TTU HSC

THIRD ANNUAL

ABILENE RESEARCH SYMPOSIUM

FRIDAY, OCTOBER 30

9:45AM-2:15PM

AGENDA

9:45 AM
10:00 AM

OPENING REMARKS ..... SANJAY K. SRIVASTAVA, PH.D.

Distinguished Professor + Chair
DEPARTMENT OF IMMUNOTHERAPEUTICS AND BIOTECHNOLOGY
Texas Tech University Health Sciences Center | Abilene, Texas

LORI RICE-SPEARMAN, PH.D.
President | *Texas Tech University Health Sciences Center*

10:00 AM
11:00 AM

KEYNOTE SPEAKER ..... ANNA KRICHEVSKY, PH.D.

Associate Professor, DEPARTMENT OF NEUROLOGY
Harvard Medical School | Boston, Massachusettes
"Expanding the Repertoire of Therapeutic Targets for Brain Tumors: the Focus on Non-coding RNA"

11:00 AM
11:30 AM

DISTINGUISHED SPEAKER ..... RUSTY KRUZELOCK, PH.D.

Vice President of Research
Abilene Christian University | Abilene, Texas
"Development of a Diagnostic Toolset that Supports a Combined Antibiotics – Biologics Treatment for Inflammatory Bowel Disease"

11:30 AM
12:00 PM

DISTINGUISHED SPEAKER ..... DIANNA WILLIS, PH.D.

Associate Director, BURKE NEUROLOGICAL INSTITUTE
Weill Cornell Medicine | White Plains, New York
"Development of non-opioid drugs for the treatment of chemotherapy-induced peripheral neuropathy"

12:00 PM
12:30 PM

DISTINGUISHED SPEAKER ..... DIPONGKOR SAHA, PH.D.

Assistant Professor, DEPARTMENT OF IMMUNOTHERAPEUTICS AND BIOTECHNOLOGY
Texas Tech University Health Sciences Center | Abilene, Texas
"Temozolomide antagonizes oncolytic immunovirotherapy in glioblastoma"

12:30 PM
1:00 PM

DISTINGUISHED SPEAKER ..... EMILY BAILEY, PH.D.

Assistant Professor, DEPARTMENT OF PUBLIC HEALTH
Texas Tech University Health Sciences Center | Abilene, Texas
"SARS-CoV-2 in Student Athletes: The Conflict of Asymptomatic Cases"

1:00 PM
2:00 PM

LIVE POSTER PRESENTATIONS ..... STUDENTS

Abilene Christian University
Cisco College
Hardin Simmons University
McMurry University
Texas Tech University Health Sciences Center
(Jerry H. Hodge School of Pharmacy, School of Nursing, Public Health Program)

2:00 PM
2:15 PM

CLOSING REMARKS ..... PEARL MERRITT, PH.D.

Regional Dean-Abilene, SCHOOL OF NURSING
Texas Tech University Health Sciences Center | Abilene, Texas

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Director, COMMUNITY OUTREACH, ABILENE

KEYNOTE SPEAKER

ANNA KRICHEVSKY, PH.D.
Associate Professor
DEPARTMENT OF NEUROLOGY
Harvard Medical School
Boston, Massachusettes

Anna Krichevsky, Ph.D., is an associate professor of Neurology/Neurobiology at Brigham and Women's Hospital and Harvard Medical School, Boston, USA. She received her M.Sc. and Ph.D. degrees from the Hebrew University of Jerusalem, Israel, and completed postdoctoral training at Harvard Medical School in Boston.

As a postdoctoral fellow, Krichevsky isolated neuronal RNA granules and pioneered the work that led to the recognition of microRNA (miRNA) functions and RNA interference mechanisms in brain physiology and pathology. She performed the first successful RNA interference in mammalian neurons, contributed to the identification of miRNAs in the mammalian brain, developed the first high-throughput arrays for miRNA expression profiling, and discovered one of the first oncogenic miRNA, miR-21, that is currently a promising target for various human diseases.

Krichevsky's laboratory identified and studied key miRNAs involved in brain tumors and neurodegenerative disorders such as Alzheimer's disease. Her laboratory also pioneered the identification of miRNA biomarkers for diagnostics and monitoring of primary and metastatic brain tumors. Krichevsky's innovative research, featured in HMS Focus, NIH, Reuters Science News, Health Canal and The Boston Globe, is geared towards RNA medicine and based on multiples collaborations. She also serves on the Executive Committee of the HMS Initiative for RNA Medicine, established to translate RNA research to clinical practice.

DISTINGUISHED SPEAKERS

RUSSELL KRUZELOCK, PH.D.
Vice President of Research
Abilene Christian University
Abilene, Texas

Russell "Rusty" Kruzelock, Ph.D., has a 25-year track record in research and technology business development. At Virginia Tech University, Kruzelock's laboratory developed high-throughput methods for identifying important genes that influence disease susceptibility including an internationally recognized bead-based liquid microarray technology.

Shortly after the anthrax attacks of 2001, the increased awareness of a biological attack dictated that the Air Force take stronger actions to protect our personnel, both overseas and at home. Kruzelock helped conceptualize the Epidemic Outbreak Surveillance (EOS) program, which provided the framework for the development of a model biodefense system that reduced the loss of personnel, resources and time secondary to an outbreak or release of an infectious agent. In 2002, the Air Force offered Kruzelock a new role as director of the Advanced Diagnostics Research Laboratories for the United States Air Force Office of the Surgeon General and Advanced Diagnostics team leader for the Air Force EOS Program developing advanced molecular diagnostics for 100s of diseases including avian flu, SARS and Ebola.

In 2004, Kruzelock headed the PharmacoGenomics Department for the University of Texas's Institute for Drug Development developing predictive biomarkers for cancer drug response. Kruzelock helped the Institute for Drug Development grow into one of the largest Phase I oncology clinical trial programs in the United States which was highlighted by the successful sale of Ilex Oncology to Genzyme for $1 billion.

In 2007, Kruzelock was again recruited by the Department of Defense to help form three Government think tanks evaluating technologies and recommending investment strategies for the Department of Defense. He formed a company, Cenovance, which met an urgent Department of Defense need for independent and objective analysis of technologies that have potential engagement value to US and Coalition partners. He also co-founded and served as chief science officer of a molecular diagnostics company in Austin, Texas.

In 2013, Kruzelock joined the West Virginia Regional Technology Park as the executive director and chief executive officer. During his six-year tenure, the Tech Park grew 92% making it one of the fastest growing Research Parks in the United States. While at the Tech Park, Kruzelock designed a strategy to remediate hazardous metals from coal ash and separate strategically important rare earth elements from the mix. This process was validated by the Department of Energy's Critical Materials Institute who is now partnering with WV-based Pinzon Metals to develop a completely United States sourced rare earth metals supply chain.

In September 2020, Kruzelock joined Abilene Christian University as their first vice president of Research.

DISTINGUISHED SPEAKERS

DIANNA WILLIS, PH.D.
Associate Director
BURKE NEUROLOGICAL INSTITUTE
Weill Cornell Medicine
White Plains, New York

Dianna E. Willis, Ph.D., is the head of the Laboratory for Axonal and RNA Biology, director of the Center for Pain Research and associate director at the Burke Neurological Institute, an assistant professor of Neuroscience at Weill Cornell Medicine and director of the Burke-Blythedale Program in Pediatric Clinic Neuroscience. Willis received her undergraduate degree in Biology from the University of Pittsburgh in 1994 and her Ph.D. in Molecular Biology and Genetics from the University of Delaware in 2002. Her postdoctoral training at Nemours Biomedical Research at the Alfred I. duPont Hospital for Children from 2002 – 2007 focused on the newly emerging understanding of local translation in neuronal axons. After completing a visiting scientist position in the Department of Molecular and Cellular Neurobiology at Vrije Universiteit in the Netherlands in 2007, she returned to Nemours as an assistant research scientist in the Center for Translational Neurobiology. In 2010, Willis was recruited to be the director of the Center for Pain Research at the Burke Neurological Institute. Her research has focused on understanding how aberrant axonal translation may lead to maladaptive plasticity as is evident in neuropathic pain and neuropathy. In 2016, she was named associate director of the Burke Neurological Institute, and in 2018, Willis became director of the Burke-Blythedale Program in Pediatric Clinical Neuroscience.

DIPONGKOR SAHA, PH.D.
Assistant Professor
DEPARTMENT OF IMMUNOTHERAPEUTICS
AND BIOTECHNOLOGY
Texas Tech University Health Sciences Center
Abilene, Texas

Dipongkor Saha, Ph.D., is an assistant professor for the Department of Immunotherapeutics and Biotechnology in the Jerry H. Hodge School of Pharmacy at Texas Tech University Health Sciences Center. Saha's lab focuses on studying oncolytic viruses and their application in cancer therapy. More specifically, they study oncolytic virus resistance mechanisms, virus-mediated in situ vaccine effects to break tumor immune tolerance, and different combination immunovirotherapeutic approaches to improve the therapeutic outcome for glioblastoma. Recently, they have expanded our virus-based immunotherapeutic strategies to treat breast cancer.

DISTINGUISHED SPEAKERS

EMILY BAILEY, PH.D.
Assistant Professor
DEPARTMENT OF PUBLIC HEALTH
Texas Tech University Health Sciences Center
Abilene, Texas

Emily Bailey, Ph.D., is an assistant professor for the Department of Public Health in the Graduate School of Biomedical Sciences at Texas Tech University Health Sciences Center in Abilene, Texas. Bailey completed her Ph.D. in environmental science and engineering at the University of North Carolina at Chapel Hill in the Gillings School of Global Public Health. She then spent two years as a postdoctoral research associate at the Duke Global Health Institute. She has research interests and experience in emerging infectious disease, zoonotic disease, and viral pathogens. Bailey has considerable laboratory experience, specifically in microbiology and molecular diagnostics.

ACKNOWLEDGEMENTS

We would like to acknowledge the following symposium sponsor:

Laura W. Bush Institute for Women's Health

Thank you to the following college and universities for their participation in this symposium:

Abilene Christian University
Cisco College
Hardin-Simmons University
McMurry University
TTUHSC Abilene, School of Nursing
TTUHSC Abilene, Master of Public Health

ABSTRACTS

UTILIZATION OF FLUORESCENT MEDICAL MARKING TO IMPROVE PATCH TESTING METHODOLOGY

Layan Al-Sukhni, BS, BA, MS3; Ganesh Maniam, BA, MBA, MS4; Dr. Jack Waller, MD; Dr. Scott D Miller, MD
DEPARTMENT OF INTERNAL MEDICINE, TTUHSC SCHOOL OF MEDICINE AT AMARILLO

Background: Patients have often expressed frustrations with the number of return visits needed to identify and confirm allergic reactions, especially in rural settings when patients often live many hours away from the clinic. A novel approach to denoting the location of the patch test panel notches, using a highlighter (or any other fluorescent medical marker) rather than a medical marking pen, may be useful in reducing the number of scheduled visits while minimally sacrificing any specificity and sensitivity of the test; indeed this approach may even improve test accuracy and thereby promote patient safety through reducing missed diagnoses.
Objective: This purpose of this article is to improve patch testing methodology in diagnosing contact allergies, as international guidelines continue to reference studies that were published prior to the invention of fluorescent markers.
Methods: This clinical pearl was written after years of successful utilization of fluorescent markers in diagnosing contact allergies via patch testing.
Results:
Challenge: Patch testing is the gold standard diagnostic tool for contact allergies. However, given that some allergens are considered late reactors in that they become positive at day 7 or even later, the fading of the medical marking ink can cause additional difficulties in locating the exact matchup of Finn chamber map cards, which may decrease accuracy of patch test interpretations. Additionally, the number of scheduled appointments required to accurately read a patch test is frequently a point of frustration for patients – especially those with limited mobility or who live far away from their closest dermatology clinic, such as in rural settings. International patch testing guidelines released as recently as 2015 continue to reference the original 1966 guidelines in their recommendations, but these references predate the invention of fluorescent markers, which were first manufactured by Dennison Company in 1978.
Solution: Fluorescence persists for weeks with Wood's lamp examination even under normal bathing conditions. The use of fluorescent medical marking (highlighters) would increase test accuracy in the interpretation of test readings for late allergen reactions, thereby minimizing lost results due to unintended mapping failures. Additionally, in situations for which patients would be better served by less frequent visits to their provider for patch test readings, it may be beneficial to consider using a fluorescent highlighter in marking the location of the patch testing panels. The use of fluorescent medical marking tools is an improvement in patch testing procedures, especially in situations of reading late allergen reactions or minimizing patient visits.
Limitations: Clinical pearls, such as this article, represent the domain of experienced-based medicine rather than evidenced-based medicine.
Conclusion: Utilization of fluorescent markers with Wood's lamp examination serves to improve procedure on patch testing thereby increasing test accuracy and promoting patient surgery by minimizing lost results due to mapping failures, along with an additional benefit of reducing patient return visits.

EVALUATING THE INDEPENDENT IMPACT OF SOCIAL MEDIA ON SLEEP QUALITY

Hannah Booher, PA-S, Ian Patterson, PA-S, & Brittany Pigott, PA-S
HSU PA PROGRAM

With social media use on the rise, it is vital to confirm that social media can be a cause of significant sleep problems in young adults. We hypothesized that a review of current literature on sleep disturbances related to social media use in young adults would reveal that at least some sleep disturbances are caused by social media itself, and not just the confounding variable of screen time that accompanies social media use. Our meta-analyses found that social media screen time causes more sleep disturbance than an equivocal amount of screen time in mixed forms in adolescents/young adults aged 10-32.

The overall odds ratio for 2-5 hours of social media time per day to cause sleep disturbance was 1.435, while the overall odds ratio for 2-5 hours of mixed screen time per day to cause sleep disturbance was 1.247, revealing a significantly higher likelihood for social media screen time to cause sleep disturbance than mixed screen time.

MALTOSE BINDING PROTEIN FUSED TO MEMBRANE PROTEINS AS A BIOCHEMICAL TOOL FOR STRUCTURE DETERMINATION.

Stephanie Boston and Luis G. Cuello
CENTER FOR MEMBRANE PROTEIN RESEARCH. CELL PHYSIOLOGY AND MOLECULAR BIOPHYSICS DEPARTMENT. TTUHSC. LUBBOCK TX.

The structure determination of membrane proteins, whether by crystallography or Cryo-Electron Microscopy, often requires the use of antibody fragments that can provide crystallizable macromolecular complexes (target protein and the antibody fragment complex) or increase their sizes to reach the minimum limit in size and rigidity required to solve their structure by single particle reconstruction and Cryo-EM methods. A relatively new methodological strategy to increase the crystallizable surface of a "protein target" or to increase its size to make it suitable for Cryo-EM structural determination is based on the generation of a fusion construct between the "protein target" and the maltose binding protein (MBP). This strategy has been very successful in the structural determination of several soluble proteins but has failed so far in assisting the crystallization of membrane proteins, presumably due to the inherent flexibility of the MBP. A way to circumvent these limitations is to generate synthetic antibodies to 1) rigidize the structure of the MBP attached to the "target protein" and 2) increase the crystallizable surfaces of the protein of interest for X-ray crystallography methods and/or increase the size for Cryo-EM structural determination. In here we are presenting a biochemical procedure to express synthetic antibody fragments (sAB) directed to either the closed or open conformation of MBP in the cytoplasm of E. coli and a strategy for their purification to homogeneity for crystallization purposes. As a proof of concept we have tested one of this antibody fragment to and bound it to a MBP-ion channel fusion protein for structural determination purposes. *Support: NIH 2R01GM097159-06, Welch Foundation BI-1949*

A BACKDOOR STRATEGY FOR THE FUNCTIONAL AND STRUCTURAL CHARACTERIZATION OF THE HERG CHANNEL AND ITS ROLE IN DRUG INDUCED CARDIAC ARRYTHMIA.

Victoria A. Cuello, D. Marien Cortes and Luis G. Cuello
CENTER FOR MEMBRANE PROTEIN RESEARCH. CELL PHYSIOLOGY AND MOLECULAR BIOPHYSICS DEPARTMENT. TTUHSC. LUBBOCK TX.

Presently, it is well known that inherited mutations in the HERG gene cause long QT syndrome (LQTS), a rare pathological condition that produces severe cardiac arrhythmias1. Likewise, the blockade of the hERG channel by structurally diverse drugs also leads to acquired (or induced) LQTS, which results in a high propensity for sudden death due to ventricular arrhythmias (drug-induced arrhythmias, DIA). The promiscuous nature of the hERG drug block have tantalized scientist for many years and it is an aspect of human cardiac physiology that must be answer, since newer and safer therapeutic drugs are greatly needed. To provide a mechanistic explanation to this distinct hERG functional behavior, a high-resolution crystal structure of its pore domain is urgently required. A recent hERG's Cryo-EM structure at 3.8 Å has provided us with high-quality structural information about the channel 3D-architecture. However, it failed to provide reliable structural information about the channel's inner cavity in the apo and drug-bound states due to two perplexing results: 1) the existence of a strong electron-density at the center of the channel's cavity even in the apo form, and 2) the asymmetric binding of drug molecules to the channel's cavity that impedes unambiguous docking of the drug molecule. We submit that to overcome these limitations, the crystal structure of the pore domain of the hERG channel can be cloned as a fusion protein with Maltose Binding Protein (MBP), which it can increase its protein expression level and promote the correct folding

state of the pore domain. We have cloned the hERG pore domain and expressed as an MBP fusion protein and shown that the pore retains all the functional hallmarks of the full-length channel. Although the pore domain is fully functional its apparent affinity for blockers is very low, a result that is compatible with the idea that the affinity for blockers is low when the hERG channel activation gate is closed. For this reason, two different approaches were implemented in parallel to generate a hERG pore domain with its activation gate hold open. First, we engineered cysteine pairs between different positions within the activation gate that apparently should yielded open and second, a Proline mutation at the position I663 that presumably kinks open the pore lining transmembrane segment (S6) can also generate an open channel. The channel mutants (either the double cysteine or the proline mutants) can be expressed in large quantities and currently their drug blockade affinity is beinsg addressed.

Support: NIH 2R01GM097159-06, Welch Foundation BI-1949

A STUDY OF THE ENVIRONMENT OF PHYSICIAN ASSISTANT STUDENTS AND ITS POSITIVE AND NEGATIVE EFFECTS ON STRESS OUTCOMES

Kelsey Dowdall

HARDIN-SIMMONS UNIVERSITY PHYSICIAN ASSISTANT PROGRAM

The curriculum and demanding nature of Physician Assistant (PA) programs serves as one of the most discouraging factors that shape an individual's decision when considering a post-baccalaureate education. These variables not only deter individuals from these programs, but they also negatively affect academic performance and stress levels once enrolled in a PA program. Our research sought to identify and mitigate various modifiable stressors that may affect an individual's experience while in PA school, outside of the inalterable variables, such as curriculum and program requirements. By utilizing a cross-sectional quantitative analysis, administered through SurveyGizmo, we sought to identify specific positive and negative factors that contributed to individual levels of stress. The positive factors found to decrease stress levels included living near family members, having a relationship with a significant other, and practicing religious beliefs. The negative factors found to increase stress levels included increasing age, having children at home, unhappiness with didactic academic performance, and inability to balance coursework with personal life. Based on these findings, a correlation can be made between certain modifiable factors and their positive and negative effects on stress. Through these findings, faculty can ensure essential strides are taken to alleviate some of the burden these negative stressors impose on students, or in the very least, provide students with the proper tools and resources needed to succeed in their PA education.

INCREASING DERMATOLOGICAL HEALTH LITERACY IN UNDERSERVED POPULATIONS THROUGH QUICK RESPONSE (QR) CODES FOR PATIENT EDUCATION

Ganesh Maniam[1], BA, MBA; Brooke Walterscheid[1], BS, MBA; Christine P. Lin[1], BA; Jonathan Aldrete[1], BA; Dr. Jay Truitt[2], MD, PhD, PharmD, MPH; Dr. Michelle Tarbox[2], MD

[1] TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER, SCHOOL OF MEDICINE

[2] TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER, DEPARTMENT OF DERMATOLOGY

This quality improvement project utilizes QR codes to increase patient access to educational materials. The pre-implementation survey revealed that department physicians find educational materials (handouts or brochures) helpful for both physicians (87.5%) and patients (100%). However, most physicians anticipate that patients retain these paper materials for less than a day before they are lost or forgotten (62.5%). Most respondents believe that patient access to educational materials would increase by implementing internet-based solutions to allow continued online access to English PDFs (75%), Spanish PDF translations (62.5%), and large-text PDFs for the visually impaired (75%). Sixteen existing paper educational materials were digitized, uploaded, and linked to QR codes; the same was done after Spanish translations and large-text conversions. Laminated code sheets

were created and placed in clinic rooms with instructions on their use. A review of published literature indicates that QR codes are generally well-received, but few projects utilize QR codes for patient education. A family medicine clinic used QR codes to connect patients to information about medications and equipment, while an orthopedics department placed QR code stickers onto casts that linked to the healthcare team website. Our project is particularly unique given its goal of increasing access for Spanish-only patients and the visually impaired, and such innovative solutions may be helpful to bridge the health gap in underserved populations. After 6 months, providers will be surveyed regarding perceived improvements in patient access to educational information and the overall role of QR codes in the clinic.

RETROSPECTIVE REVIEW: CONVALESCENT PLASMA & DEXAMETHASONE MAY BE EFFECTIVE IN TREATMENT OF ACUTE RESPIRATORY DISTRESS SYNDROME SECONDARY TO COVID-19

Ganesh Maniam[1], BA, MBA; Jonathan Young[1], PhD; Stacy Philip[1], BS, MBA; Bella Kalayilparampil[1], BA; Jim Tseng[1], MD; Rishi Pahuja1, PharmD; Jerry Vettenthadathil[1], PharmD, MBA, MSHS; Angela Purvines[1], PharmD; Thien Vo[1], MD; Manish Patel[1], MD; Mark Sigler[1], MD; Tarek Naguib[1], MD

[1] TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

Objectives: The outbreak of COVID-19 disease due to novel coronavirus (SARS-CoV-2), leading to severe acute respiratory distress syndrome (ARDS), was first documented in late December 2019 in Wuhan, China. Following this, international spread occurred rapidly. Preliminary data has been released and multiple studies are ongoing, including the SOLIDARITY and RECOVERY trials, concerning potential treatment regimens for COVID-19. However, there is currently insufficient evidence to declare a general first line treatment regimen for COVID-19. This retrospective analysis may suggest treatments that warrant further study or provide supporting evidence for management evaluated in other trials. In this study, we will describe our initial institutional practices and outcomes, focusing on mortality and length of stay data.

Methods: In this retrospective chart review, patients who were admitted to our institution between March 14, 2020 and June 9, 2020 with a laboratory-confirmed COVID-19 diagnosis were analyzed for treatments administered and clinical outcomes including in-hospital mortality, intensive care unit (ICU) length of stay and hospital length of stay.

Results: Our study did not find statistical significance in mortality with the utilization of convalescent plasma, remdesivir, hydroxychloroquine, tocilizumab, lopinavir/ritonavir, or dexamethasone ($p>0.05$). Our study demonstrated significant increases for length of stay in the hospital setting for convalescent plasma ($p < 0.05$), remdesivir ($p < 0.05$), tocilizumab ($p<0.05$), and dexamethasone ($p<0.05$) but not for hydroxychloroquine or lopinavir/ritonavir ($p>0.05$); these findings did not demonstrate significant differences for length of stay in the ICU setting for convalescent plasma, remdesivir, hydroxychloroquine, tocilizumab, lopinavir/ritonavir, or dexamethasone ($p>0.05$ for all treatment groups and effects on ICU LOS). Overall ($n = 213$), this study had 55 patients with ARDS and 22 patients died due to ARDS. However, when compared to supportive care in ARDS mortality (50%), there was improvement with convalescent plasma (32%) and dexamethasone (33%).

Conclusions: The limitations of this study include small sample sizes across treatment groups which may lead to weaker statistical power, utilization of mSOFA in propensity matching which is limited by the unknown nature of this pandemic and isolated respiratory symptoms in COVID-19 disease, and utilization of LOS as secondary outcomes of this study leading to significant differences but does not account for severity of disease. Although our study suggests potential benefit in patients with severe COVID-19 treated with convalescent plasma or dexamethasone, further data in prospective, randomized trials is necessary to effectively guide decision-making.

ABSTRACTS

BIOTECHNOLOGY IN PSYCHIATRY: TRANSCRANIAL MAGNETIC STIMULATION (TMS) TREATMENT OUTCOMES FOR MAJOR DEPRESSIVE DISORDER (MDD) AND ASSESSMENT OF GENDER DIFFERENCES

Parsa Azam[1]; Trisha Modi[2]; Ganesh Maniam[3]; Cinthya Vigil[4]; Amy Stark, MD[5]

[1] UNIVERSITY OF TEXAS HEALTH SCIENCES CENTER, TEXAS COLLEGE OF OSTEOPATHIC MEDICINE, FORT WORTH, TX

[2] TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER, SCHOOL OF MEDICINE, LUBBOCK, TX

[3] TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER, SCHOOL OF MEDICINE, AMARILLO, TX

Background: Transcranial Magnetic Stimulation is an FDA-approved treatment option for patients with treatment refractory major depressive disorder and obsessive compulsive disorder. Previous studies have suggested that there are significant differences in treatment outcomes for MDD based on gender1. The objective of this study was to determine if this difference was reproduced in the patient population of a new TMS clinic.

Methods: A retrospective analysis of recent cases of patients ages 28 to 72 who underwent treatment with TMS for refractory major depressive disorder in 2019. The Beck's Depression Inventory-II (BDI-II) was used to gauge symptom severity at the initiation and completion of treatment, and the differences between the BDI-II for each patient was used to calculate the change in BDI-II as the primary outcome measure. The BDI-II changes divided by patient sex, and the averages of each group were analyzed using the two-sample T-test. A secondary analysis was performed after separating the female cohort into premenopausal up to age 50 and postmenopausal groups.

Results: Of the 22 individuals in the study, 16 were female and 6 were male. The statistical analysis of treatment outcomes revealed no significant differences in BDI-II changes between females versus male patients, even when separating the female cohort into premenopausal (n=3) and postmenopausal groups (n=13); $p > 0.05$, two-tailed test.

Conclusions: Conclusions are limited due to sample size. The results of this preliminary analysis found no evidence of significant differences between female and male patients in the treatment of MDD using TMS, even when taking menopausal status into consideration. Caveats to this study include a small sample size with a particularly small sampling of male patients, lack of control for additional therapies or medications, and a possible selection bias for insurance status. Additionally, these findings represent a single institutional experience in the utilization of TMS in the treatment of MDD amongst a diverse patient population.

TREGS, TGF-B, AND TRANSPLANTS: HOW SERTOLI CELLS PREVENT ACUTE GRAFT REJECTION

Taylor Hibler

TTUHSC DEPARTMENT IMMUNOLOGY AND MOLECULAR MICROBIOLOGY

The current treatment for Type I Diabetes, insulin replacement, has limited success as it is difficult to achieve glucose homeostasis and is increasingly expensive. A promising alternative treatment is islet transplantation. Transplanted human islets can successfully produce insulin in response to elevated blood glucose, allowing 60% of recipients to produce their own insulin for upwards of four years. However, this procedure requires harsh immunosuppressive drugs that can inhibit insulin production and result in infections and cancers; and even with these drugs, the 85% require exogenous insulin at five years post-transplantation. Thus, an alternative is needed for the immunosuppressive drugs used in islet transplantation. Our lab focuses on improving islet transplant survival by co-grafting them with Sertoli cells (SC), an immune protective cell type found in the testes. When co-transplanted with islets, 59% of grafts survived upwards of 100 days with no immunosuppressive drugs. Thus, understanding the mechanism by which SC protect co-transplant islets will lead to increased graft survival. Previously, it has been shown that Tregs (T regulatory cells) play an important role in allotransplant survival. Analysis of the Treg population in our SC grafts via flow cytometry and immunohistochemistry revealed the presence of both CD4+ and CD8+ Tregs in surviving SC grafts in the first 14 days. Rejecting control grafts

had only CD4+ Tregs that appeared after 14 days, suggesting they were present only to suppress the inflammatory immune response after rejection was complete. CD8+ Tregs have been poorly represented in the literature, but newer studies have begun to suggest they are a potent protective cell in transplantation. Further data from our lab shows that when Tregs are depleted in vivo via anti-CD25 monoclonal antibodies, grafts without SC rejected 100% within 20 days. Interestingly, 57% of SC grafts in Treg depleted mice survived. Flow cytometry revealed that 100% of surviving SC grafts had Tregs, indicating that SC are able to induce Tregs from naïve T cells, and that they are critical for SC graft survival. Given the importance in allograft survival and Treg induction, TGF-β (tumor growth factor beta) was selected for additional study. Immunohistochemical analysis of SC grafts revealed activation of pSMAD2 (part of a TGF- β activation pathway associated with Treg induction) at early time points in surviving SC allografts. To examine the role of TGF- β in vivo, BALB/c SC were transplanted into SMAD2/3 floxed mice (SMAD2/3 is a downstream indicator of active TGF-β) and control mice. 100% graft rejection was seen in SAMD2/3 floxed mice, while 100% survival was seen in control mice. Combined, our data demonstrate that SC can promote graft survival in a TGF-β dependent manner and through induction of Tregs. Further study of the mechanism of SC protection will improve graft survival and quality of life for patients

PHARMACISTS AND NATIONAL INSTITUTES OF HEALTH R03 AND R21 FUNDING AT UNITED STATES SCHOOLS OF PHARMACY

Princy John, PharmD Candidate, MSc, MBA

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TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER, JERRY H. HODGE SCHOOL OF PHARMACY

Purpose: The National Institutes of Health (NIH) provides more than $40 billion in grants to support biomedical research each year. R03 and R21 grants are often considered an intermediate step to R01 funding. Receiving an NIH R03 or R21 grant as the lead principal investigator (PI) is recognized by most United States (US) Schools of Pharmacy (SOP) as a major step towards independence and is viewed favorably by most US SOP during promotion and/or tenure review. To our knowledge, no one has described how often pharmacists are lead PIs on funded NIH R03 or R21 grant awards. The purpose of this study was to determine the frequency of pharmacists receiving NIH R03 or R21 funding within US SOP from 2015-2019.

Methods: The NIH Research Portfolio Online Reporting Tools Expenditures and Results (RePORTER) website was used to retrieve R03 and R21 grants awarded from all NIH institutes and centers to lead PIs affiliated with US SOP for fiscal years (FY) 2015-2019. The results of these searches included the grant title, names of the lead and other PIs, the institutional affiliation of the lead PI with associated geographic characteristics, the fiscal years funding was received, the amount of costs per fiscal year, and the institute or center that awarded the grant. As this data is publicly available information, approval from the Institutional Review Board (IRB) was not required. Professional degrees obtained for the PIs included Doctor of Philosophy (PhD), Doctor of Medicine (MD), pharmacy (Bachelor of Science in Pharmacy or PharmD), and Master of Public Health (MPH). MD and pharmacy degrees obtained outside of the US were excluded.

This data was primarily acquired from the PI's institutional faculty profile, however, additional sources included LinkedIn profiles, personal lab websites, and news or institutional articles written about the recipient. Multiple funding years for the same project and funding for equipment and diversity supplements were excluded to identify the total number of unique projects in their first year of funding. All data were analyzed using Stata version 15.1 (StataCorp LLC, College Station, Texas).

Results: There were 50 new R03 grants and 218 new R21 grants awarded to a total of 230 lead PIs associated with US SOP for FY 2015-2019. The vast majority (n=201) of lead PIs had only a PhD degree (87%) and 8 had only a PharmD degree (3.5%). There were 23 pharmacists total, of which

14 also had a PhD degree (61%). Other degrees included PhD/MPH (n=4), MD only (n=1) and MD/PhD (n=1). Four lead PIs were pharmacists with MPH degrees, three of these also had a PhD as a third degree. There were 254 projects with lead PIs who had a PhD with or without another degree (95%). The number of grants awarded based on degree type was similar across all five years. The mean total cost for the first year of new awards was $182,896 for pharmacists and $185,868 for non-pharmacist PIs (p=0.82). The Agency for Healthcare Research and Quality (AHRQ) (21%) most frequently funded pharmacists followed by the National Institute of Allergy and Infectious Diseases (NIAID) (14%) and the National Institute of Aging (NIA) (14%). The NIAID (24%), the National Cancer Institute (NCI) (16%), the NIA (10%), and the National Institute on Drug Abuse (NIDA) (10%) were the most frequently funded work by non-pharmacists. Conclusion: Pharmacists are underrepresented as lead PIs for NIH funded R03 and R21 grants to US SOP. From 2015-2019, pharmacists represented 52% of faculty in US SOP but only 10% of new NIH funded R03 and R21 grants. The vast majority of NIH R03 and R21 grant recipients had at least a PhD degree and approximately three-fifths of funded pharmacists also had a PhD degree. Based on these results, pharmacy-related topics important to public health may be less likely to be funded, which may negatively affect patients' health. US SOP may need to increase clinical and translational PhD training programs for pharmacists to increase pharmacist competitiveness for NIH funding.

HICKAM'S DICTUM VS. OCCAM'S RAZOR IN DIAGNOSING SUBACUTE BACTERIAL INFECTIVE ENDOCARDITIS

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Introduction: Early detection of infective endocarditis (IE) is imperative for improving morbidity and mortality. IE, originating from bacterial infection of prosthetic heart valves, intravenous drug use, or immunosuppression, can prove fatal, with the production of septic emboli and end-organ damage. This case report elucidates the severe, yet subtle, presentation of subacute bacterial IE.

Case: A 56-year-old male presented with acute cerebrovascular accident; labs revealed vitamin B12 deficiency and pancytopenia. The patient was discharged, but returned with progressive dysphagia and significant weight loss. Labs indicated a worsening pancytopenia, acute kidney injury, and hypocomplementemia. Upon discharge after this encounter, he was readmitted for respiratory symptoms and tested positive for influenza A. He met sepsis criteria and blood cultures grew Enterococcus faecalis. Physical exam revealed a new diastolic murmur and widened pulse pressure. Transesophageal echocardiogram revealed IE with aortic valve perforation.

Discussion: This patient presented with several systemic signs and symptoms of IE including ischemic stroke, acute kidney injury, dysphagia, weight loss, vitamin deficiencies, and cutaneous lesions. Each diagnosis was managed separately with every hospitalization, without consideration for one etiology. Using Hickam's dictum to separately explain this patient's presentation, rather than utilizing Occam's razor to identify one encompassing diagnosis, led to delays in proper management.

Conclusion: IE can be difficult to diagnose due to various subtleties in the clinical picture that are patient-specific. Blood cultures should be part of pancytopenia workup without identifiable cause. In diagnostic uncertainty, clinicians should attempt to connect all clinical manifestations under a single encompassing diagnosis.

MOXIDECTIN, A NOVEL THERAPEUTIC CANDIDATE FOR PEDIATRIC MEDULLOBLASTOMA

Itishree Kaushik and Sanjay K. Srivastava

Medulloblastoma (MB) is one of the most malignant and common brain tumors in children.

It has a profound impact on the morbidity and mortality of these patients. Sonic hedgehog (Shh) activated subgroup of MB is considered to be highly aggressive and metastatic in nature. Shh-MB is characterized by mutations in PTCH1, SMO and SuFu along with amplified activation of Gli1, a major transcription factor of this signaling pathway. In the current study, we have evaluated the anti- cancer effects of moxidectin. Several MB cell lines such as Daoy, UW426, UW228, ONS76, and PFSK1 cells were treated with moxidectin in a concentration and time dependent manner. Our results demonstrated that moxidectin treatment resulted in significantly reduced proliferation of MB cells. The IC50 of moxidectin in all the MB cell lines ranged 10-17μM after 24, 48 and 72 hours of treatment. Moreover, moxidectin was able to induce 3-4 fold apoptosis in all the MB cell lines as evaluated by Annexin V-FITC/ PI assay, and increased cleavage of caspase3 and PARP. Western blotting analysis demonstrated that moxidectin treatment significantly reduced the expression of Gli1 and its downstream effector molecules such as Pax-6, Oct-4, Sox-2 and Nanog. Efficacy of moxidectin was evaluated in in vivo tumor models. In subcutaneous model, human Daoy MB cells were injected in the right flank of the mice. Our results demonstrated that 2.5mg/kg moxidectin by oral administration everyday suppressed the growth of Daoy tumors by 52%. Additionally, moxidectin also suppressed the proliferation of intracranially injected human Daoy luc cells by 55%. Western blotting analysis of the tumor samples from both experiments showed inhibition of Gli1 and its downstream effector molecules. The clinical chemistry analysis of the blood samples of control and treatment group indicated that moxidectin has no significant effect on the major liver and kidney enzymes. Similarly, the weight of critical organs in the control and treatment group remain unchanged. Conclusively, our results indicate that moxidectin effectively reduces the growth of MB tumors by inhibiting Shh signaling.

DOES PATIENT WAIT TIME INFLUENCE PROVIDER PREFERENCE?

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HARDIN-SIMMONS PA PROGRAM

Objective - PA's are known to increase efficiency and decrease wait times in many different health care settings. We investigated how prolonged wait times in the outpatient clinic setting influenced patients' provider preference. Methods - Our research consisted of a 9-item questionnaire survey posted and shared on Facebook by all co-investigators. The study collected data from responders and observed how the general population's perception of wait time changed their preference of seeing either a physician or a physician assistant. The research team used a control of no wait time and analyzed how the provider preferences changed as the wait time increased from hours to days. All data was analyzed at the .05 alpha level using SPSS statistical software. Results - Our survey correspondents included 302 individuals. The data collected showed 66.78% would choose to see a physician, and 33.22% choose to see a PA when there is no wait time. When the wait time is increased to two hours wait for a physician versus thirty minutes wait to see a PA, 91.39% of people preferred to be seen by the PA, and 8.61% chose to wait to see the physician. When the wait time increased to four hours, 96.35% of people preferred to see a PA within one hour and 3.65% chose to wait and see a physician in 4 hours. According to the data, 74.09% would prefer to see a PA in the primary care setting if the appointment was the same day, compared to 25.91% of the respondents who would prefer to wait and see a physician the following day. Similarly, 84.11% of respondents chose to see a PA in two days, compared to 15.89% who preferred to wait one week to see a physician. Conclusion - This study supports the belief that patients trust PAs to evaluate and manage their health and are comfortable with seeing a PA when faced with prolonged wait times. Based on this study, our research team proposes that PAs are uniquely positioned to reduce wait times, improve patient volume, and increase patient satisfaction with their care.

ABSTRACTS

ENHANCING PATIENT AGENCY IN PSYCHIATRIC HEALTHCARE USING QUICK RESPONSE CODES

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In psychiatric healthcare settings, patient agency is variously represented and can be limited through the language of health information and mediation of resources used by providers. Also, patients construct their identity and act as agents in response to the healthcare system, become knowledgeable, and manage their health conditions. [1] A patient's level of health literacy is variable and it can be difficult to accurately remember and organize new medical information presented in an appointment or counseling session. [2] For example, paper handouts are common educational resources provided to patients in outpatient psychiatric clinics. However, most resources are in English, which may not be inclusive to all patient demographics. The utilization of quick response (QR) codes can prove to be a nuanced method to improve patient agency via health education.[3] Research indicates that QR codes are generally well-received, but are rarely used for patient health and the healthcare system.[4] Pre-implementation surveys revealed that 80% of department providers and staff find educational materials (handouts or brochures) helpful or very helpful for patients. However, over 90% of providers and clinical staff anticipate that patients retain these paper materials for less than a month before they are lost or forgotten. Over 80% of respondents believed that patient access to educational materials would increase by implementing digital solutions to allow continued online access along with Spanish translated resources to promote inclusive patient agency. Following QIRB approval, study standardized binders with laminated QR coded sheets dedicated to ifferent psychiatric disease states (such as common child psychiatry disorders and adult psychiatry disorders), navigating the healthcare system, and the cultural dimensions to health will be created and distributed to the providers of outpatient psychiatric clinics. This nuanced resource will be offered to patients during their appointments or counseling sessions. With any smartphone camera, patients will scan these QR codes and retrieve provider approved health and healthcare system resources in either English or Spanish. Once retrieved, patients will have continued access to any information linked to previously scanned QR codes. Our goal is to improve psychiatric patient access to and utilization of health information by at least 20% in 6 months. After 6 months, providers will be surveyed again regarding perceived improvements in patient access to educational information and the overall role of QR codes in the clinic. The pre- and post-implementation study-created survey data will be assessed in order to gather physician and patient feedback. Based on feedback from providers, changes will be implemented in the next cycle of implementation. This quality improvement project is particularly unique given its goal of increasing access for primarily Spanish-speaking patients. Furthermore, such innovative and sustainable solutions may also serve to close the health literacy gap and increase patient agency in underserved populations.

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RAD6 INHIBITOR OVERCOMES ACQUIRED CHEMORESISTANCE IN OVARIAN CANCER (OC) AND ELICITS SYNERGISTIC RESPONSE WITH STANDARD CHEMOTHERAPY

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Ovarian cancer (OC) is one of the most lethal gynecological malignancies and 5th leading cause of cancer related deaths in women. Primary therapeutic regimen of OC involves surgical resection of the tumor and removing all visible tumor mass followed by platinum based chemotherapy either as single agent or in combination with a taxane. Despite promising initial responses, over 70% of OC patients develop resistance to available chemotherapeutic drugs and relapse. These resistant tumors are untreatable due to low response to existing therapies, and contribute to poor patient survival. Our previous studies showed RAD6, an E2 ubiquitin-conjugating enzyme, is significantly overexpressed in ovarian tumors, and associated with aggressive tumor cell growth, stemness, chemoresistance to platinum drugs and poor prognosis. Our results show that up-regulated RAD6 promotes chemoresistance to platinum drugs by regulating DNA damage tolerance and DNA double strand break repair by monoubiquitination of PCNA and activation of Fanconi anemia-BRCA mediated homologous recombination respectively. Additionally, RAD6 regulates epigenetic modification of H2B and other histones that triggers transcriptional reprogramming and expression of cancer stem cell signaling genes such as ALDH1A1, SOX2 and beta-catenin. Our data shows either down-regulation of RAD6 using siRNAs or our novel small molecule inhibitors (S4, R4 and R14) attenuated the expression of DNA damage response and stem cell signaling proteins, and results in re-sensitization of chemoresistant OC cell lines to platinum drugs. Collectively, these findings indicate RAD6 could be an important therapeutic target for prevention of acquired chemoresistance and treatment of relapsed OC and improve patient survival.

OPTIMIZATION OF A HIGH-THROUGHPUT LIPOSOMES FLUORESCENCE ASSAY FOR THE SCREENING OF DRUG LIBRARIES WITH POTENTIAL THERAPEUTIC USE FOR ION CHANNEL DYSFUNCTION RELATED DISEASES.

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Voltage-gated sodium and potassium channel dysregulation and overexpression have been found to be the leading cause of many channel-related diseases, including epilepsy, Alzheimer's disease, schizophrenia, and most recently, several cancer types. In relation to cancer, potassium channels can become dysregulated, allowing an increased efflux of positively charged potassium ions out of the cell, overriding many checkpoints within the cell cycle, and permitting the cell the ability to divide uncontrollably as a result. It has also been found that overexpression of potassium channels also promotes cell mobility of cancer cells, often leading to metastasis. KcsA (a prokaryotic K+ channel) is the archetypal potassium channel that would be used in the study of finding therapeutic drugs that could act as a "gatekeeper" (in the case of an inhibitor) to regulate the flow of water molecules as a consequence of positively charged ions (K+-ions) moving out of the cell. We attempt to do this by employing a liposome fluorescence assay in which the fluorescent signal decay indicates channel activity. The presence of an inhibitor can therefore "block" (or inhibit) the K+ channel activity, halting the decay in the fluorescent signal, and potentially identifying a putative therapeutic novel blocker. Finally, electrophysiology will be utilized to track the movement of K+-ions across the cell membrane, as well as the blocking properties of putative new therapeutic drugs. The development of this novel high-throughput functional assay will provide a robust and reliable first drug screening approach to identify ion channels blockers in general.

ABSTRACTS

INDUCTION OF ULK1 MEDIATED AUTOPHAGY BY PIMAVANSERIN LEADS TO APOPTOSIS IN PANCREATIC CANCER CELLS

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Pancreatic cancer patients have limited treatment options in spite of several advanced treatment strategies. Pancreatic tumors exhibit high basal autophagy compared to other cancers. Several studies including from our lab reported that enhanced autophagy can lead to apoptosis in cancer cells. In this study, we have demonstrated that pimavanserin (PVT) suppresses pancreatic tumor growth by inducing autophagy mediated apoptosis. Our results indicated that PVT induced apoptosis and reduced the proliferation of pancreatic cancer cells with IC50 ranging between 3-9μM after 24, 48 and 72 hours of treatment. In addition, PVT inhibited the colony formation of pancreatic cancer cells. Treatment of pancreatic cancer cells with increasing concentrations of PVT resulted in a concentration dependent increase in autophagy as evaluated by acridine orange assay by flow-cytometry. PVT induced the expression of autophagy markers ULK1, FIP200, Atg101, Beclin-1, LC3A/B in a concentration dependent manner in several pancreatic cancer cells. In addition, phosphorylation of ULK1 at Ser757 was inhibited with PVT treatment. Apoptotic effects of PVT in pancreatic cancer cells was validated by increase in cleavage of caspase3. ULK1 agonist LYN-1604 enhanced the autophagic and apoptotic effects of PVT. On the other hand, autophagy inhibitors chloroquine and bafilomycin blocked the autophagic and apoptotic effects of PVT in pancreatic cancer cells. Our in vivo findings demonstrated that chloroquine abrogated the growth suppressive effects of PVT by 21% in sub-cutaneously implanted BxPC3 tumor xenografts. Moreover, chloroquine reduced the effects of PVT in inducing the expression of ULK1 and increasing the cleavage of caspase 3 as evaluated by western blotting. Oral administration of PVT suppressed BxPC3 tumor xenografts by 50% in athymic nude mice. In another in vivo experiment, PVT treatment inhibited the growth of orthotopicaly implanted PANC1 tumors by 77%. Chronic administration of PVT did not exhibit any general signs of toxicity or behavioral side effects in mice. Moreover, long-term administration of PVT did not altered the clinical chemistry parameters like ALT, AST, total serum protein, calcium, creatinine, BUN and albumin. Collectively, our results indicate that PVT mediated pancreatic tumor growth suppression was associated with induction of autophagy mediated apoptosis. Since, PVT is already available in clinic with an established safety profile, our results will accelerate its clinical development for pancreatic cancer therapy.

PATIENT PERCEPTIONS OF SEEKING MEDICAL CARE IN RURAL VS. URBAN COMMUNITIES

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Background: Rural populations in the United States (U.S.) have been shown to delay health care as a coping strategy to address their unique barriers in obtaining care when compared to urban populations. Rural health research regarding specific healthcare-seeking behaviors continues to be limited based on geography and sample size.
Purpose: This study aims to analyze differences in timing to seek care between rural and urban communities as well as assess for common barriers and motivators.
Methods: An electronic survey was distributed to a convenience sample, open to U. S. residents over 18 years of age. Likert-type scales were used to assess perceptions of health status, potential barriers and motivators to seeking care, and the time frame in which respondents would seek care for specific symptoms.
Results: Urban respondents indicated waiting longer periods of time before seeking care in comparison to rural respondents for the urgent scenarios of feeling numbness or tingling ($p=0.045$), chest pain ($p=0.10$), and feeling a large lump or lymph node ($p=0.011$). Rural respondents

agreed more strongly that they would seek care if they heard something on the radio (p=0.023) or saw something on TV that inspired them to go (p=0.037).

Conclusions: Our findings suggest that rural populations do not delay seeking healthcare in comparison to urban populations, nor do they indicate more barriers that prevent them from seeking care. The findings otherwise suggest that rural populations would be more likely to seek care if they were exposed to television or radio content that inspired them to do so, a potential point of intervention to encourage rural health care awareness.

STRUCTURAL ACTIVITY RELATIONSHIP APPROACH ON A NOVEL COMPOUND FOR THE TREATMENT OF TRIPLE NEGATIVE BREAST CANCER.

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Triple-negative breast cancer (TNBC) is an aggressive breast cancer type lacking the expression of estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) genes. Therefore, it renders hormonal therapy and HER2-based treatment ineffective. Epidemiological studies suggest that TNBC is more common in younger women, primarily of African-American and Hispanic descent. TNBC is characterized by higher metastatic and reoccurrence rates, as approximately 28% of TNBC patients suffer from the brain metastases, leading to decreased survival rates compared to other breast cancer types. At the same time, TNBC shows good response to chemotherapy, and search for novel anticancer agents is vital.

Recently, we identified a novel class of anticancer agents with cytotoxicity against MDA-MB-231, ability to cross the blood-brain barrier in vitro and in vivo, and optimized toxicological profile. We synthesized and analyzed a library of more than 40 compounds to elucidate the key features responsible for the anticancer activity of these analogs. In addition, we identified molecular targets for these compounds using standard immunoblotting techniques. Here, we report the current state of structure-activity relationship studies for this class of compounds and proposed mechanisms of action associated with their anticancer activity.

DISCOVERY OF THE ELUSIVE REGULATORY SWITCH THAT CONTROLS NUCLEAR TRANSLOCATION OF DISHEVELLED PROTEINS

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For the 3rd Abilene Research Symposium at TTUHSC, I would like to present novel findings from my PhD research published in Scientific Reports (Nature). This study is the first to report that Dishevelled (DVL) nuclear entry and exit is controlled by post-translational lysine acetylation. This discovery has helped to redefine how we view DVL proteins since they have been almost exclusively studied as cytoplasmic regulators of Wnt signaling for the past 60 years. We are excited to have uncovered a novel, simple and elegant regulatory switch that controls DVL functions. These findings could help identify new therapeutic vulnerabilities in cancer biology.

Dishevelled proteins are central mediators of the Wnt signaling pathway and are versatile regulators of several cellular processes, yet little is known about their post-translational regulation. Acetylation is a reversible post-translational modification (PTM) which regulates the function of several non-histone proteins involved in tumorigenesis. Since we previously demonstrated that lysine deacetylase, SIRT-1, regulates DVL protein levels and its function, we reasoned that DVL could potentially be a substrate for SIRT-1 mediated deacetylation. To further examine the potential role of multiple families of lysine deacetylases in the regulation of DVL, we screened for novel acetylation sites using liquid chromatography mass-spectrometry analysis. Herein, we report 12 DVL-1 lysine residues

that show differential acetylation in response to changes in oxygen tension and deacetylase inhibition in triple-negative breast cancer. PTMs are well documented to influence protein activity, and cellular localization. We also identify that acetylation of two key lysine residues, K69 and K285, promote nuclear over cytoplasmic localization of DVL-1, and influences its promoter binding and regulation of genes implicated in cancer. Collectively, these findings for the first time, uncover acetylation as a novel layer of regulation of DVL-1 proteins.

INTERACTIVE LEARNING: USE OF ANATOMY BINGO IN ATTEMPT TO INCREASE SELF-CONFIDENCE ON ANATOMY WRITTEN EXAMS IN HSU PHYSICIAN ASSISTANT STUDENTS

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HARDIN-SIMMONS UNIVERSITY PHYSICIAN ASSISTANT STUDIES

Graduate-level anatomy is a high-intensity, heavy content subject that is a fundamental course for physician assistant students. This course can often lead to a decrease in self-confidence among PA students when it comes to their exam taking. The purpose of our research was to see if interactive learning through Anatomy BINGO would improve PA students' self-confidence. We additionally wanted to foster meaningful interactive learning to see improvements in performance. The cohort was blindly and evenly separated into 2 groups taking care to alternate the experimental and control group. All students were sent out a pre-exam survey asking the students to rank their level of self-confidence for the exam. On the same day, the experimental group participated in Anatomy BINGO. After the exam, both the control and the experimental group filled out a post-exam survey that assessed their self-confidence level depending on their participation. We were able to take the results of these surveys and analyze them using a 2 tailed t-test. The results showed that participants had a 0.63 increase in self-confidence between their pre, and post exam and non-participants had a 0.81 increase in self-confidence between the pre and post exam. There was a 0.18 higher increase in self-confidence of non-participants compared to the participants. Our p-value was 0.689 making this data not statistically significant. This made us accept our null hypothesis that interactive learning in the form of anatomy BINGO did not affect self- confidence levels in students' exam taking. Some limitations to our research were a small sample size, ordinal data, self-reported data, randomization, and varying levels of difficulty between exams. The statistical power may be dependent on each student's day-to-day factors such as stress, anxiety, schedule, and mood. Further research should be conducted in hopes to find a positive correlation between interactive learning and having increased self-confidence.

FACEBOOK USE AND ACADEMIC PERFORMANCE IN PHYSICIAN ASSISTANT STUDENTS

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Facebook has become a significant component in the daily routine of graduate students. In the United States, 90% of adults aged 18 to 29 years are on social media and actively use their accounts (Austin-McCain, 2017). There has yet to be an overall consensus on the relationship between Facebook use and students' academic performance, and an even greater lack of knowledge regarding the effect of Facebook use in the physician assistant student population. With increasing popularity and use of Facebook, this study aims to determine if elevated levels of Facebook activity will negatively impact the academic productivity, academic satisfaction, and academic success of a PA student. The significance of this research will serve to aid physician assistant students in identifying activities such as increased Facebook usage that may be detrimental or beneficial to academic performance. Additionally, this research may aid students in recognizing time spent on Facebook and help to improve time management, thereby enabling increased academic productivity. An analytical, prospective research design was conducted. The research focused on 90 physician assistant students from the Hardin-Simmons University Master of Physician Assistant Studies

program. The subjects included 29 students in their final semester of schooling, 31 students in their clinical rotations, and 30 students in their didactic studies. The subjects were emailed an anonymous, voluntary, 21 item web-based, firewall password protected questionnaire using Survey Monkey which assessed their Facebook usage, academic success, productivity, and satisfaction. The level of Facebook use was measured using a 7-item self-reporting, anonymous survey that used semantic differential scales and the Verbal Frequency Scale. Participants were asked to respond to each item using the following categories: 1 = Never, 2 = Infrequently, 3 = Occasionally, 4 = Often, and 5 = Always. Their responses were saved as numerical data points. The higher the numerical value, the higher the Facebook usage. Each participant's demographics were evaluated through their responses to 4 items. These questions included the confirmation that the student is a Hardin-Simmons PA Program student, as well as the participant's age, gender, and prospective year of graduation.
A multiple regression was run to predict a correlation between GPA and updating Facebook status, time spent on Facebook, and posting to Facebook. The multiple regression model did not demonstrate statistical significance as predicted by GPA, $F(3, 25) = .968$, $p = .423$, adj. $R2 = -.003$. All three variables did not add statistical significance to the prediction, $p > .05$. . According to the statistical analysis there was no correlation between Facebook usage and academic success, productivity, and satisfaction.

SERTOLI CELL EXPRESSION OF COMPLEMENT REGULATORY PROTEINS IS NECESSARY TO THEIR SURVIVAL OF HYPERACUTE REJECTION

Rachel L. Washburn, Gurvinder Kaur, Jannette M. Dufour

Transplantation is an important clinical procedure used to treat organ failure associated with various medical conditions. In 2019 there were almost 113,000 patients awaiting transplants while just under 35,000 transplants were actually performed. In fact, 20 people die each day awaiting a transplant. The utilization of pig tissue would present an endless supply of transplantable tissue, but xenografts are rapidly destroyed through hyperacute rejection mechanisms by the recipient's immune system. The primary humoral mediator of hyperacute rejection is the complement system (C"), which is activated by preformed-antibody binding to xenoantigens. C" consists of proteins that, when activated, undergo a series of proteolytic cleavages resulting in insertion of the membrane attack complex (MAC), causing lysis of the target cell. Previously, we have found that Sertoli cells (SCs) survive xenotransplantation without immune suppressive drugs. SC are immune privileged cells found in testes which physiologically function to protect maturing sperm cells from autoimmune destruction. The goal of this study was to examine the mechanisms SCs use to survive hyperacute rejection. Given that one of the major mechanisms of xenograft rejection is C" destruction, we measured SC survival of C'' in vivo and in vitro. Neonatal porcine SC (NPSCs) transplanted into rats not only survived as xenografts, but immunohistochemical analyses of the surviving grafts show some C3 deposition and no MAC deposition, suggesting that SCs are inhibiting the complement cascade after activation. Using a Human serum (HS)-C" cytotoxicity assay in vitro, we confirmed SCs survive exposure to C". We have also identified that SCs express two of the main complement regulatory proteins (CRPs), CD46 (membrane cofactor protein, MCP) and CD55 (decay accelerating factor, DAF). Furthermore, mRNA and protein quantification indicated elevated expression of these CRPs by NPSCs, as compared to neonatal porcine islets, which are killed by complement. Therefore, we knocked down expression of CD46 and CD55 using shRNA to confirm their importance. No more than 10% of the transformed cells survived exposure to the HS-C" cytotoxicity assay, which indicates that CD46 and CD55 are important in NPSC xenograft survival in vitro. Finally, microarray data of mouse SCs showed expression of multiple other CRPs. We intend to investigate other CRPs produced by SCs and confirm their role in SC-mediated complement inhibition. Data gained from these experiments will be critical in determining the mechanism of SC immune-privilege and could increase the viability of allo- and xeno-grafts clinically.

ABSTRACTS

CEFIDEROCOL, A NEW SIDEROPHORE CEPHALOSPORIN FOR THE TREATMENT OF COMPLICATED URINARY TRACT INFECTIONS CAUSED BY MULTIDRUG-RESISTANT PATHOGENS: PRECLINICAL AND CLINICAL PHARMACOKINETICS, PHARMACODYNAMICS, EFFICACY AND SAFETY

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Cefiderocol (Fetroja®) is a siderophore cephalosporin and has demonstrated potent activity against extended-spectrum beta-lactamases producing Enterobacteriaceae, carbapenem-resistant Enterobacteriaceae, and nonfermenting Gram-negative bacilli, including Pseudomonas aeruginosa, Stenotrophomonas maltophilia, and Acinetobacter baumannii, Burkholderia cepacia, and Klebsiella pneumoniae. However, cefiderocol has limited activity against Gram-positive bacteria and anaerobes like Bacterodies fragilis. In the APEKS-cUTI study, 183 (73%) of 252 patients in the cefiderocol group versus 65 (55%) of 119 patients in the imipenem-cilastatin group achieved the composite outcome of clinical and microbiological eradication of Gram-negative bacteria (treatment difference of 18.58%; 95% CI 8.23–28.92, p = 0.0004) in complicated urinary tract infections (cUTIs). Cefiderocol was non-inferior to imipenem-cilastatin in cUTIs caused by Gram-negative bacteria such as E. coli, K. pneumoniae, P. aeruginosa, Proteus mirabilis, Enterobacter cloacae, Morganella morganii, and Citrobacter freundii. Cefiderocol required dose adjustment in patients with renal impairment and percentage of time that free drug concentrations above the minimum inhibitory concentration (%fT > MIC) best correlated with clinical outcomes. The most common adverse events with cefiderocol were gastrointestinal symptoms such as diarrhea, constipation, nausea, vomiting, or upper abdominal pain. Two phase III clinical trials, the CREDIBLE-CR study and the APEKS-NP study, investigated the efficacy and safety of cefiderocol for the treatment of pneumonia or cUTI, and both studies showed higher all-cause mortality associated with cefiderocol. Therefore, the use of cefiderocol should be limited only to the treatment of cUTIs from Gram-negative bacteria, especially in patients who have limited or no alternative treatment options.

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