in terms of flow rate of 0.5 ml/min, 800 rpm rotation speed, and order of addition aqueous to organic solvent. The nanoparticle size ranged from 250 to 400 nm, with a CAI-29 encapsulation efficiency up to 25%.

Conclusion: The PLGA nanoparticles were successfully formed and optimized for loading of the lipophilic CAI-29 into their cores.

Poster 22

Nader Afifi*, Dennis Colussi[1] and Dr. Oscar Perez[2]

Multiplex Gene Tagging of Stem Cells for the Development of Kidney Organoids for Drug Discovery

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Purpose: Kidney organoids derived from induced pluripotent stem cells (iPSCs) offer a promising in vitro system to study renal development and disease mechanisms. However, the detection of specific cell types or protein targets in kidney organoids typically requires cell fixation and immunostaining, limiting live cell analysis. This project aims to differentiate kidney organoids from iPSCs engineered via CRISPR gene editing with kidney-specific endogenously labeled proteins fused to fluorescent proteins to facilitate real-time visualization of specific cell types and cellular organelles in live kidney organoids. This kidney-specific protein tagging will enable the detection of changes in specific cell types in response to genetic mutations or pharmaceutical compounds, aiding in the identification of pathogenic mechanisms and potential therapeutic interventions.

Methods: We developed a novel genetic tool to enhance CRISPR-mediated homology-directed repair to engineer iPSCs with multiplex tagging of three endogenous genes: a universal nuclear protein to identify all cells, a protein exclusively expressed in kidney podocytes, and a protein specific to renal tubular cells. This engineered cell line was differentiated into kidney organoids using an established protocol. Live-cell confocal microscopy was used to assess differentiation efficiency, protein localization, and cellular changes associated with nephrotoxic compounds.

Results: Using our novel gene editing tool for endogenous tagging, we successfully generated edited iPSCs that differentiated into kidney organoids exhibiting nephron-like structures with fluorescently tagged proteins that were not expressed in undifferentiated iPSCs. The fluorescent labels enabled high-resolution imaging of protein dynamics in live organoids. Treatment with known nephrotoxic compounds revealed distinct cellular and molecular alterations, confirming the organoids' utility as models for high-content imaging-based cellular analysis.

Conclusion: Our new gene editing tool facilitates CRISPR-mediated genetic tagging for developing cellular models from iPSCs that, upon differentiation, allow real-time detection of specific cell types and cellular organelles in kidney organoids. Nephrotoxic compounds can be detected with this live-cell model, demonstrating its potential for drug screening applications. Future research will focus on developing enhanced cellular models to track multiple cell types and biological processes in the context of genetic kidney diseases.

Poster 24

Dr. Mirza Feroz Baig*, Lauren Morelli†, Drs. Daniel J. Canney[1] and Benjamin E. Blass[1]

Synthesis and Evaluation of Novel Sigma-1 Ligands as a Potential Therapeutic Agents

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The sigma receptors were originally discovered in 1976 when W. R. Martin et. al. classified opioids based on their impact on chronic spinal dogs. Their initial report described a single sigma receptor based on the pharmacological response elicited by (rac)-SKF-100047, but it was later determined by W. D. Bowen et. al. that there are two sub-types, sigma-1 (σ1) and sigma-2 (σ2), each with their own unique pharmacology. An x-ray crystal structure of σ1 was reported by H. R. Schmidt et. al. in 2016, and this protein has been linked to addiction, Alzheimer's disease, juvenile-onset amyotrophic lateral sclerosis , and multiple sclerosis. Shortly thereafter, it was demonstrated that σ2 is identical to the protein designated asTMEM97, and this receptor has been shown to play a role in Niemann-Pick disease, schizophrenia, Alzheimer's disease, neuropathic pain, traumatic brain injury, and cancer. As part of our on-going efforts to develop novel therapeutic agents, we have been exploring a series of functionalized γ-lactones that are highly selective for σ2 over σ1 receptors. During the course of our structure-activity studies of these sigma ligands, we observed a surprising inversion of this selectivity. Herein, we describe the preparation and evaluation of a novel series of ligands selective for σ1 over σ2 receptors.

Poster 25

Drs. Adil Shareef Mohammed*, Lori A. Knackstedt[1] , Youssef Sari[2], Wayne Childers[3] and Magid Abou-Gharbia[3]

Design and synthesis of β-Lactam GLT-1 enhancers for the treatment of Drug addiction related disorders

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Glutamate transporter-1 (GLT-1), also known as excitatory amino acid transporter 2 (EAAT2) is the most abundant glutamate transporter and is primarily responsible for glutamate homeostasis in the forebrain. Down-regulation of GLT-1 is reported in various neurological diseases such as epilepsy, stroke, ALS, Alzheimer's disease and movement disorders besides cocaine addiction. Preclinical studies revealed that β-Lactam antibiotic, Ceftriaxone has good brain permeability, increases the cellular glutamate uptake by activating the Glutamate transporter-1 (GLT-1), enhancing GLT-1 expression, to attenuate the reinstatement of cocaine seeking that is primed by cocaine administration. However, there are limitations associated with using ceftriaxone subchronically as a drug for preventing cocaine relapse, including its lack of oral bioavailability, its poor CNS penetration (1–2%), and the risk for developing bacterial resistance. To overcome these issues, we embarked on a phenotypically driven SAR campaign to identify β-lactam analogs that retained the ability to enhance expression of GLT-1 while eliminating antibiotic activity and increasing oral and CNS bioavailability. Among them, we have identified β-lactam analog MC-100093, a lead molecule, as a potent up-regulator of GLT-1 expression that is orally bioavailable, brain penetrant, and induces GLT-1 up-regulation in an accepted model of cocaine addiction and withdrawal. MC-100093, with drug-like physicochemical properties, has demonstrated in vivo efficacy of restoring GLT-1 Expression after Cocaine Self –Administration and Significantly reduced ethanol consumption thereby restoring the Dysregulation in Glutamatergic System.

Poster 28

Kishore Pathivada* and Dr. Patrick M. Glassman[1]

Fatty acid derivatization of tissue plasminogen activator for half-life extension

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Purpose: Tissue-type plasminogen activator (tPA) is FDA-approved for the treatment of acute thrombotic disorders. Its poor pharmacokinetics (PK) and severe side effects, namely bleeding complications and aberrant vascular remodeling, necessitate improvements in its pharmacologic properties. Several FDA-approved drugs are engineered for prolonged exposure through coupling to serum albumin. We hypothesize that fatty acid derivatization of tPA will confer it with improved in vivo pharmacology through reversible binding to albumin.

Methods: tPA was conjugated to fatty acids of varying acyl chain length through amine-reactive chemistry. The potency of tPA to both prevent (prophylactic) and lyse (therapeutic) clots in vitro was assessed using a plate-based clotting assay. PK of total protein (ELISA) and enzymatic activity (plasminogen activation) were assessed in mice following IV injection of 0.9 mg/kg tPA or fatty acid derivatives.

Results: The potency of tPA was assessed in vitro in prophylactic (IC50: 13.1 ± 1.0 nM) and therapeutic (IC50: 5.48 ± 0.87 nM) settings. Coupling of palmitic (Therapeutic: 1.96 ± 0.35 nM) or arachidic (Prophylactic: 21.10 ± 2 nM; Therapeutic: 2.62 ± 0.48 nM) acid to tPA had minor effects on IC50. Following IV injection, palmitic acid-tPA had a 37% increase in total protein exposure and ~66% increase in activity exposure vs. unmodified tPA, as measured by area under the curve (AUC).

Conclusions: Fatty acid derivatization of tPA had a minor effect on potency; however, palmitic acid-tPA trended towards improved exposure and in vivo activity vs. unmodified tPA. This suggests that fatty acid derivatization is a viable strategy for improving the in vivo pharmacology of tPA. Future studies will focus on derivatization with other fatty acids to establish a structure-function relationship, molecular characterization and PK, safety, and efficacy of fatty acid-derivatized tPA.