TEXAS TECH UNIVERSITY
HEALTH SCIENCES CENTER™

Jerry H. Hodge School *of* Pharmacy

Office of Sciences

Nineteenth Annual

RESEARCH DAYS

Overton Hotel / Lubbock, TX
June 13-14, 2022

Connecting Through Research

A Special Thanks

to

Texas Tech University Health Sciences Center

Office of Research

Schedule of Events

MONDAY, JUNE 13, 2022

8:00-8:50 am:	**Breakfast and Registration**
8:50-9:00 am:	**Opening Ceremony -** Ulrich Bickel, M.D.
9:00-9:30 am:	**Opening Speaker –** Darrin D'Agostino, DO, MPH, MBA *Provost, Texas Tech University Health Sciences Center*
9:30-9:35 am:	**Keynote Speaker Introduction -** Ron Hall, Ph.D.
9:35-10:35 am:	**Keynote Speaker –** Kerry LaPlante, Pharm.D. *"The Secret Life of a PI"*
10:35-11:05 am:	**Attendees to meet with Kerry LaPlante, Pharm.D.**
11:05-11:25 pm:	**Break**
11:25-11:30 am:	**Podium Presentations Introduction –** Devin Lowe, Ph.D.
11:30-11:45 am:	**Junior Graduate Student Presentation –** Prathysusha Naidu *"Ferutinin Induces Osteogenic Differentiation of Dental Pulp-Derived Stem Cells (Dpscs) by Upregulating BMP2 Signaling"*
11:45-12:00 pm:	**PGY2 Resident Presentation** - Megan Ferry, Pharm.D. *"Utilization of Continuous Glucose Monitoring in Older Adult Patients with Type 2 Diabetes Mellitus"*
12:00-1:00 pm:	**Lunch**
1:00-1:05 pm:	**Keynote Speaker Introduction –** Vardan Karamyan, Pharm.D., Ph.D.
1:05-2:05 pm	**Keynote Speaker –** Alan Saghatelian, Ph.D. *"Molecular Profiling to Identify Bioactive Molecules"*
2:05-2:15 pm:	**Coffee Break & Judges meeting**
2:15-2:45 pm:	**Attendees to meet with Alan Saghatelian, Ph.D.**
2:45-2:50 pm:	**Seed Grant Awardee Introduction –** Nadezhda German, Ph.D.
2:45-3:15 pm:	**Seed Grant Awardee Presentation -** Meredith Sigler, Pharm.D. *"Effectiveness of empagliflozin for the management of heart failure with reduced ejection fraction initiated within 30-days of a heart failure hospitalization in a Veterans Affairs population with type 2 diabetes mellitus."*
3:15-4:45 pm:	**Poster Session #1 and Judging** *(Sciences and Residents)*
6:00 pm:	**Annual Dinner**

Schedule of Events

TUESDAY, JUNE 14, 2022

8:00-8:45 am: **Breakfast**

8:45-9:00 am: **Morning Presentations -** Devin Lowe, Ph.D.

9:00-9:30 am: **Opening Speaker -** Grace Kuo, Pharm.D., MPH, Ph.D.,
Dean, School of Pharmacy

9:30-11:00 am: **Poster Session #2 and Judging** *(Sciences and Residents)*

11:00-11:05 am: **Podium Presentations Introduction –** Meredith Sigler, Pharm.D.

11:05-11:20 am: **Senior Graduate Student Presentation –** Iqra Pervaiz
"Modeling Glut1 Deficiency Syndrome at the Human Blood-Brain Barrier In Vitro using CRISPR-Cas9 Edited Induced Pluripotent Stem Cells"

11:20-11:35 am: **Post-Doctoral Research Associate Presentation –** Quynh Do, Ph.D.
"Interaction Interface between 5-HT3A Serotonin Receptor and RIC-3 Chaperone"

11:35-11:50 am: **PGY1 Resident Presentation -** Sze Yi Kong, Pharm.D.
"Impact of a Layered Learning Model on Student Pharmacists' Academic Performance in the Inpatient Setting"

12:00-1:00 pm: **Lunch**

1:00-1:05 pm: **Distinguished Speaker Introductions –** Ron Hall, Pharm.D.

1:05-1:35 pm: **Distinguished Speaker –** John Griswold, M.D.
"Clinical Research Institute (CRI) – an all-inclusive clinical research support service for faculty and trainees"

1:40-2:10 pm: **Distinguished Speaker –** Theresa Byrd, DrPH, MPH, RN
"Examples of Behavioral Science Research in Public Health"

2:10-2:50 pm: **Awards Ceremony**

Keynote Speaker

Keynote Speaker

Alan Saghatelian, Ph.D.

Professor
Clayton Foundation Laboratories for Peptide Biology
Dr. Frederik Paulsen Chair
Salk Institute

Dr. Saghatelian's lab dives into the discovery and characterization of novel molecules associated with human disease, such as diabetes, cancer and autoimmune disease. What makes his lab unique in this endeavor is the focus on the biology of metabolites and peptides—two classes of molecules that are extremely important in biology but understudied because of technical challenges. Exploring this uncharted territory has enabled the Saghatelian lab to discover novel lipids that reduce inflammation and improve the symptoms of diabetes and identify a previously unknown cluster of human genes that produce peptides and small proteins that control fundamental cellular processes, such as DNA repair, highlighting their potential importance in cancer.

Alan Saghatelian's work touches on virtually all areas of human biology. He has developed and applied new mass spectrometry strategies that measure changes in small molecules overlooked by traditional biological methods, which typically focus on DNA, RNA and proteins. In particular, Saghatelian focuses on metabolites and peptides, which have been understudied because of technical challenges in their detection. Exploring this uncharted territory has enabled Saghatelian to make important discoveries, including the recent finding of a novel human lipid that reduces inflammation and reverses the symptoms of diabetes. Saghatelian hopes to use the knowledge gained from his lab's work to accelerate the development of new medicines in the area of diabetes. He is also collaborating with many laboratories at Salk to understand the roles of peptides and metabolites in cancer and neurodegenerative and immunologic disorders.

Keynote Speaker

Kerry LaPlante, Pharm.D., FCCP, FIDSA, FIDP

Professor and Chair of Pharmacy,
University of Rhode Island, Kingston, RI

Adjunct Professor of Medicine,
Brown University, Providence, RI

Dr. LaPlante is the Department Chairperson and a tenured Professor of Pharmacy, as well as the founding Director of the Rhode Island Infectious Diseases Antibiotic Research Program at the Providence VA Medical Center.

As a licensed clinical pharmacist, LaPlante is an internationally recognized expert on antibiotic use, antimicrobial resistance, as well as health policy implementation. She remains on the frontline of the antimicrobial resistance public health crisis by leading statewide initiatives and serving as an advisor to the Centers of Diseases Control and Prevention, PEW Research Center and The Joint Commission.

She currently serves as chairperson for the Rhode Island Department of Health's Antimicrobial Stewardship and Environmental Task Force where she led the Rhode Island Antimicrobial Stewardship Expansion Initiative. In this role, she has created guidance and provided education for Antimicrobial Stewardship across Acute Care, Long Term Care and Urgent Care facilities throughout the State of Rhode Island, specifically for the CVS Minute Clinics Provider meeting at the at CVS National Headquarters in Rhode Island. During the COVID-19 pandemic, she was appointed to the COVID-19 vaccine subcommittee by the governor of Rhode Island.

Combining a clinical and scientific career, Dr. LaPlante has published over 120 peer-reviewed research articles, and she has received continuous uninterrupted funding with over 30 successfully awarded grants totaling over 20 million from the National Institutes of Health, the Department of Veterans Affairs, and Investigator-Initiated Research from Research and Development divisions of the pharmaceutical industry.

She is also Director of the Pharmacology Core for the Rhode Island NIH-COBRE Center for Antimicrobial Resistance and Therapeutic Discovery (1P20GM121344-01A1), a member of the Antimicrobial Resistance Leadership Group (ARLG), an elected Fellow of the Infectious Diseases Society of America (FIDSA) and the American College of Clinical Pharmacy, and a past president of the Society of Infectious Diseases Pharmacists (SIDP; 2018-2019). Her pharmacy research fellowship (2012-present) awarded from the Office of Academic Affiliations (OAA) at the VA's National Office is one of a limited number of nationally recommended fellowships by the American College of Clinical Pharmacy (ACCP). She is a vice-president at Making a Difference in Infectious Diseases (MAD-ID), and an Associate Editor for Clinical Infectious Diseases.

Research Advisory Committee Members

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Committee Chair
Assistant Professor, Department of Immunotherapeutics and Biotechnology

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Vice Chair, Department of Pharmaceutical Sciences

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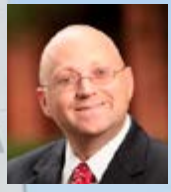

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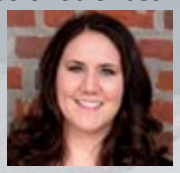

MEGAN FERRY
Pharmacy Resident Liaison
Department of Pharmacy Practice

Opening Speakers

Darrin D'Agostino, DO, MPH, MBA

Provost | Texas Tech University Health Sciences Center | Lubbock

Grace Kuo, Pharm.D., MPH, Ph.D.

Dean | Jerry H. Hodge School of Pharmacy |Amarillo

Distinquished Speakers

John Griswold, M.D., FACS

Director |Clinical Research Institute | Lubbock

Theresa Byrd, DrPH, MPH, RN

Chair & Associate Dean |Department of Public Health | Lubbock

Seed Grant Awardee Speaker

Meredith Sigler, Pharm.D

Assistant Professor | Department of Pharmacy Practice | Dallas

Podium Presentation

Interaction Interface between 5-HT3A Serotonin Receptor and RIC-3 Chaperone

Hoa Quynh Do PhD[1], Michaela Jansen PharmD -PhD[1]

[1]Department of Cell Physiology and Molecular Biophysics and Center for Membrane Protein Research, School of Medicine, Texas Tech University Health Sciences Center, Lubbock, Texas

Serotonin or 5-hydroxytryptamine receptors type 3 (5-HT3) belong to the family of pentameric ligand-gated ion channels (pLGICs), which also includes other neurotransmitter-gated ion channels as nicotinic acetylcholine receptors. pLGICs have been long-standing clinical targets for treating psychiatric disorders such as anxiety, schizophrenia, addiction, and neurological diseases like Alzheimer's and Parkinson's disease. Due to the highly-homologous structures of pLGICs' extracellular and transmembrane domains, clinical trials for drug candidates targeting these domains have been largely hampered by undesired effects mediated by off-subunit modulation. With the present study, we explore the interaction interface of the 5-HT3A intracellular domain (ICD) with the resistance to inhibitors of choline esterase (RIC-3) chaperone. Previously, we have shown that RIC-3 physically interacts with 5-HT3A subunits, and we identified the L1-MX fragment of the ICD fused to maltose-binding protein as sufficient for the interaction. For the present study, synthetic L1-MX-based fragments, Ala-scanning, and a pull-down assay were used to probe binding to RIC-3. In complementary studies with full-length 5-HT3A subunits, we investigated the impact of the Ala substitutions on modulation of functional surface expression by RIC-3 using two-electrode voltage-clamp recording and Xenopus laevis oocytes. Our data demonstrate that the 5-HT3A-MX segment contains the interaction interface, and that residues W347, R349, and L353 disrupt the interaction with RIC-3.

Utilization of Continuous Glucose Monitoring in Older Adult Patients with Type 2 Diabetes Mellitus

Megan E. Ferry, Les P. Covington, Levi S. Campbell, Lindsay A. Courtney, Rodney B. Young, Karen J. Cutts, Michelle J. Lofranco, Eric J. MacLaughlin

Texas Tech Physicians of Amarillo Family Medicine or Internal Medicine, Amarillo, Texas

Purpose: To determine if continuous glucose monitoring (CGM) is associated with improved A1c levels in older adults with type 2 diabetes mellitus (T2DM).

Background: Uncontrolled T2DM exacerbates issues impacting many older adults. Use of CGMs in older patients is attractive due to the potential for increased risk of hypo- or hyperglycemia. While CGMs have demonstrated improved glycemic control and fewer adverse events in younger patients with T2DM, few studies have assessed their utility in older adult patients.

Methods: This study is prospective, self-controlled utilizing a pre-post pragmatic design. Eligible subjects were identified through an electronic health record (EHR) query from October 1, 2020 through September 30, 2021. Inclusion criteria include age ≥65 years, ≥1 appointment with a Family Medicine or Internal Medicine provider during the query timeframe, an ICD-10 diagnosis of T2DM, and prescriptions for prandial insulin. Exclusion criteria include being wards of the state, utilizing a CGM device prior to the study, <3 injections of insulin/day, or documented cognitive impairment. The primary outcome is change in A1c before initiation of a CGM device and 3 months following initiation. Secondary outcomes include A1c at 6 months, time-in-therapeutic range, average glucose, Glucose Management Indicator, other pertinent CGM metrics, total daily dose of insulin prescribed, and change in reported hypoglycemia symptoms. Descriptive statistics will be used for the analysis of patient characteristics. For the primary outcome and ordinal data, a Wilcoxon Signed Rank test will be utilized, and a McNemar test will be used to compare nominal variables. A sensitivity analysis will be performed on patients who have low sensor utilization.

Results: 200 subjects were identified, 74 met inclusion criteria, and 50 were eligible for study enrollment. Five subjects are currently enrolled, and recruitment is ongoing. Additional results are in progress.

Conclusion: Research in progress.

Impact of a Layered Learning Model on Student Pharmacists' Academic Performance in the Inpatient Setting

Celine Zhong, PharmD, BCPS, Sze Yi Kong, PharmD, Craig Cox, PharmD, FCCP, BCPS

Texas Tech University Health Sciences Center, Amarillo, Texas

Purpose: Over the past two decades, the number of pharmacy schools in the United States has increased by almost 80%, urging the American Society of Health-System Pharmacists to recommend the use of a layered learning model to facilitate experiential training of student pharmacists and clinical teaching of pharmacy residents simultaneously. The primary aim of this study is to evaluate the impact of a layered learning model on student pharmacists' academic performance in the inpatient setting.

Methods: This is a multi-campus, retrospective, observational cohort study of student pharmacists in graduating classes of 2019 and 2020 between 5/1/2018 and 5/31/2020 who completed both Introductory Pharmacy Practice Experiences (IPPE) and Advanced Pharmacy Practice Experiences (APPE) in the adult medicine setting. The primary outcome is the summative/overall adult medicine clinical clerkship score received by IPPE student pharmacists precepted by a pharmacy resident versus full-time/adjunct pharmacy faculty. Secondary outcomes include final learning outcome scores on patient care process, rotation-specific, and interprofessional competencies, and professionalism for IPPE and APPE, retention of knowledge between IPPE and APPE, and IPPE student pharmacists' perception of preceptorship model. All data are obtained and blinded from the experiential office. Statistical analysis include t-tests and chi-square tests to compare continuous data and categorical data, respectively.

Results: IPPE students in the pharmacy resident group receive statistically significant higher scores in patient care process (89.9% vs 87.4%, p=0.04) and interprofessional (96.8% vs 95.4%, p=0.0001) competencies when compared to the full time/adjunct pharmacy faculty group. The IPPE students' perception for the preceptors's commitment on educational experience was more positive in the pharmacy resident group than the full time/adjunct pharmacy faculty group (94.8%, 92.3%, p=0.04). There was no statistically difference in the other outcomes.

Conclusion: The layered learning model provides comparable/favorable academic performance outcomes on the students and a positive perception of having a resident preceptor.

Ferutinin Induces Osteogenic Differentiation of Dental Pulp-Derived Stem Cells (DPSCs) by Upregulating BMP2 Signaling

Prathyusha Naidu, Daniela Rolph, Hiranmoy Das

Department of Pharmaceutical Sciences, Jerry H. Hodge School of Pharmacy, Texas Tech University Health Sciences Center, Amarillo, Texas

Osteoporosis is a systemic metabolic bone disorder causes bone deterioration. Even though numerous medicines are available for osteoporosis, most of them are helping only to slow the loss of bone density. So, it is crucial to gain insight into underlying mechanisms and be able to develop novel therapies accordingly. The bone morphogenetic proteins (BMP) are a group of proteins within the superfamily of transforming growth factor-beta (TGF-β) proteins. These proteins are very important for bone biology, and their associated downstream effectors are involved almost in every aspect of osteoblastic differentiation and maturation. Thus, we concentrated on studying the role of Ferutinin in regulating osteogenesis via the BMP2 pathway and elucidate the effects of ferutinin on structural and functional molecules related to osteogenesis. Dental pulp derived stem cells are self-renewing multipotent cells that are capable of mediating tissue regeneration. Our lab has shown that the phytoestrogen ferutinin activates DPSCs by epigenetically regulating Wnt/β-catenin signaling. As studies have indicated BMP-2 is known to enhance osteogenic differentiation, and because of the relationship between BMP-2 and canonical Wnt pathway signaling, our goal is to develop a potential stem cell therapy using human DPSCs. Based on our preliminary results, increased gene expression of BMP2, Runx2, and SMAD 1, 5, and 8, demonstrate that the ferutinin promotes expression of BMP2 pathway molecules at the mRNA and protein levels (both western blot and immunostaining). Moreover, these observations are consistent with previous work from our lab, which found that ferutinin upregulates canonical Wnt signaling in DPSCs. Both Wnt and BMP2 signaling are important to osteogenic differentiation, and crosstalk between the two pathways has been observed. These findings indicate that ferutinin promotes osteogenic differentiation in DPSCs.

Modeling Glut1 Deficiency Syndrome at the Human Blood-Brain Barrier *In Vitro* using CRISPR-Cas9 Edited Induced Pluripotent Stem Cells

Iqra Pervaiz, Fatema Tuz Zahra, Constantinos M. Mikelis and Abraham J. Alahmad

Texas Tech University Health Sciences Center; Jerry H. Hodge School of Pharmacy; Dept. of Pharmaceutical Sciences, Amarillo Texas

Glucose is an important source of energy for the central nervous system. Its uptake at the blood-brain barrier (BBB) is mostly mediated via glucose transporter 1 (GLUT1), a facilitated transporter encoded by the SLC2A1 gene. GLUT1 Deficiency Syndrome (GLUT1DS) is a haploinsufficiency characterized by mutations in the SLC2A1 gene, resulting in impaired glucose uptake at the BBB and clinically characterized by epilectic seizures and movement disorder. A major limitation is the absence of in vitro models of the BBB reproducing the disease. This study aimed to characterize a in vitro model of GLUT1DS using human pluripotent stem cells (iPSCs). Two GLUT1DS clones were generated (GLUT1-iPSC) from their original parental clone iPS(IMR90)-c4 by CRISPR/Cas9 and differentiated into brain microvascular endothelial cells (iBMECs). Cells were characterized in terms of SLC2A1 expression, changes in the barrier function, glucose uptake and metabolism, and angiogenesis. GLUT1DS iPSCs and iBMECs showed comparable phenotype than their parental control, with exception of reduced GLUT1 expression at protein level. Although no major disruption in the barrier function was reported in the two clones, a significant reduction in glucose uptake accompanied by an increase in glycolysis and mitochondrial respiration were reported in both GLUT1DS-iBMECs. Finally, impaired angiogenic features were reported in such clones compared to the parental clone. Our study provides the first documented characterization of GLUT1DS-iBMECs generated by CRISPR-Cas9, suggesting that GLUT1 truncation appears detrimental on brain angiogenesis and brain endothelial bioenergetics, but maybe not detrimental on iBMECs differentiation and barrier integrity. Our future direction is to further characterize the functional outcome of such truncated product, as well as its impact on other cells of the neurovascular unit.

Repurposing an Anti-psychotic Drug Pimavanserin (PVT) for the Treatment of Glioblastoma

Manas Yogendra Agrawal, Sharavan Ramachandran, Carson Zabel, Sanjay K. Srivastava

Department of Immunotherapeutics and Biotechnology,
Center for Tumor Immunology and targeted Cancer Therapy, Abilene, Texas

Glioblastoma multiforme (GBM) is a highly aggressive grade IV malignant brain tumor with an average survival time of 12 - 18 months. Although there are several current treatment strategies, they all prove to be inefficient as the 5 year survival rate still remains 5%. In terms of chemotherapy, drug resistance and passage through the blood-brain barrier (BBB) are the major caveats of concern. Thus, in the current study, we propose the use of an FDA-approved anti-psychotic agent Pimavanserin (PVT) as a substitute for Temozolomide (TMZ), the current standard therapy for GBM. To confirm the oncolytic efficacy of PVT, we performed preliminary cytotoxicity assays on various GBM cell lines. This was followed by Annexin assay to confirm the mode of cell-death caused by the drug. Apoptosis was further confirmed using apoptotic markers through western blot assay. To further elucidate the molecular mechanism of PVT, we performed protein gel electrophoresis; and deciphered the probable mechanism by which the drug exhibits its anti-cancer activity. We also studied the cell-cycle arrest profile due to PVT using flow cytometry. The IC50 values for different human GBM cell lines were in the range of 5µM to 8µM at 48 and 72 hours after treatment. A 70% increase in apoptotic cells was observed at the highest concentration treatment of PVT compared to control. Western blot analysis revealed a modulation in the PI3K/Akt and MAPK pathways in a dose-dependent manner at 48-hour time-point. These initial findings provide us with a robust platform signifying the potential of PVT to treat GBM via the PI3K/Akt and MAPK signaling. In order to corroborate our findings, we plan to perform in vivo experiments in GBM orthotopic model. We also plan to delineate the mechanism of PVT by performing immunoblot assays rt-PCR, Immunohistochemistry, etc. Our preliminary comparative studies with TMZ showed that PVT is more effective than TMZ

Internalization and Endocytic Pathway of T-cell Receptor Mimic Antibodies (TCRm) RL6A in Human Brain Endothelial Cells

Yeseul Ahn, Ehsan Nozohouri, Sumaih Zoubi, Ulrich Bickel

Department of Pharmaceutical Sciences, Jerry H. Hodge School of Pharmacy,
Texas Tech University Health Science Center, Amarillo, Texas

T-cell receptor mimic antibodies (TCRm), a novel class of antibodies, recognize specific peptides in the context of MHC class I molecules with higher specificity and binding affinity than T-cell receptor (TCR). RL6A is one of TCRm antibodies that detects the endogenous peptide/MHC complex, YLLPAIVHI/HLA-A2 (YLL-A2). This peptide is derived from human P68 RNA helicase, which is extensively expressed in human breast cancer cells and, as well as in human brain endothelial cells. Our lab previously showed RL6A antibodies traffic via clathrin-independent endocytosis (CIE) in brain endothelial cells. In this study, we investigated RL6A internalization and trafficking mechanism, especially at the early endocytic pathway.

For quantification of the internalization process, we analyzed the amount of surface-bound TCRm antibodies on the human brain endothelial cells using flow cytometry. RL6A internalized from the surface of hCMEC/D3 cells in a biphasic pattern, rapid internalization in the early time points (>30% internalized within 10min) followed by a much slower phase at later time points. The signals for surface-bound RL6A were significantly reduced 120min after endocytosis initiation by induced Pluri-potent Stem Cells (iPSC) derived human brain microvascular endothelial cells (hBMEC). Furthermore, the mean fluorescence intensity (MFI) for surface-bound RL6A increased by around two-fold for the interferon-gamma (IFN-γ) treated cells. 3-D confocal images of a monolayer of hCMEC/D3 cells were obtained and analyzed for colocalization. RL6A colocalized with small GTPase ARF6 and rab5 after 30min. Object-based colocalization analysis indicated that early endosome marker (EEA1) is involved in the trafficking of RL6A at all time points with a peak at 10min. This result confirms the previous result that RL6A undergoes CIE, which is characteristic of MHC I trafficking. In conclusion, RL6A enters the brain endothelial cells at the BBB, which can be a potential immunotherapeutic for brain tumors and neurodegenerative diseases.

Listeria Monocytogenes-Based Vaccines to Mediate Targeted Ablation of the Tumor-Associated Vasculature in Colorectal

Anderson TS, Wooster AL, Oladejo M, Wood LM, Lowe DB

Department of Immunotherapeutics and Biotechnology, Jerry H. Hodge School of Pharmacy, Texas Tech University Health Sciences Center, Abilene, Texas

Anti-cancer vaccines are consequential and useful tools in eliciting long-term immune responses against tumor-associated antigens (TAAs). Attenuated Listeria monocytogenes (Lm) represents one such vaccine modality for inducing durable immune-driven responses against MHC class I/II presented antigens. Rather than direct this form of therapy against the dynamic assortment of targets expressed directly by tumor cells, we have instead conjugated Lm-derived truncated listeriolysin O (tLLO) to RGS5, a critical molecule for cancer angiogenesis. Intriguingly, RGS5 is upregulated by pericytes in nascent blood vessels within the tumor microenvironment, and the destabilization of such blood vessel networks can effectively induce regressions of vascularized tumors like colon cancer. Our initial in vivo studies in mice immunized with the RGS5-LLO vaccine demonstrated significant protection against the aggressive colon cancer line MC38. Such findings provide the rationale for continuing efforts in developing a Lm-based therapeutic regimen against RGS5 and understanding the mechanistic interplay between vaccine-directed immune cells and tumor-derived blood vessels in this model.

Potential Postnatal Neurotoxicity Induced by Maternal E-Cigarette Exposure: Alteration of Blood-Brain Barrier (BBB) Integrity and Worsening of Ischemic Stroke Outcomes

Sabrina Rahman Archie, Ali Ehsan Sifat, Heidi Villalba, Sejal Sharma, Saeideh Nozohouri, Yong Zhang, Thomas J Abbruscato

Department of Pharmaceutical Sciences, Texas Tech University Health Sciences Center, Amarillo, Texas

Despite the prevalence perception about electronic cigarette (e-Cig) as a safe alternative of smoking for pregnant women, growing concern related to its potential toxic impact on neonatal health warrants adequate investigation. Several studies have demonstrated the toxic effects of prenatal tobacco smoking on postnatal health however, no such data is available with reference to e-Cig exposure during pregnancy. Due to the noticeable growth in e-Cig usage during pregnancy (~15%), it has become critical to study the long-term impact of maternal e-Cig smoking on postnatal health outcomes. Hence, in this study, we have evaluated the consequences of prenatal e-Cig use during pregnancy on postnatal blood-brain barrier (BBB) integrity, neuro-inflammation, and ischemic stroke outcomes in offspring. Pregnant CD1 mice (E5) were exposed to e-Cig vapor (2.4% nicotine) till postnatal day (PD) 7. The expression level of structural elements of the BBB including, tight junction proteins (ZO-1, claudin-5, occludin), astrocyte (GFAP), pericyte (PDGFRβ), basement membrane (Laminin α1, Laminin α4), NeuN, AQP4 and GLUT-1 were analyzed in offspring using western blot and immunohistochemistry at PD 7, PD 23, PD 45 and PD 90. Relevant neuro-inflammatory markers were quantified at PD 7 and PD 90. Ischemic stroke outcomes were evaluated by middle cerebral artery occlusion (MCAO) method in prenatally e-Cig exposed adult female offspring. In our study, significantly reduced expression of tight junction proteins and astrocyte marker were observed in male and female offspring till PD 90 ($P < 0.05$). Moreover, higher level of cytokines was found in offspring brain at PD 7. Additionally, prenatally e-Cig exposed female adult offspring had worsened ischemic stroke injury and neurological score compared to control offspring ($P < 0.05$). Our findings suggest that prenatal e-Cig exposure induces some long-term neurotoxic effects on neonates by disrupting postnatal blood-brain barrier integrity, inducing neuro-inflammation, and worsening ischemic stroke outcomes.

Evaluation of Macrophage Lipid Metabolism after Liposomal Treatment

Patricia Ines Back, Qisheng Zhang, Ninh M. La-Beck

Dept. of Immunotherapeutics and Biotechnology, Texas Tech Health Sciences Center, Abilene, TX
Dept. of Pharmacology, University of North Carolina at Chapel Hill, Chapel Hill, NC

Background: Liposomes are the most studied nanoparticle to enhance drug delivery and retention in tumors as a strategy to increase efficacy and decrease toxicity of cancer drugs. However, the biological impact of this lipid delivery system is poorly understood and viewed as secondary to the pharmacology of the drug cargo. The primary route of clearance for systemically administered liposomes is through macrophage internalization. Recently, we have found that liposomes induce M2 polarization in macrophages, suggesting they can modulate antitumor immune responses. We hypothesize that such effect may be related to the carrier's lipid composition, in particular cholesterol, which can be endogenously oxidized into oxysterols. Oxysterol production is related to cholesterol homeostasis and can directly affect macrophage metabolism and polarization state. Oxysterol metabolism is complex and many different oxysterols with different biological effects can be generated. Oxysterol 27-HC is linked to M2 polarization and tumor proliferation, and 25-HC can induce pro-inflammatory cytokine production. The impact and mechanisms by which liposome-derived cholesterol regulates macrophage functionality in the tumor milieu is unknown. This knowledge is necessary to engineer cholesterol analogs without protumoral activity, thereby improving the efficacy of liposomal drugs. The objective of this study is to characterize the impact of liposomes on macrophage lipid metabolism.

Methods: Macrophages were differentiated from bone marrow cells of C57Bl/6 mice and M0, M1 or M2 macrophages were generated using vehicle (no polarization stimulus), LPS 100 ng/mL or IL-4, respectively. After incubation overnight, cells were treated with liposomes (standardized at 55.7 µM phospholipids) or dextrose vehicle. After 24h, cells were collected and processed for lipidomics analyses.

Results/Conclusion: Sample analyses are ongoing and we anticipate to have results in May. We expect that the effects of liposomes on different lipid pathways will depend on macrophage polarization states.

Simultaneous Quantification and Validation of Serotonin, Dopamine, and Norepinephrine by LC-MS/MS in the Mouse Brain

Sounak Bagchi, Nausheen Syeara,Dhavalkumar Patel, Vardan T. Karamyan

Texas Tech University Health Sciences Center, School of Pharmacy, Amarillo, Texas

Background: Monoamines (MAs) are involved in several neurological disorders, including stroke, and contribute significantly to the pathogenic mechanisms of these diseases. We developed and validated the method for simultaneous quantification of the three main MAs, serotonin (5-HT), dopamine (DA), and norepinephrine (NE), in mouse cerebral cortical homogenates using highly sensitive liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS).

Method: The quantitative analysis of 5-HT, DA and NE was executed using a reversed-phase Raptor Biphenyl column (100 × 2.1 mm, 2.7µm) coupled to an API-QTRAP 5500 (AB SCIEX) mass spectrometer under a gradient mode, using a 0.2% formic acid in water and 0.2% formic acid in methanol at a flow rate of 0.2 mL/min. The method was validated by determining the linearity, intra and interday (precision and accuracy), recovery, matrix effect, carry-over and stability in cerebral cortical samples obtained from CD-1 mice. In addition, the basal levels of the MAs were compared in samples obtained from male and female mice.

Result: The MAs were detected and quantified by LC-MS/MS with positive electrospray ionization, which operates in a multiple reaction monitoring mode. The linearity for 5-HT and NE was achieved at concentrations ranging from 1.953 – 1000 ng/ml and DA at 7.812 – 2000ng/ml with an r2 value > 0.99. The method exhibited good intra and inter-day precisions (RSD < 15%) with good accuracy (85-115%). Recovery ranges were between 88% and 106%. Other factors like matrix effect, carry-over and stability were consistent with the requirements of regulatory agencies. No significant differences were observed in the basal levels of the MAs in both genders.

Conclusion and ongoing studies: A new method was developed and applied to quantify MAs in brain homogenates. Our ongoing studies focus on evaluating alteration of MA levels in the brain following treatments that promote functional recovery after ischemic stroke in mice.

Evaluation of Use of Intravenous Iron at BSA Health System

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BSA Health System

Exogenous iron supplementation improves hemoglobin synthesis and aids in the repletion of iron reserves for various indications. Parenteral, or intravenous (IV), iron supplementation comes in various forms which are often utilized in cases of severe deficiency or when oral formulations are not able to be used. BSA Health System (BSAHS) currently carries three IV iron products; iron sucrose, iron dextran, and ferric gluconate. Considering the differences in cost, approved indications, and recommended dosages across these available formulations, a medication use evaluation was performed. Results are currently pending. Analysis and conclusion will be presented at Texas Tech University Health Sciences Center Jerry H. Hodge School of Pharmacy Research Days.

In-Hospital Antihypertensive Prescribing After Acute Ischemic Stroke

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Purpose: Stroke is the leading cause of serious long-term disability in the United States. Although current guidelines recommend against the use of antihypertensive therapy in patients with a blood pressure less than 220/120 mmHg, prescribing patterns have shown to be inconsistent with this data. The purpose of this study is to assess the use of antihypertensive medications within the first 24 hours after hospitalization in relation to current guideline recommendations and to characterize process variables and outcomes associated with specific use patterns.

Methods: Retrospective cohort study of patients 40-89 years of age who were admitted to the hospital acute ischemic stroke between January 1, 2019, and December 31, 2021. Subjects were identified through ICD-10 codes and confirmed through manual chart review. Patients were excluded if transferred from an outside facility > 6 hours after start of stroke symptoms, hospital survival < 24 hours, severe stroke, coma at presentation, concomitant hemorrhagic stroke, COVID-19 infection, or history of atrial fibrillation or flutter. Patient demographics, comorbidities, antihypertensive medication use prior to hospitalization, and stroke treatments (e.g., receipt of alteplase) were collected. Prescribing patterns were assessed including antihypertensive medication, route, frequency, schedule, and the type of prescriber. Primary analysis was performed using basic descriptive statistics. Chi square test or Fisher's exact test were used to assess differences in prescribing patterns and other categorical data. Student's t-test was used to compare continuous data including blood pressure variables. Multivariable logistic regression will be used to assess the association between prescribing patterns and outcomes.

Results: Data collection and analysis are currently in process.

Conclusion: Conclusion to be presented following the completion of data collection and analysis.

Correlation of Population Specific Risk Factors and Prevalence of Developing Severe Hypoglycemia at a Large Medical Center

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Purpose: To determine the risk factors for developing severe inpatient hypoglycemia in patients at Covenant Medical Center. Results will support the creation of a population-specific tool to more accurately identify patients for pharmacist intervention.

Background: Our organization was challenged to evaluate potential contributing factors for severe hypoglycemia in the facility due to exceeding the ministry goal of 4.5% by double, at 8.97%. Our organization defines severe hypoglycemia as any blood glucose value <50 mg/dL. Review of patients with severe hypoglycemia utilizing a validated risk-assessment calculator published by Elliot et al. did not provide the expected patient specific risk score. Therefore, more detailed review of our patient population was needed to elucidate correlating risk factors.

Methods: A retrospective chart review was completed for 736 at-risk patients, any patient with active anti-diabetic orders, admitted to Covenant Medical Center from January 2021 through March 2021. Patient demographics and high-risk characteristics were collected including units/kg/day and BID schedule of long-acting insulin, corticosteroid use and taper, dietary intake, AKI or ESRD, and sulfonylurea use. Patients were excluded if receiving insulin through pump, continuous infusion or for hyperkalemia treatment, or in cases with inadequate information within chart. A multiple logistic regression was performed on the collected data to predict the probability of developing severe hypoglycemia in relation to the included risk factors.

Results & Conclusion: Yet to be determined.

Are Myotoxin-Derived Peptides Activators of Amyloid Beta-Degrading Enzymes,Endothelin Converting Enzyme-1 and Neprilysin?

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Introduction: The aim of this study was to reproduce findings of a recent report suggesting that two Bothrops asper Myotoxin-derived peptides, peptides 1 and 2, enhance activity of endothelin converting enzyme-1 (ECE-1) and neprilysin (NEP) – two metallopeptidases deemed to participate in degradation of amyloid beta (Aβ) and pathogenesis of Alzheimer's disease. For this purpose, we have designed in vitro pharmacological experiments to evaluate the effect of peptides 1 and 2 on activity of ECE1 and NEP, and several other peptidases from the same family.

Methods: Concentration-dependent effect of the peptides on activity of recombinant human NEP, ECE1, angiotensin converting enzyme (ACE), ACE2, neurolysin (Nln), and thimet oligopeptidase (TOP) was measured in a continuous enzymatic assay at different conditions. The identity of NEP and ECE1 used in these experiments was confirmed by well-characterized selective inhibitors and immunoblotting.

Results: In contrast to the original report, we did not observe enhanced activity of NEP in the presence of 0.1 to 30 μM peptides 1 and 2, wheras at higher concentrations the peptides inhibited activity of NEP. Peptides 1 and 2 enhanced the activity of ECE-1 at 0.1 to 10 μM concentrations (~two-fold), while at higher concentrations inhibition of ECE-1 was observed. Both peptides had negligible effect on activities of ACE, ACE2, NEP and Nln and showed slight inhibitory effect at high concentrations. Conventional Western Blotting experiments with validated antibodies confirmed the identity of commercially purchased NEP and ECE-1 used in our experiments. Furthemore, we observed concentration-dependent inhibition of both peptidases in response to selective inhibitors with potency values in line with literature reports.

Conclusions: Our experimental observations challenge the earlier proposition that Bothrops asper Myotoxin-derived peptides 1 and 2 are NEP and ECE-1 activators. Our ongoing experiments focus on evaluating the effect of these peptides on degradation of Aβ by NEP and ECE-1

A Novel Anti-Parasitic Drug Suppresses Pancreatic Cancer by Modulating the Immune Microenvironment

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Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive cancer and is predicted to be the second leading cause of cancer-related deaths by 2030 with a death toll of approximately 800,000 worldwide. The tumor biology of PDAC, being a solid tumor is complex and has been one of the most difficult to treat tumors. Successful therapeutic developments against PDAC have been limited due to factors such as drug resistance, low drug infiltration, and adverse effects of therapies affecting the patient's performance status. Recently, immunotherapy has shown surprisingly positive results in cancers such as melanoma, however, immunotherapies majorly failed in PDAC clinical trials. The stiff desmoplasia and reduced infiltration of immune cells is considered to be a critical factor for this failure. Using drug repurposing strategy, we identified anti-cancer and immunomodulatory effects of MBO, an anti-parasitic drug in the PDAC tumor microenvironment. We observed concentration-dependent growth inhibition of PDAC cell lines AsPC-1, MiaPaca-2, SUIT-2, Panc-1, and murine PDAC cell line PO2. The IC50 of MBO in PDAC cell lines ranged from 4-6 µM. MBO induced 3-4-fold apoptosis in PDAC cells and its apoptotic activity was monitored using Annexin/APC assay. Next, we studied the anti-cancer activity of MBO in a subcutaneous PDAC model wherein we observed 70-80% tumor growth suppression. We also observed an 80% tumor growth suppression in syngenic orthotopic PDAC mice model. In the orthotopic PDAC model, we performed immune analysis and interestingly, we observed higher infiltration of cytotoxic CD8 T cells within the MBO treated tumor groups when compared to control tumors. Subsequently, we analyzed the effect of MBO in co-culture assay using isolated human peripheral blood mononuclear cells (PBMC). MBO sensitized the cancer cells to the cytotoxic activity of T cell population. Additionally, co-culture studies showed increased activation of T cells and dendritic cells which was monitored using activation markers in flow cytometric analysis.

The immunomodulatory effect of MBO in PDAC is a novel identification and is critical for therapeutic development against PDAC. The failure of immunotherapy in PDAC can be addressed by combining immune checkpoint inhibitors such as anti-PD-1/PD-L1 with repurposed compounds having immunomodulatory activity. This new approach might prove beneficial for reviving the failed immunotherapeutic development against PDAC and move the therapy towards clinical approval

The Impact of a Pharmacist-Led Ketogenic Weight Loss Protocol in a Community Pharmacy Setting

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Purpose: The purpose of this study is to evaluate the impact of a pharmacist-led ketogenic weight loss program in a community pharmacy setting.

Background: Obesity is a complex disease state that is typically said to occur when energy intake exceeds energy expenditure; however, this definition of obesity is an oversimplification. Many factors play a role in obesity, including genetics, environment, lifestyle factors, hormonal imbalance, and the gut microbiome. Diet and lifestyle modification have been a mainstay of obesity management for decades; however, there has not been a specific diet that has shown more benefit than another. Many of these programs provide education and counseling on diet, physical activity, and behavioral therapy designed to lose and maintain 5-10% of total body weight.. Although weight loss has been the cornerstone for obesity, diet and lifestyle modification education rarely occur due to time constraints, limited access to resources, and low provider reimbursement. Community pharmacists are in a unique position to fill in the gap of obesity management.

Methods: In this retrospective review, charts will be reviewed from patients enrolled in our ketogenic weight-loss program at an independent community pharmacy in Denton, TX from January 2021 to December 2021. Key inclusion criteria include patients over the age of 18 who are overweight (BMI: 25-29.9) or obese (BMI>30). The primary outcome is the achievement of 5% total body weight loss from baseline. Secondary outcomes include achievement of 10% total body weight loss from baseline, mean percent reduction in weight loss, reduction in anthropometric measurements (arm, chest, waist, hips, thigh), reduction in body fat, and change in BMI from baseline. For the primary outcome and secondary outcomes, a Wilcoxon Sign-Rank test will evaluate statistical significance. A P value of less than 0.05 was considered to indicate statistical significance.

Results / Conclusion: In progress.

Impact of SGLT-2 Inhibitors Prescribed in a Clinic Setting on Reducing the Risk of HFrEF Hospitalizations in a Community Hospital System

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Purpose: Approximately 1 in 4 heart failure (HF) patients are readmitted within 30 days of discharge and nearly half are readmitted within 6 months. The DAPA-HF and EMPEROR-Reduced landmark trials analyzed a composite cardiovascular (CV) death or heart failure with reduced ejection fraction (HFrEF) hospitalization reduction when using sodium glucose-cotransporter-2 protein (SGLT-2) inhibitors dapagliflozin and empagliflozin, respectively. Currently, there is no literature that compares the role of dapagliflozin and empagliflozin in reducing hospitalizations in an outpatient HF clinic or community hospital setting. Hendrick Medical Center (HMC) has had an interprofessional outpatient HF clinic that services Abilene community members. The purpose of this study is to determine hospitalization or urgent HF clinic readmission reduction rates in HFrEF patients who were prescribed dapagliflozin or empagliflozin post-index date. Index date is defined as an initial hospitalization or urgent HF clinic visit.

Methods: HMC both inpatient and outpatient services utilize the Allscripts electronic medical record system. This resource will be utilized to evaluate patients admitted to the HF clinic from October 2019 to August 2021 with a focus on hospitalization and readmission history. Data will be collected by electronic chart review of patients in the Hendrick Health Outpatient Heart Failure Clinic, including patient demographics, hospital and clinic record history, ejection fraction, SGLT-2 prescription use, matched by age, gender, and severity of HF. Patients will be sorted into groups by whether or not they were prescribed dapagliflozin or empagliflozin post-index date. Outcomes will be compared to a matched cohort of HF patients prescribed an SGLT-2 inhibitor versus patients not prescribed an SGLT-2 inhibitor. This study will also utilize the similar criteria as the DAPA-HF and EMPEROR-Reduced trials.

Results: Statisitical analyses are currently in progress.

Conclusion: Statisitcal analyses are currently in progress.

Vancomycin Area under the Curve Target Attainment using a First Order Analytic Equations Calculator

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Purpose: Vancomycin trough serum concentrations have been utilized as a surrogate marker for therapeutic attainment of area under the curve to minimum inhibitory concentration (AUC:MIC) goal of 400 mcg*h/mL. Recent updated dosing guidelines recommend using Bayesian software or first order analytic equations to estimate vancomycin AUC due to the reduction in nephrotoxicity. The use of pharmacokinetic (PK) equations has been favored in institutions that do not have the means to purchase Bayesian software. The purpose of this study is to evaluate accuracy of analytic PK equations in attaining therapeutic AUC levels.

Methods: Retrospective, single center, observational study of 403 adult hospitalized patients conducted from July to November 2021 received intravenous vancomycin therapy greater than 24 hours for indications requiring an AUC:MIC of 400 – 600 mcg*h/mL were included. Patients were excluded if they received any form of renal replacement therapy within 72 hours of vancomycin initiation, had creatinine clearance <30 ml/min, pregnant, or vancomycin indications for surgical prophylaxis, urinary tract infections, or skin & soft tissue infections. Vancomycin was dosed utilizing a home-grown first-order PK equation calculator. Outcomes include observed AUC:MIC within therapeutic goal at steady state with empiric dose. The rates of target attainment and AKI were assessed.

Results: A total of 1455 patients were reviewed, and 402 patients were included. Of the 402, 210 (52%) were therapeutic at steady state after empiric calculations. There were 129 (32%) patients that were subtherapeutic, and 63 (15.8%) patients that were supratherapeutic. Overall, 247 out of 402 (61%) achieved therapeutic AUC goal, while 31 out of 402 (7.69%) met criteria for nephrotoxicity.

Conclusions: The use of a first-order pharmacokinetic calculator resulted in AUC target attainment for more than half of patients with low rates of AKI. Improvement in target attainment was noted as pharmacists gained experience with the dosing tool.

Pharmacist-Initiated Spirometry Clinic within a Family Medicine Residency Clinic

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Purpose: The purpose of this study was to evaluate the impact of a pharmacist-initiated spirometry clinic in patients with chronic obstructive pulmonary disease (COPD) and describe drug therapy modifications made by the pharmacist.

Methods: This is a prospective single site study of outpatients seen at Texas Tech Physicians of Amarillo Family Medicine clinic starting 12/01/2021-present. Patients are included if they are ≥18 years old, seen in the clinic within 10/2020-12/2021, and diagnosed with COPD based off ICD-10 codes. Patients are excluded if they are unable to perform spirometry (e.g., dementia, Alzheimer's disease), have contraindications to spirometry, are pregnant, or if they have had spirometry within the last year of the index date. The primary objective of the number of COPD patients that complete spirometry with the pharmacist, and secondary objectives of pharmacist-initiated therapeutic interventions after spirometry, were analyzed using descriptive statistics.

Results: A total of 42 patients have been included to date, with a total of 8 seen in clinic by a pharmacist. Three of the eight patients that completed spirometry in the clinic did not have results conducive to a COPD diagnosis and subsequently were referred to their primary care for further evaluation. The average Modified Medical Research Council Dyspnea Scale (mMRC) score was 1.88+0.83, the average COPD Assessment Test (CAT) score was 21.4+6.84, the average FEV1 percent predicted post bronchodilator was 64.4%+20.14, and the average FEV1/FVC ratio post bronchodilator was 71.3%+16.38. One-half (50%) of the patients seen by the pharmacist had new therapy recommendations due to their spirometry results and symptomology. Forty percent of patients had their current drug therapy modified, following national guidelines, based on the medical history and spirometry results (e.g., change from a long-acting beta-agonist (LABA)/inhaled corticosteroid (ICS) combination to a LABA/long-acting muscarinic antagonist (LAMA).

Conclusions: Research is ongoing.

KLF2 Modulates the Function and Activity of Mitochondria in Osteoclast Differentiation

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We have previously demonstrated that Kruppel-like factor 2 (KLF2) promotes autophagy during osteoclastogenesis. However, it remains unclear how KLF2 regulates autophagy during the process that produces a bone loss in a variety of bone disorders, including osteoporosis, osteoarthritis, and rheumatoid arthritis. In this current investigation, we found that the number and mass of mitochondria and the mitochondrial membrane potentiality were augmented during osteoclastic differentiation, mediated by the addition of soluble receptor activator of nuclear factor- kappaB ligand (sRANKL) to the RAW 264.7 cells and that these measures were significantly reduced by chemical induction of KLF2 (induced by addition of GGTI298). As a result of the increased number of mitochondria, oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) increased, which were almost restored by overexpression of KLF2. Furthermore, scanning electron microscopy and western blot data indicated that osteoclast differentiation increased mitochondrial fission by increasing mitophagy; this process was reduced by overexpression of KLF2. Finally, we observed high expression of autophagy molecules in the late endosome of myeloid cells, as determined by immune co-localization and western blot. In conclusion, we have shown for the first time that mitochondrial activity and functions significantly influence osteoclastic differentiation and that KLF2 plays a significant role in orchestrating these processes. Through identifying the regulatory mechanisms of KLF2, novel therapeutic strategies could be developed to treat a wide range of bone-related diseases by targeting osteoclast cells.

Characterizing the Impact of Liposome Co-Encapsulated Alendronate-Doxorubicin on the Tumor Immunologic Milieu in a Murine Fibrosarcoma Model

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Background: Fibrosarcoma is a rare and aggressive soft tissue sarcoma that occurs in infants and adults alike. For surgically unresectable or late-stage fibrosarcoma, doxorubicin is the standard of care but it has significant limitations in terms of its toxicity profile and response rate. A major mechanism of resistance to this anti-cancer therapy is immunosuppression in the tumor microenvironment (TME) mediated by myeloid and T-regulatory cells. In this study we explore the strategy to co-encapsulate doxorubicin with alendronate, an amino-bisphosphonate which modulates tumor infiltrated myeloid cells, in pegylated liposomes to make a safer and effective alternative to the standard of care. We postulate that co-encapsulating alendronate with doxorubicin in pegylated liposomes (PLAD) will favorably modulate the TME and increase the efficacy of doxorubicin since alendronate abrogates the activity of myeloid cells and liposomes target drug delivery to tumors.

Methods: WEHI-164 fibrosarcoma cells were implanted in 8-10 weeks-old male balb/c mice. Animals were randomized to PLAD, pegylated liposomal doxorubicin (Doxil), or free doxorubicin (FDox) at 8 mg/kg of doxorubicin (n=9/group), or dextrose (vehicle) or pegylated liposomal alendronate (PLA) at 3.28 mg/kg alendronate (same dose as PLAD) (n=5/group). Five days post-treatment, animals were euthanized, and tumors were processed for flow cytometric analyses.

Results: PLAD and Doxil decreased M2-polarized macrophages, T-regulatory cells, and CD4/CD8 ratios in tumors, while activated natural killer cells were increased compared to the control. PLA decreased M2-polarized macrophages but did not have any impact on T-regs, while FDox had the opposite effect. Doxil and PLAD significantly increased uptake of doxorubicin in acrophages and other myeloids, compared to FDox. These effects were greater with PLAD than Doxil.

Conclusion: Co-delivery of doxorubicin and alendronate remodeled the TME towards an immune-permissive milieu. Ongoing studies will determine the anticancer efficacy of PLAD.

Concordance with Guideline-Directed Therapy for Secondary Prevention of Ischemic Stroke at Hospital Discharge

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Purpose: To characterize prescribing practices, including the use of guideline-recommended treatments for secondary stroke prevention at discharge and factors that influence concordant prescribing in a primary stroke center in West Texas. Prior studies have emphasized the importance of appropriate prescribing of secondary prevention medications at discharge. Appropriate and timely follow-up after discharge is also imperative. Overall, medications prescribed on discharge may be associated with improved long-term adherence.

Methods: This is a retrospective cohort study of adult patients admitted between January 2018 and March 2020 with a diagnosis of acute ischemic stroke or transient ischemic attack based on ICD-10 codes. Patients with a history of atrial fibrillation/flutter, use of an oral anticoagulant before hospital admission, intracranial bleeding during admission, history of prior stroke, and patients designated hospice or palliative care were excluded. We collected retrospective data from the institution's electronic medical records, and reviewed medication administration records for high-intensity statins and antiplatelet agents. Select secondary endpoints included patient demographics, stroke severity, renal function, discharge location, planned follow-up appointments and type of specialist to be seen, and agent and dose of antihypertensives, statins and antiplatelets. Basic descriptive statistics were used to assess the primary objective. Multiple regression analysis will be used to evaluate factors associated with specific prescribing patterns.

Results: Data collection is ongoing.

Conclusion: To be determined upon result analysis.

Antagonists of the Prostaglandin E2 EP2 and EP3 Receptors Modulates Central Post-Stroke Pain and Associated Protein Expression through Antiapoptotic and Anti-Inflammatory Mechanisms

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Neuropathic pain following stroke, termed central post-stroke pain (CPSP), is reported in as many as 18% of poststroke patients, often manifesting as spontaneous or evoked pain in the form of mechanical allodynia and thermal hyperalgesia. To date, there is no viable treatment available for the alleviation of CPSP due to the lack of sufficient data needed to understand the pain perception pathway involved. Here, we will investigate a potential pain perception pathway that is activated after stroke, as well as its implications in the generation of CPSP. In addition, we aim to find a suitable treatment approach to alleviate stroke patient pain for maximal engagement in post stroke rehabilitation. Previous reports have shown that antagonists of the prostaglandin E2 (PGE2), EP2 and EP3 receptors, could be involved in modulating the secondary injury mechanisms responsible for the inflammatory and apoptotic reactions occurring in the ischemic cortex, demonstrating its potential involvement in neuroprotection, as well a possible role in attenuating CPSP. During stroke, a hypoxic and nutrient deprived environment proliferates at the site of lesion, resulting in neuronal damage and astrocyte activation, which may then bring about the release of various pain associated inflammatory markers associated with a prolonged, persistent pain state. In this study, we will utilize immunoblotting to examine the expression of CPSP related proteins in neurons, such as, nuclear factor kappa B, tumor necrosis factor alpha, interleukin-1 beta, cyclooxygenase-2, mitochondrial PGE2 synthase-1, PGE2 EP2 receptor, PGE2 EP3 receptor, and Neu-N. These CPSP related proteins will be examined in primary neurons exposed to the oxygen glucose deprived (OGD) condition for 3 hours, followed by recovery for various time periods under normal oxygen-glucose conditions. In addition, we will also examine the expression of CPSP related proteins in neurons treated with EP2 and EP3 receptor antagonists during the post-OGD recovery periods.

Evaluation of Discharge Prescription Errors at a Large Urban Emergency Department

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Purpose: Optimization of discharge prescriptions represents an area for pharmacy intervention. Studies indicate the most common classes of medications attributed to an error include antimicrobials, steroids, and inhalants. The purpose of this study is to investigate if there are medication prescription errors at discharge from the Texas Health Harris Methodist Fort Worth (THFW) ED, determine the clinical severity, and assess where pharmacy can provide optimization.

Methods: In this retrospective, cross-sectional review of discharge prescriptions, we assessed the appropriateness of a random selection of prescriptions. Specifically, inhalants, antimicrobials, and anticoagulants were evaluated for accuracy. The primary outcome was prevalence of moderate, serious, or potentially lethal medication errors among adult patients during the month of July 2021. Secondary outcomes included clinical severity of errors. The categories included optimal, area for optimization, moderate, serious, and potentially lethal errors.

Results: Of 8,876 prescriptions from July 2021 there were 210 inhalants, 1,311 antimicrobials, and 16 anticoagulants; of those, 50 orders were randomly selected from each group. As there were only 16 anticoagulants for July 2021, we included March through July 2021. There were no potentially lethal errors and the only group to have a serious error was anticoagulants prescribed for Atrial Fibrillation (AF), of which 56% had a serious error. A moderate error occurred in 21/50 (42%) of antimicrobials, 22/50 (44%) of inhalants, and 1/40 (3%) of anticoagulants.

Conclusion: Our results are descriptive and cannot be determined to be statistically significant, but there is an obvious area of intervention for pharmacists in the ED here at THFW. In all three categories there was at an area in which pharmacists could assist in optimization. The most clinically important intervention is needed for anticoagulants for AF. Additionally, optimization of the duration of antimicrobial therapy and choice of agent is a large area of pharmacist opportunity.

Evaluation of Use of Custom Vs. Premade Total Parenteral Nutrition Products at BSA Health System

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Malnutrition is something that can occur often in critically ill patients. Acute malnutrition can be a caloric deficit due to overall starvation on presentation or even from catabolic effects such as (muscle wasting, insulin resistance, as well as electrolyte imbalances due to infection severity. Although the goal is to correct the nutrition balance in a timely manner, doing this too fast can increase the risk for fatal outcomes. Malnutrition in critically ill patients is typically treated with supplemental nutrition. The ability to adequately provide patients with nutritional support can positively impact morbidity, mortality, as well as hospitalization stay. The purpose of this study was to evaluate the appropriateness of custom vs premixed TPN in patients at risk for malnutrition and identify opportunities for improvement in its use and monitoring. This is a retrospective chart review of patients with TPN or Clinimix ordered between January 1, 2019 and December 1, 2019 at Baptist Saint Anthony Hospital in Amarillo, Texas. Baseline characteristics will include indication, eligibility for enteral nutrition, primary diagnosis, location, malnutrition risk, NUTRIC score, timeframe to initiation, length of use. The purpose of this review is to evaluate if TPN is being used appropriately in the setting of malnutrition. Data collection and analysis is currently ongoing. Conclusion to be presented following the completion of data collection and analysis.

Listeria-Based Vaccines Targeting Interferon-Stimulated Gene 15 (ISG15) for Renal Cell Carcinoma and Colorectal Cancer

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Both renal cell carcinoma (RCC) and colorectal cancer (CRC) are leading causes of cancer-related deaths in the United States. There is an urgent need to develop new treatment regimen(s) for advanced RCC and CRC patients due to (i) their current 5-year survival rates are below 15% and (ii) the prevalence of resistance to currently available systemic therapies. Immunotherapy is an emerging approach in advanced RCC and CRC. A Listeria-based vaccine is an active form of cancer immunotherapy with demonstrated anti-tumor efficacy in several pre-clinical models of cancer and in clinical trials. The Listeria-based vaccine is developed from an attenuated Listeria monocytogenes (Lm) bacterium which has the unique ability to preferentially infect dendritic cells (DCs), deliver the tumor antigen-of-interest and induce robust cytotoxic T lymphocyte (CTL) responses to eradicate tumors. One such tumor-associated antigen, Interferon-stimulated gene 15 (ISG15), is the first identified ubiquitin-like modifier and has been implicated for its central role in innate immunity against intracellular pathogens. While the anti-viral mechanism of ISG15 is well-established, the protein is recently being explored for its contribution to cancer development. ISG15 expression is highly elevated and significantly associated with unfavorable prognosis in a multitude of cancers including RCC and CRC. Therefore, targeting ISG15 by means of a Lm-based vaccine could be a promising approach in RCC and CRC. Our preliminary studies found that ISG15 is highly upregulated in both murine RCC and CRC cell lines compared to the normal fibroblast 3T3 cell line. The expression of ISG15 is further enhanced after stimulation with IFN-β. In subcutaneous syngeneic mouse models of RCC and CRC, vaccination with a Lm-based vaccine targeting ISG15, Lm-LLO-ISG15, significantly controls primary tumor burden and extends median survival compared to control-treated animals. Our findings suggest that Lm-LLO-ISG15 can be a potential candidate for the treatment of RCC and CRC.

Effect of Propofol on BBB Integrity of iPSC-Derived Human Brain Microvascular Endothelial Cells (hBMECs)

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Enhanced fluidity of lipid membranes caused by volatile anesthetic agents at clinically relevant concentrations, including isoflurane and sevoflurane, increases the permeability of the blood-brain barrier. In endothelial cell monolayers exposed to 3% (v/v) isoflurane, permeability coefficients rose by 40% for stable isotope-labeled [13C]sucrose, while transendothelial resistance and cell viability remained unaffected. On the other hand, injectable anesthetic agents such as Propofol, the most commonly used IV general anesthetic, could have the same impact on BBB and thus contribute to a leaky barrier phenotype. This anesthetic agent has a minimal aqueous solubility and is produced as 1% w/v of oil/water emulsion. To study the potential effect of Propofol on iPSC-derived human brain microvascular endothelial cells (hBMECs), the change in the permeability of [13C] sucrose as an excellent marker was evaluated in this study. A CCK-8 assay was initially performed to determine cell viability. Subsequently, two different sets of experiments were performed to assess the permeability: I) DMSO treated vs. media treated BMECs, and II) Propofol treated vs. DMSO treated BMECs. No significant change was observed between the permeability of [13C] sucrose in the first set.

In contrast, a statistically significant difference was observed in the 2nd set of experiments between Propofol treated vs. DMSO treated BMECs (permeability coefficients respectively: 6.3e-007 and 4.7e-007), which refers to an increased leakiness of BBB in the Propofol treated group. To further investigate the effect of Propofol on BBB, tight junction proteins of the blood-brain barrier were stained with appropriate primary and secondary antibodies, and they were observed with a superresolution confocal microscope. Based on the imaging achieved from the confocal microscope and by comparing the control group with the Propofol treated group, it can be concluded that the tight junction proteins in the latter group are compromised.

A Listeria Based Vaccine Directed against CD105 In Renal Cell Carcinoma

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Renal Cell Carcinoma (RCC) is the deadliest urological cancer with an abysmal overall survival probability of 12% after metastasizing. Various factors contribute to the aggressive phenotype of RCC, the most prominent of them being related to vascularization. CD105 is a 180kDa transmembrane glycoprotein that is a co-receptor for the TGF-β signaling complex and is implicated in angiogenesis in various forms of cancers including RCC. In RCC CD105's expression is modulated on both the tumor cells and vasculature and this expression corelates with a poor prognosis. This dual enrichment also makes CD105 an antigen of high potential that can be targeted by an active vaccination platform such as Listeria monocytogenes-based vaccine.

The efficacy of a Listeria based vaccine directed against CD105 (Lm-LLO-CD105) was tested in syngeneic subcutaneous and orthotopic models of RCC utilizing murine renca cell line in male Balb/c mice. Lm-LLO CD105 significantly reduced the tumor growth in a subcutaneous model. Flow cytometry analysis further confirmed that this vaccine increased the population of polyfunctional tumor infiltrating lymphocytes and reduces the population of T-regs in the tumor microenvironment of the CD105 vaccine treatment group compared to the control vaccine group. Furthermore, we confirmed that the efficacy of Lm-LLO-CD105 is dependent on the activity of cytotoxic CD8+ T cells in an orthotopic model, we further observed that Lm-LLO-CD105 has appreciable effect on angiogenesis as observed by a reduced hemoglobin content in the CD105 vaccine treated tumors. Lastly, Lm-LLO-CD105 demonstrates an acceptable safety profile with minimal effect on wound healing process in vaccinated mice.

In conclusion, Lm-LLO-CD105 demonstrates a high therapeutic efficacy with minimal side effect and a high potential for translation into clinical settings.

Mitragynine Reverses Paclitaxel Chemotherapy-Induced Peripheral Neuropathy and Is Mediated Via Opioid Receptor Involvement

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**Mentor of Yuma Ortiz*

Chemotherapy-induced peripheral neuropathy (CIPN) is a problematic side effect in patients receiving chemotherapeutic cancer treatments. Clinical use of approved analgesic drugs often does not adequately control the pathological pain arising from CIPN and does not account for potential abuse with opioid therapeutics. Mitragyna speciosa (kratom) contains the alkaloid mitragynine, which exhibits analgesic properties. However, the underlying pharmacological mechanisms that underlie these analgesic properties are complex and not completely understood. Male and female C57bl/6 mice received 8 mg/kg intraperitoneal injections of paclitaxel, a taxane class chemotherapeutic, every other day over the course of 7 days. To confirm the development of CIPN, the von Frey assay was utilized to determine the onset mechanical allodynia, which arises when a previously non-painful stimulus is perceived as painful. Intraperitoneal mitragynine and the prototypical opioid agonist morphine both dose-relatedly reversed CIPN-induced mechanical allodynia. Effective doses (ED)50 were as follows – morphine: 7.02 (6.56 – 7.51) mg/kg, mitragynine: 109.80 (104.27 – 115.62) mg/kg. Pretreatment with the opioid antagonist naltrexone 0.032 mg/kg, intraperitoneally produced a rightward shift in both morphine and mitragynine dose-response curves. Effective doses (ED)50 were as follows – naltrexone + morphine: 27.93 (24.84 – 31.40), naltrexone + mitragynine: 245.41 (211.76 – 284.39), resulting in a 3.98 and 2.24 fold shift of dose response curves, respectively. Here we show that mitragynine reverses mechanical allodynia associated with paclitaxel CIPN in a manner likely mediated through opioid receptor activity. Mitragynine may be an effective analgesic treatment option for patients experiencing painful CIPN.

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Metformin Alleviates Oxidative Injury by the Pyruvate Dehydrogenase Complex in Primary Mouse Astrocytes Subjected to Oxygen-Glucose Deprivation

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Immediate after stroke, a rapid transition from aerobic to anaerobic metabolism in ischemic tissue causes disruption of the modulatory activity of the pyruvate dehydrogenase complex (PDHC), pyruvate dehydrogenase kinase (PDK), and pyruvate dehydrogenase phosphatase (PDP). The changes of PDHC, PDK, and PDP activity provide vital indexes to determine the severity of oxidative damage underlying ischemic injury after stroke. Emerging evidence showed that PDC-PDK-LDH axis is an important link that plays a vital role in metabolic reprogramming and brain injury. During stroke, a hypoxic and nutrient deprived condition interferes with this connection and provokes oxidative damage in the brain. Oxygen-glucose deprivation (OGD) in primary astrocytes is the recognized model for inducing ischemic injury in vitro. Previous studies have shown the regulatory effect of metformin on mouse astrocyte activation. Here we investigated the modulatory effect of metformin (100 μM) pretreatment on the PDK-PDH-LDH pathway in mouse astrocytes exposed to different time points (2 and 4 hours) of OGD and determine the expression of key proteins using the Western blot analysis. Our data shows that metformin modulates PDHC activity by upregulating the expression of PDP and downregulating the expression of PDK at 4 hr OGD. Interestingly, metformin significantly reduces the expression of LDH, a marker for increased lactic acidosis, and LDH/PDH ratio, a potential indicator for the status of ischemic brain recovery. Together these results suggest that metformin alleviates oxidative damage of primary mouse astrocytes after OGD conditions by the PDK-PDH-LDH pathway.

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Accessibility of Board-Certified Pharmacists for Patients Living in Rural Areas of Texas

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Purpose: Board-certified specialty pharmacist services improve patient care and can enhance care in rural areas. Previous reports describe geographical disparities in the general services provided by pharmacists. It is not known whether disparities exist in advanced practice roles such as comprehensive medication management. Geographic distribution of board-certified specialty pharmacists may provide insight into service accessibility. The purpose of this study is to characterize board-certified specialty pharmacists in respect to geographic location, including rural and non-rural areas of the state of Texas and relation to the demography of healthcare populations and access.

Methods: Data were collected from the Board of Pharmacy Specialties (BPS) public record database and manually cross-referenced with the Texas State Board of Pharmacy (TSBP) website. Workplace zip codes for BPS pharmacists were then evaluated with the National Healthcare Quality and Disparities Report. Descriptive statistics were utilized as appropriate.

Results: 3276 BPS pharmacists are registered in Texas, with approximately 50% being Pharmacotherapy specialists. Texas accounts for 7% of total BPS certifications in the U.S. Current TSBP records characterize 20,614 actively licensed pharmacists practicing within the state. Percentages with one or more BPS certifications will be presented in aggregate based on location and in proportion to population.

Conclusion: This study addresses a potentially significant issue regarding access to pharmacist-provided patient care and comprehensive medication management services.

Epigallocatechin-3-Gallate Inhibits Osteoclastic Differentiation and Maturation by Modulating Mitophagy and Mitochondrial Functions

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Osteoclasts (OCs) play a critical role in bone resorption and maintain homeostasis. To reduce the side effect of hormonal and some pharmaceuticals drugs, natural plant extract and their derived compounds were verified for their effectiveness in the regulation of osteoclasogenesis. In this study, we wanted to investigate the role of epigallocatechin-3-gallate (EGCG), a tea catechin in the osteoclastogenesis. We found that EGCG inhibited the OCs differentiation in RAW264.7 cells and in bone marrow-derived cells in the K/BxN serum-induced arthritis mice in a dose-dependent manner. RT-PCR studies confirmed that EGCG reduced expression of OCs differentiation markers like NFATC1, TRAP, Cathepsin K, and MMP9. DCFDA, MitoSOX, and JC-1 staining revealed that EGCG attenuated the intracellular and mitochondrial reactive oxygen species (ROS), and mitochondrial membrane potential, and Seahorse analysis corroborated the effect of EGCG. Using the confocal, western blot, and RT-PCR studies we found that the EGCG inhibited mRNA and protein expressions of mitophagy-related molecules like PINK1, PARKIN, FIS1, and DRP1. Our findings confirmed that the OCs differentiation and maturations were significantly inhibited by EGCG by modulating autophagy, specifically mitophagy using in vitro and in vivo models using Akt and P38 MAPK pathways. We also evaluated the mode of binding of EGCG with the RANK receptor by in silico analysis and found that EGCG inhibited the RANK and RANKL binding, which is essential for OC differentiation and maturation. Overall, these findings confirmed the mechanisms of bone resorption during RA and that will help in developing a new therapy using natural compounds beside the existing therapeutics.

In-Vitro and *In-Vivo* Evaluation of Metformin across the Blood-Brain Barrier

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Metformin is first-line anti-diabetic therapy. Studies from our lab and collaborators showed metformin to attenuate post-ischemic brain injury promoted by stroke through AMPK activation. Metformin is a small hydrophilic molecule that accumulates into the cells driven by membrane potential. Its potential interaction with transporters (uptake and efflux) expressed at the blood-brain barrier (BBB) and the brain pharmacokinetics parameters are unknown. First, to determine the permeability value of metformin, we used an established in-vitro co-culture model of the BBB. Next, we performed apical uptake studies in mouse brain endothelial cells using transporters-specific inhibitors and metformin's interaction with the efflux transporter, plasma glycoprotein. Furthermore, for the in-vivo study, we developed and validated LC-MS/MS method for metformin in plasma and brain matrices. We then performed intravenous administration of metformin to evaluate the brain uptake clearance (Kin) value. Our results showed that metformin is a highly permeable molecule with a permeability coefficient value of almost 10 folds higher than the high permeable threshold range. Additionally, apical uptake studies showed involvement of cationic selective uptake for the drug, in which OCT-3 and PMAT transporters played a major role in drug uptake while P-gp had no interaction with metformin. Furthermore, the high Kin value of metformin at an earlier time point compared to mannitol suggested the involvement of active transport mediated uptake for the drug in-vivo. For our future studies, we will characterize the transporters involved in metformin transport across the established in-vitro coculture model of BBB and evaluate the Kin values for metformin at more sampling time points.

Real-world Utilization of SARS-CoV-2 Antibodies in Outpatients with COVID-19 (Covid Antibodies)

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University Medical Center in Collaboration with Covenant Medical Center

Purpose: The aim of this research was to evaluate the impact of early administration of SARS-CoV-2 targeted monoclonal antibodies to patients with mild to moderate COVID-19 who are at high risk for hospitalization. Since the beginning of the Covid-19 pandemic, it has become apparent that certain patients are more likely to suffer from a more severe case of the disease than others often leading to hospitalization and sometimes death. In November of 2020, two monoclonal antibody drugs were granted emergency use authorizations (EUAs) by the FDA for the treatment of mild to moderate COVID-19 in persons who are at high risk for progressing to severe disease and/or hospitalization. These potent antispike neutralizing monoclonal antibodies include bamlanivimab (LY-CoV55) and casirivimab/imdevimab (REGN10933/REGN10987). Despite the approved EUA by the FDA, and subsequent loss of EUA by bamlanivumab, the efficacy of these antibodies has not been fully established and is still under investigation in randomized clinical trials. Herein we describe the rate of hospitalization/emergency department visits among a group of high-risk patients after administration of SARS-CoV-2 targeted monoclonal antibodies (bamlanivimab or casirivimab-imdevimab).

Methods: This was a dual center retrospective chart review, performed at University Medical Center and Covenant Medical centers, of patients who were diagnosed with mild to moderate COVID-19 who were had received bamlanivimab or casirivimab/imdevimab injections from November 23rd, 2020 to January 28, 2021. This data was compiled from Lubbock County public health records and patient outcomes were tracked for 29 days following the infusion date meaning the last date of record was February 26th 2021. Outcomes tracked included hospitalization, emergency dept visits, or death that occurred within the study period.

Results / Conclusion: Research in progress.

Impact of an Interdisciplinary Heart Failure Clinic Versus Standard Inpatient Hospital Care on Patient Outcomes

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Purpose: A previous study at a hospital in West Central Texas showed a slight increase in heart failure (HF) related hospital readmissions amongst patients managed in an interdisciplinary HF-clinic versus hospital patients with no focused HF-clinic follow-up. The study also showed an increase in all-cause readmission amongst HF-clinic patients, but the mortality rate amongst HF-clinic patients was significantly lower than patients with no HF-clinic visit. The purpose of this study is to investigate the impact the HF-clinic has had on patients' overall hospital length of stay after being readmitted for acute decompensated heart failure versus those not followed in the HF-clinic.

Methods: The hospital utilizes an electronic medical records software for all its inpatient and outpatient services. Data is being collected for HF-clinic patients from January 1, 2016 to January 1, 2021. The data collected from these patients will be reviewed from the time of admission to the HF-clinic to subsequent visits within a 12-month period. Data from a matched cohort of HF patients who received standard inpatient care but no HF-clinic referral will be reviewed in comparison. The data collected includes patient demographics, comorbidities, NYHA HF class, prior hospitalizations, emergency department visits, primary residency, pertinent labs and vitals, inpatient and discharge medications, length of stay, requirement for ICU stay, and insurance status. Data amongst both groups will be matched by age, gender, HF severity, comorbidities, and any other pertinent information.

Results / Conclusion: In progress

The Impact of a Benzodiazepine-Sparing Strategy on Alcohol Withdrawal Management

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Purpose: The objective of this study was to assess the impact of a benzodiazepine-sparing strategy on overall benzodiazepine use in alcohol withdrawal management. Commonly utilized agents in benzodiazepine-sparing strategies include clonidine, gabapentin, and dexmedetomidine. These agents are less potent than benzodiazepines individually, but literature reveals using higher doses and combinations of these agents to target multiple pathways may provide similar efficacy with less adverse events.

Methods: This is an IRB-approved retrospective, chart review of trauma and surgical patients at a large, community hospital. An electronic health record (EHR) database search was conducted to identify historic patients who received treatment for alcohol withdrawal before the implementation of a benzodiazepine-sparing protocol. A separate EHR database search was conducted to identify patients who received a benzodiazepine-sparing protocol. Patients were included if they had a Prediction of Alcohol Withdrawal Severity Scale (PAWSS) score ≥ 4 or clinical suspicion of alcohol withdrawal. Patients were excluded if they had a creatinine clearance (CrCl) < 30 ml/min or if they were incarcerated, < 18 years of age, or pregnant at the time of admission. The primary outcome is decreased overall benzodiazepine use in lorazepam equivalents in milligrams. Secondary outcomes will evaluate duration of alcohol withdrawal symptoms and adverse effects leading to protocol discontinuation.

Results: A total of 159 patients were in the control group and a total of 25 patients received a benzodiazepine-sparing strategy. Patients who received a benzodiazepine-sparing strategy required a lower overall milligram amount of benzodiazepines in lorazepam equivalents (median [IQR], 2.0 mg [0.0, 14.3] vs 10.0 mg [1.5, 27.5]). The treatment group experienced fewer days of alcohol withdrawal symptoms (median [IQR], 1.0 [0.0, 6.0] vs 5.0 [0.0, 4.0]).

Conclusion: The results of this study implicate a need for further robust trials to establish the safety and efficacy of benzodiazepine-sparing protocols.

Pharmacist Impact on Concordance with Guideline-Directed Medical Therapy for Cardiac Patients

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Purpose: While studies have shown that guideline-directed medical therapy (GDMT) reduces morbidity and mortality in patients undergoing coronary revascularization or receiving an implantable cardioverter-defibrillator, real-world compliance remains low, and many patients are not prescribed GDMT at discharge. Additionally, pharmacists involved in interdisciplinary care teams and transitions of care can improve guideline concordance and patient outcomes including length of stay and readmission rates. The purpose of this study is to evaluate the impact of pharmacist intervention to improve GDMT prescribing rates for patients presenting with cardiac conditions.

Methods: This is a retrospective cohort study of 200 adult patients admitted for a percutaneous coronary intervention, coronary artery bypass graft, or implantable cardioverter-defibrillator procedure. Patients were identified through ICD-10 codes and manual review. Patient demographics, cardiac procedure, medications at discharge, and other variables were collected through manual review of medical records for the patient's first admission or the admission in which the procedure occurred. A multivariable logistic regression model was used to assess concordance with GDMT at discharge.

Results: Data collection and analysis currently in progress.

Conclusion: The results of this study will be presented following completion of data collection and analysis.

Developing a Prediction Model for Extended-Spectrum-Beta-Lactamase-Producing Enterobacteriaceae in Admitted Patients with Urinary Tract Infection

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Purpose: The prevalence of extended-spectrum-beta-lactamase (ESBL) organsims in hospitals is increasing, including those associated with urinary tract infection (UTI). Optimal treatment strategies depend on mechanisms to accurately predict the presence of these organisms. The purpose of this study is to develop a prediction tool to aid in identifying patients at increased risk for UTI due to ESBL-produding Enterobacteriaceae at time of hospital admission. The study also characterizes treatment outcomes for ESBL versus non-ESBL infections.

Methods: This is a retrospective cohort study of 200 adult patients admitted with a diagnosis of UTI. Patients were identified through manual review. Patient demographics, culture findings, and potential risk variables were collected through manual review of electronic health records. Candidate variables were selected and evaluated using a two-step process. Each collected variable was assessed for inclusion feasibility based on the availability of data in medical records. Variables that were adequately represented in both ESBL+ and ESBL- samples were then evaluated to construct a multivariable logistic regression model.

Results: Data collection and analysis currently in progress.

Conclusion: Conclusion to be presented following the completion of data collection and analysis.

Analysis of the Effects of Therapeutic Vaccination with Tumor Vascular-Primed Dendritic Cells In a Mouse Model of Colon Cancer

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Colorectal cancer remains the third leading cause of cancer-related death in the United States despite advances in targeted therapies such as monoclonal antibodies and tyrosine kinase inhibitors. Progression of vascularized tumors, including colorectal cancer, is reliant on a functioning blood system that provides cancer cells sufficient nutrients and oxygen. This process is ultimately driven by a concerted effort of pro-angiogenic factors, namely vascular endothelial growth factors (VEGFs) and their cognate receptors – the VEGF receptors (VEGFRs). However, tumor vascularization tends to be an unregulated process that results in the overexpression of angiogenic molecules that promote the development of abnormal and chaotic blood vessels, which ultimately impede the perfusion and efficacy of small molecule drugs or immune-based approaches that incorporate cytotoxic CD8+ T cells. FDA-approved targeted agents have been developed against major angiogenic components such as VEGF and VEGFRs, but, despite short-term clinical benefits, these drugs are generally cytostatic and quickly lead to resistance in most patients. To address such shortcomings, active immunotherapeutic strategies directed at auxiliary targets within the tumor vasculature represent a potentially improved direction toward prolonging cancer protection by instituting the long-term destruction of endothelial cell and pericyte networks that provide tumors critical support. We hypothesize that therapeutic vaccination using autologous alpha-type-1 polarized dendritic cells (DCs) pulsed with endothelial cell-and pericyte-derived peptides will induce a protective and safe cytotoxic T cell response in animals. This clinically-relevant DC approach should ultimately lead to colon cancer regressions in mice and allow our group to identify immunologic-based mechanisms that contribute to lasting immunity against the disease.

Evaluation of Bleeding in Orthopedic Surgery with Perioperative Use of Selective Serotonin Reuptake Inhibitors

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Selective serotonin reuptake inhibitors (SSRIs) are the preferred first line therapy for depression because of their higher tolerability and lower toxicity, however, there are data that SSRIs block the reuptake of serotonin causing the depletion of serotonin from platelets which plays an important role in platelet aggregation. This effect is associated with an increase in bleeding, and there have been concerns that SSRI exposure during the perioperative period has the potential bleeding risk in patients undergoing surgical operations. The purpose of this study is to compare the rate of major bleeding events between patients who were on perioperative SSRIs and those not on SSRIs in orthopedic surgery.

This is a retrospective cohort study of adult subjects who were admitted to University Medical Center (UMC) in Lubbock Texas. This study included all adult patients who were admitted to UMC for orthopedic surgery including hip fracture, and total hip or knee replacement. Screening of patients' home medications was completed to evaluate patients on anticoagulants, non-steroidal anti-inflammatory drugs (NSAIDs), and antiplatelet agents including SSRIs. Patient demographics, type of surgery, comorbidities, name, and dose of SSRIs, duration of SSRIs exposure peri operation, CBC, estimated blood loss, amount of transfusion during the surgery and after surgery, use of alcohol, and HAS-BLED score will be collected.

From a total of 120 patients who underwent orthopedic surgery, subjects were matched 1:1 based on whether preoperative use of SSRIs or not. Most patients were female (67%) and white (75%), with a median age of 66 years at the time of orthopedic surgeries. Compared with those who did not receive SSRIs, patients who received SSRIs had a higher transfusion rate (30.0% vs 15.0%; P=0.0491). Patients who received transfusion were more likely to be elderly (median age of 79 years vs 66 years; P=0.0095). Additional data analysis is in progress.

An Assessment of Cardiovascular Outcomes in Hypertensive Patients through the Evaluation of the Fraction of Time Maintained within a Given Blood Pressure Range

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Background/purpose: Many recommendations exist regarding blood pressure targets to reach and maintain with patients based on a variety of factors. Despite this, there remains conflicting evidence regarding intensification of antihypertensive therapy and the associated benefit in select patient populations.1,2 The primary outcome of this study is to assess cardiovascular outcomes in hypertensive patients by analyzing the percent of time in which they are within a given blood pressure range, to evaluate if this correlates with an improvement in cardiovascular outcomes, and if so, which range this is. Cardiovascular outcomes include ischemic stroke, hemorrhagic stroke, and myocardial infarction. The secondary outcome is to assess if maintaining patients within a specific range for a given fraction of follow-up visits, as opposed to targeting a specific blood pressure target, results in decreased hospital utilization.

Methods: This is a retrospective study of hypertensive patients with or without established cardiovascular disease followed over a period of two years. Hypertension control in the outpatient setting will be assessed and any associated hospital admissions or emergency department (ED) visits. Data will be collected using Cerner Health Facts database, and ICD-10 codes will be used to obtain de-identified patient data.

Conclusions: This study may provide insight into the management of hypertension in patients that is different from the goal blood pressure range that has been targeted for years.

Potential Role Of Astrocyte Ace2 In The Neural Transmission of Covid-19 and a Neuroinflammatory State Induced by Smoking and Vaping

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Knowledge of the entry receptors responsible for SARS-CoV-2 is key to understanding the neural transmission and pathogenesis of COVID-19 characterized by a neuroinflammatory scenario. The current understanding of the brain distribution of angiotensin converting enzyme 2 (ACE2), the primary entry receptor for SARS-CoV-2, remains mixed. In this study, we systematically examined the spatial- and cell-type-specific distribution of ACE2 in mouse brains to help understand the neuropsychological manifestations in COVID-19 patients. Immunohistochemistry assays reveal ubiquitous expression but uneven brain distribution of ACE2, with high expression in the cerebral microvasculature, medulla oblongata, hypothalamus, ventricular choroid plexus, subventricular zones, and meninges around medulla oblongata and hypothalamus. Co-staining with cell type-specific markers demonstrates ACE2 is primarily expressed in astrocytes around the microvasculature, medulla oblongata, hypothalamus, subventricular zones, and subependymal zones in the rhinoceles and rostral migratory streams, radial glial progenitor cells in the lateral subventricular zones, tanycytes around the third ventricle, epithelial cells and stroma in the ventricular choroid plexus, as well as pericytes in the cerebral microvessels, but rarely detected in neurons and endothelial cells. ACE2 expression in astrocytes is further confirmed in primary cultured cells, indicating astrocytes are indeed vulnerable to SARS-CoV-2. Furthermore, we explore the effect of smoking, a risk factor related to COVID-19 severity, on the brain. The data show experimental smoking exposure increases proinflammatory and immunomodulatory cytokine IL-1a, IL-6 and IL-5 without significantly affecting ACE2 expression in the brain, suggesting a pre-conditioned neuroinflammatory and immunocompromised scenario might attribute to COVID-19 severity in the smokers. Taken together, our data highlight the potential roles of astrocyte ACE2 in neural transmission of COVID-19, choroid plexus in brain entry of SARS-CoV-2, and smoking exposure in exacerbated neuropathogenesis of the pandemic.

Development of LC-MS/MS method for the Measurement of Plasma and Brain Acetaminophen

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The blood–brain barrier (BBB) prevents the brain uptake of most pharmaceuticals. This property arises from the tight junctions between brain microvascular endothelial cells. Recent (unpublished) studies by colleagues suggest that acetaminophen (APAP) increases leakiness of the BBB by modulating the expression of tight junction proteins. The ultimate goal of the present study is to measure BBB permeability of stable isotope labeled [13C]sucrose after administration of APAP in mice. As a first step we need to ensure that APAP plasma concentrations are in a pharmacologically relevant, non-toxic range after IP administration. We developed a LC-MS/MS method on the SCIEX 5500 triple quadrupole mass spectrometer for APAP quantitation in plasma and brain samples. The analytes and internal standard, APAP deuterated analog Acetaminophen-d4, were separated on a C18 column, using gradient elution of mobile phase containing 0.1% Formic Acid in water and Methanol, at a flow rate of 0.35 mL/min. Analysis was carried out within 4 min. APAP and the internal standard eluted at a retention time of ?1.4 min. Standard curves were linear over the concentration range of 5–1000 ng/mL for plasma and 1.56-400 ng/mL for brain. Matrix effect, recovery, accuracy and precision have been investigated for the analyte and internal standard in neat solvent and post-extraction matrix from plasma and brain. Both plasma and brain values were within the limits of Food and Drug Administration (FDA) guidelines for the method validation. The LC-MS/MS method for determination of APAP in plasma and brain will allow to correlate APAP plasma and brain concentrations to BBB permeability, as measured by brain uptake of [13C]sucrose using our established protocol, . We will also use high resolution confocal imaging of tight junctions to investigate whether structural changes of cell membranes at clinical APAP concentrations can be detected.

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