4th ANNUAL TRANSLATIONAL RESEARCH SYMPOSIUM

January 31, 2020

Program & Abstracts

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The 4th Annual CNU Translational Research Symposium
January 31, 2020 8:00 AM-5:00 PM

Start Time	Duration	Agenda
8:00 am	45	Registration
8:45 am	15	Opening Remarks **Dr. Alvin Cheung, PharmD, MHSA, CNU President**
Oral Presentation Session 1 (Moderators: Drs. Xiaodong Feng (COP), Ruth Vinall (COP), Linh Ho (COP))		
9:00 am	**45**	*Keynote Speaker* **Dr. Yuanpei Li, Ph.D., Associate Professor, UC Davis** *Transformable Nano-Theranostics for Precision Cancer Imaging and Therapy*
9:45 am	20	**Hang Nguyen, P2 Student, CNUCOP Summer Research Fellowship** *Natural Plant Extracts Modulate OA-induced Steatosis in Human C3A (Hep2/C3A)*
10:05 am	20	**Ayeh Barekat, P3 Student, CNUCOP Summer Research Fellowship** *Pharmacodynamics of Ampicillin Against Enterococcus Faecalis Cultured with Escherichia Coli*
10:25 am	20	**Steven Sprenger, M3 Student, CNUCOM** *Induction of Adipogenic Genes by Novel Serum-free Conditions in Pre-adipocyte 3T3-L1 and ST2 Cells*
10:45 am	15	**POSTER PRESENTATIONS** - Coffee break
Oral Presentation Session 2 (Moderators: Drs. Catherine Yang (MPS), Damon Meyer (CHS))		
11:00 am	*20*	**Dr. Abdelbasset Farahat, CNUMPS Faculty** *Indole and Benzimidazole Diamidines: Synthesis, DNA Binding and Antiparasitic Activity*
11:20 am	20	**Emily Nguyen, M2 Student, CNUCOM** *Generating a Stable Hepatitis B Virus Cell-based Infectious System for Drug Screening*
11:40 am	20	**Nancy Le, 3+ BSMD Student, CNUCHS** *Testing of the BRCA2 Protein in Repairing Double Stranded Breaks in rad52 Mutated Cells*
12:00 pm	60	**POSTER PRESENTATIONS** - Lunch Break
Oral Presentation Session 3 (Moderators: Drs. Yihui Shi (COM), Welly Mente (COP))		
1:00 pm	**45**	*Keynote Speaker* **Dr. Paul Glassman, DDS, MA, MBA, Assistant Dean for Research, CNUCDM** *On the Road to Value-Based Care Systems: Oral Health Care and Telehealth-Connected Teams*
1:45 pm	20	**Dr. Gordon Sproul, PGY1 Resident, CNUCOP** *Evaluating 30-day Surgical Site Infection (SSI) Rates Using Protocol-guided Timing and Dosage of Perioperative Antibiotics*
2:05 pm	20	**Kyle Cartier, P1 Student, CNUCOP/CNUMPS** *The Dual Role of the PARK2 gene: a Cross-talk between Neurological Disorders and Cancer*
2:25 pm	20	**Elizabeth Browning, P3 Student, CNUCOP Summer Research Fellowship** *Dysregulation of Nrdp1 Expression Levels and Cellular Localization Occurs in Prostate Cancer Patients and is Associated with Worse Patient Outcomes*
2:45 pm	60	**POSTER PRESENTATIONS** - Coffee break
Oral Presentation Session 4 (Moderators: Drs. Ahmed ElShamy (MPS), Shankar Chaturvedi (COP), Tuan Tran (COP))		
3:45 pm	20	**Dr. Ghalib Alkhatib, CNUCOM Faculty** *Low levels of HIV-1 envelope-mediated fusion are associated with long-term survival of an infected CCR5-/- patient*
4:05 pm	55	Awards for Poster and Oral Presentations
5:00 pm		Adjournment

Keynote Speaker Biography

Dr. Yuanpei Li is a tenured Associate Professor in the Department of Biochemistry and Molecular Medicine at the University of California Davis. He is also an active member at UC Davis Comprehensive Cancer Center. Dr. Li's group aims to 1) develop next generation nano-medicine platforms and novel therapeutics by learning from Mother Nature and clinical practices, 2) obtain fundamental knowledge on how these subjects interact with biological systems, and 3) apply them to solve complex medical problems that are associated with cancer and other diseases. These research projects integrate recent advances in interdisciplinary fields, such as nanotechnology, medicinal chemistry, material sciences, engineering and biology, to create innovative technologies and therapeutics. Significant efforts have also been devoted to the rapid "bench to bed side" translation of these innovative technologies and therapeutics that can tremendously benefit the health of human and companion animals. Dr. Li has successfully led four nano-formulations from the initial design to the stage of filing the Investigational New Drug (IND) application to the FDA for clinical trials in human. Dr. Li has published over 50 research papers and 3 book chapters and filed over 10 patents applications in the field of nanomedicine and molecular imaging. Many of his papers were published in high-impact journals, such as Nature Nanotechnology, Nature Communications, Advanced Materials, Angewandte Chemie and Biomaterials. Dr. Li has been the Principal investigator on 12 nano-medicine grants (total ~$7 million) and the Co-investigator on 14 federal grants (> $15 million total cost). He has received the Fellowship Award from the Department of Defense Prostate Cancer Research Program, multiple 5-year R01 awards from the National Institute of Health and a number of awards from UC Davis. Dr. Li is a member of the American Chemical Society (ACS), American Association for Cancer Research (AACR), Controlled Release Society (CRS) and World Molecular Imaging Society (WMIC). Dr. Li also serves as the reviewer for numerous high-rank journals and many NIH and DoD study sections for grant review.

Transformable Nano-theranostiscs for Precision Cancer Imaging and Therapy

Yuanpei Li[1], Xiangdong Xue[1] and Tzu-yin Lin[2]

1) *Department of Biochemistry and Molecular Medicine, UC Davis Comprehensive Cancer Center, University of California Davis, Sacramento, CA 95817, USA. Email: lypli@ucdavis.edu, Tel: 1-916-734-4420*
2) *Division of Hematology/Oncology, Department of Internal Medicine, University of California Davis, Sacramento, California 95817, USA.*

Nanoparticle-based theranostic agents are emerging as a promising paradigm towards personalized nanomedicine for disease- and patient-specific diagnosis and treatment. The integration of imaging and therapeutic functions into a single nano-formulation allows precise diagnosis of disease, individualized selection of treatment modality, real-time monitoring of drug distribution/delivery and assessment of therapeutic outcomes. Although conceptually impressive, these theranostic agents are still at an early stage of development. Concerns also remain with many multifunctional nanoparticles regarding complexity of fabrication, variations in formulations, limited *in vivo* stability, unfavorable biodistribution, limited ability to regulate release of payload and limited data on the fate and toxicity of nanocarriers once they enter the blood circulation. Furthermore, high background noise and lack of an amplification strategy to increase target signal output are major factors hampering advances in nanoparticle imaging functions. We have developed a series of highly innovative transformable nano-theranostics that were highly capable to circumvent the sequential biological barriers which had hindered the drug delivery to tumors. These nano-theranostics have intrinsic fluorescence and are able to chelate various metal ions for non-invasive "visualization" of tumor, drug delivery and therapeutic effect by magnetic resonance imaging (MRI) and near infrared fluorescence imaging (NIRFI). Moreover, the synergistic multi-modality therapy (photothermal-, photodynamic-, chemo- and immuno-therapies) with these nano-theranostics were demonstrated to be highly effective with high complete cure rate in a variety of subcutaneous and orthotopic cancer xenograft models. These nano-platforms with powerful delivery efficiency and versatile theranostic functions shows enormous potentials to improve cancer diagnosis and therapy.

Keynote Speaker Biography

Paul Glassman DDS, MA, MBA is the Associate Dean for Research and Community Engagement at the College of Dental Medicine at California Northstate University in Elk Grove, CA and Professor Emeritus at the University of the Pacific, Arthur A. Dugoni, School of Dentistry in San Francisco, CA. He has served on many national panels including the Institute of Medicine's (IOM) Committee on Oral Health Access to Services which produced the IOM report on *Improving Access to Oral Health Care for Vulnerable and Underserved Populations*.

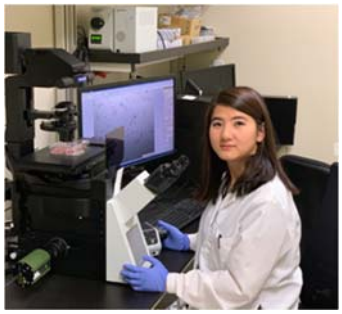
Dr. Glassman has had many years of dental practice experience treating patients with complex conditions and has published and lectured extensively in the areas of Hospital Dentistry, Dentistry for Patients with Special Needs, Dentistry for Individuals with Medical Disabilities, Dentistry for Patients with Dental Fear, Geriatric Dentistry, and Oral Health Systems reform. He has a long career working with special populations in a variety of practice and community settings. Dr. Glassman has been PI or Co-PI on over $30 million in grants and contracts over the last 30 years devoted to community-service demonstration and research programs designed to improve oral health for people with disabilities and other underserved populations. Dr. Glassman has led the national movement to improve oral health using telehealth-connected teams and Virtual Dental Homes.

On the Road to Value-Based Care Systems: Oral Health Care and Telehealth-Connected Teams

The U.S. oral health care system primarily serves the wealthiest and healthiest segments of society. Those groups and individuals with the greatest burden of disease face many barriers in accessing oral health services in the traditional oral health delivery structures. At the same time, there are several promising developments in oral health care. These include increased focus on value-based outcomes, new materials and understanding in prevention, treatment, and behavior support science, and innovations in delivery systems including expanded roles for allied personnel and the use of telehealth-connected teams to "bring care to where people are.". All these trends and developments provide opportunities for CNU to receive funding and excel at community-delivery and translational science research.

ORAL PRESENTATIONS

Title: Natural Plant Extracts Modulate OA-induced Steatosis in Human C3A (Hep2/C3A)



Authors:

Hang Nguyen, College of Pharmacy, CNSU, Hang.Nguyen2562@cnsu.edu

Advisor: Lakshmi Shankar Chaturvedi, Ph.D. Dept of Pharmaceutical & Biomedical Sciences-College of Pharmacy; Dept of Basic Sciences and Surgery-College of Medicine, CNSU Lakshmi.Chaturved@cnsu.edu

Tibebe Woldemariam, PhD, Department of Pharmaceutical & Biomedical Sciences, CNSU College of Pharmacy, Elk Grove CA, TWoldemariam@cnsu.edu

Introduction: NAFLD is the most common form of chronic liver disease and there is no effective therapy available for this devastating disease. The natural plant product (NPP) extracts of Barberry (*Berberis vulgaris*), Goji (*Lycium Barbarum)*, Sumac (*Rhus coriana*), and Ginger (*Zingiber officinale*) have been commonly used in "traditional" herbal medicines. However, the use of these NPP in the modulation in vitro NAFLD and molecular targets has not been fully elucidated. We investigated effect of NPPs in the modulation of oleic acid (OA)-induced free fatty acid accumulation (FFA) and studied molecular targets in *in vitro* C3A cell-culture system.

Methods: C3A were cultured in EMEM with FBS. Cell viability was assessed via CCK-8 kit. Cells were treated with various concentrations OA (0-1.5 mM) to induce steatosis and quantified using Oil Red O (ORO) staining. Cells were untreated or treated with various concentrations of NPP extracts with or without OA (0.5mM) for 24 hours. Quantitative-RT-PCR was performed using *delta-delta Ct method.* RPLPO was used as house-keeping gene for quantitation of relative expressions. Genes involved in fatty acid biosynthesis PPARγ, FASN, PNPLA3 and RAC1 were studied.

Results: A dose dependent increase induction of FAA with OA in comparison to untreated cells by ORO. All NPPs significantly reverse/decrease the FFA accumulation induced by OA. Real-time PCR data revealed that Goji ameliorates OA-induced PPARγ, FASN, PNPLA3, and RAC1 genes involved in hepatosteatosis. However, other NPPs found to have a differential effect on various genes studied.

Conclusion: Natural bioactive aqueous extract from Goji might have beneficial effects on hepatic steatosis by targeting PPARγ, FASN, PNPLA3, and RAC1 gene expression in OA-induced steatosis in C3A cells. This study suggests that bioactive NPP of Goji might have promising therapeutic potential in the reversal or treatment of NAFLD.

Title: Pharmacodynamics of Ampicillin Against Enterococcus Faecalis Cultured with Escherichia coli

Authors:

Ayeh Barekat, MS, PharmD Candidate, College of Pharmacy, CNSU
ayeh.barekat6108@cnsu.edu

Tiffany McMurtry, Pharm.D./MPS Candidate, College of Pharmacy, CNSU,
tiffany.mcmurtry7036@cnsu.edu

Parwinder Purewal, Pharm.D. Candidate, College of Pharmacy, CNSU,
parwinder.purewal5909@cnsu.edu

Fantasia Rodriguez, PharmD Candidate, College of Pharmacy, CNSU,
fantasia.rodriguez2760@cnsu.edu

Advisor: Justin Lenhard, PharmD, College of Pharmacy, CNSU, Justin.lenhard@cnsu.edu

Introduction: The purpose of the current study was to explore if β-lactamase producing strain of *Escherichia Coli* are able to protect *Enterococcus faecalis* from β-lactam exposure. These two species are frequently co-cultured together in variety of infections such as urinary tract infections.

Methods: *E. faecalis* isolate AR Bank 0671 was used in monoculture experiments and co-culture experiments with *E. coli* isolate AR Bank 0019 (TEM-1 β-lactamase producing strain) or *E. coli* AR Bank 0017 (no β-lactamase). The time-killing experiments were done over 24 hours with the initial inoculum of 10^6 CFU/ml to examine the extent of killing by ampicillin at concentrations of 0.023, 0.093, 0.375, 1.5, 6, 24, and 96 mg/L. To assess ampicillin pharmacodynamics, bacterial killing was analyzed using a Hill-type mathematical model and the AUCFU curves of each ampicillin concentration.

Results: Ampicillin at concentrations of 24 and 96 mg/L was able to completely eradicate the *E. faecalis*. Interestingly, no strength of ampicillin was able to achieve any killing of the *E. faecalis* when co-cultured with the β-lactamase producing *E. coli*, and the max log reduction of *E. faecalis* was about 1.5, which eventually reached near control levels by 24 hr. In the Hill-type analysis, the maximal killing of *E. faecalis* was significantly lower during co-culture with β-lactamase producing *E. coli* (E_{max} = 1.23, 95% CI: 0.94 –1.53) compared to monoculture (E_{max} = 4.62, 95% CI 4.32 – 4.94). As expected, β-lactamase deficient *E. coli* was not able to protect the *E. faecalis* from ampicillin (E_{max} = 3.5, 95% CI 3.32 – 3.68) compared to monoculture (E_{max} = 3.76, 95% CI 3.36 – 3.40).

Conclusion: β-lactamase producing *E. Coli* was able to protect *E. faecalis* during exposure to ampicillin. These results can have important implications for the selection of appropriate antimicrobial agent when facing polymicrobial infections involving *E. faecalis*.

Title: Induction of Adipogenic Genes by Novel Serum-free Conditions in Pre-adipocyte 3T3-L1 and ST2 Cells

Author:
Steven Sprenger, BS, College of Medicine, CNSU

Advisors: Lakshmi S. Chaturvedi, PhD* Dept of Basic Sciences and Surgery-College of Medicine, CNSU
Lakshmi.Chaturved@cnsu.edu
Tibebe Woldemariam, PhD; College of Pharmacy, CNSU
Dinesh Vyas, MD, Chair, Department of Surgery, College of Medicine, CNSU

Introduction: Obesity, defined as a condition of excessive fat accumulation in adipose tissue, is a global epidemic which has a myriad of deleterious effect on human health. It has become one of the leading impediments to public health globally. The study of obesity necessitates adipocyte models, which commonly employ medium enriched with adipogenic hormones and Fetal Bovine Serum (FBS) to culture terminal adipocytes. In the current study, we developed a novel protocol for serum-free differentiation of 3T3-L1 and ST2 preadipocytes using media enriched with Free Fatty Acids (FFA) and Bovine Serum Albumin (BSA). Differentiation was characterized by measuring FFA uptake and changes in expression of adipogenic genes.

Materials and Methods: NIH-3T3-L1 and ST2 preadipocyte cells were maintained in DMEM containing 10% fetal calf serum and 1% penicillin-streptomycin and RPMI with 10% FBS and 1% penicillin-streptomycin mixture respectively at 37^0C, 5% CO_2 in a humidified atmosphere. Differentiation was induced using a mixture of Dexamethasone-0.25 µM, 3-isobutyl-1-methylxanthine (IBMX-0.5 mM), Insulin-10 µg/mL or Insulin-Transferrin-Selenium (ITS 1%). Cells were cultured in media containing DMEM with bovine serum albumin (BSA-2.5%) and Lipid mixture 1 (LM1-1%). Total RNA was extracted and quantitative-RT-PCR performed using delta-*delta Ct method*, also known as the $2^{-\Delta\Delta Ct}$ *method.* Ribosomal protein P0 (RPLP0) was used as house-keeping gene for quantitation of relative expressions.

Results: We observed an increased fatty acid accumulation relative to controls using Oil Red O neutral lipid staining and spectrophotometry. Differentiation was further confirmed by increased gene-expression of adipogenic transcription factor peroxisome proliferator-activated receptor gamma (PPARγ), and CCAAT/enhancer binding protein alpha (C/EBPα), and adipogenic genes fatty acid binding protein 4 (FABP4/aP2), fatty acid translocase (FAT/CD36) and lipogenic gene Peripilin by using quantitative-RT-PCR.

Conclusion: Our data suggest that serum-free differentiation can significantly enhance the free-fatty acid accumulation as well as adipogenic gene expression in both NIH-3T3-L1 and ST2 pre-adipocyte cells.

Title: Indole and Benzimidazole Diamidines: Synthesis, DNA Binding and Antiparasitic Activity

Author:
Dr. Abdelbasset A. Farahat (presenter), Master of Pharmaceutical Sciences program, CNSU, Abdelbasset.Farahat@cnsu.edu

Abstract: A novel series of indole and benzimidazole diamidine derivatives were prepared to study their antimicrobial activity against the tropical parasites causing African sleeping sickness and Malaria. The dicyanoindoles needed to synthesize the target diamidines were obtained through Stille coupling reactions while the biscyanobenzimidazoles intermediates were made via condensation/cyclization reactions of different aldehydes with 4-cyano-1,2-diaminobenzene. Different amidine synthesis methodologies namely, lithium bistrimethylsilylamide (LiN[Si(CH3)3]2) and Pinner methods were used to prepare the diamidines. Both types (indole and benzimidazole) derivatives of the new diamidines bind strongly with the DNA minor groove and generally show excellent in vitro antitrypanosomal activity. The diamidino-indole derivatives also showed excellent in vitro antimalarial activity while their benzimidazole counterparts were generally less active. Many Compounds were highly active in vivo and cured all mice infected with Trypanosoma brucei rhodesiense, a model that mimics the acute stage of African sleeping sickness, at a low dose of 4 x 5 mg/kg i.p. and hence these compounds are more potent in vivo than pentamidine."

Title: Generating a Stable Hepatitis B Virus Cell-based Infectious System for Drug Screening

Authors:
Emily Nguyen , College of Medicine, CNSU,
Emily.Nguyen7991@cnsu.edu
Fatima Shabaan Yasin, College of Pharmacy, CNSU,
Fatima.Yasin2916@cnsu.edu
Advisor: Dr. Ahmed El-Shamy, Ph.D., Master of Pharmaceutical Sciences, CNSU, ahmed.elshamy@cnsu.edu

Introduction: Approximately 2 billion people have been infected by hepatitis B virus (HBV). Of those, 250 million are chronically infected, including at least 1.25 million in the United States. Current anti-HBV drugs are not curative, partly due to the continued presence of transcriptionally active HBV DNA in the host nucleus that is not directly targeted by available therapies. Therefore, often life-long treatment is necessary for persistent suppression of viral replication and to reduce the risk of developing cirrhosis and liver cancer. According to the 2018 HEPATOLOGY report, the development of new therapeutics that lead to a "*functional cure*" of chronic HBV infection is currently a top priority of HBV-related research. Many clinical medications are derived from medicinal plants and thus, offer a great potential resource for developing novel antiviral agents. But first, in order to screen various natural products, a functional cell-based HBV infectious system must be established. This project aims to establish a cell culture system that supports the complete life cycle of HBV.

Methods: This cell culture will comprise of hepatoma-derived cell lines, called Huh7. These cell lines alone are not susceptible to HBV infection as they are not able to mediate viral entry due to low expression of the sodium taurocholate cotransporting polypeptide (NTCP), which serves as the functional receptor for HBV to gain entry into hepatocytes. By molecular cloning approaches, a vector plasmid was prepared containing the NTCP gene and an antibiotic resistance marker gene (neomycin). The plasmid was then amplified and purified using midi-prep technique. Subsequently, purified NTCP + neomycin plasmid was transfected into Huh7 cells obtained from Rice Laboratory at Rockefeller University, New York. Twenty-four hours after the lipofectamine transfection, the cells were cultured in complete media containing 500 micrograms of neomycin / mL and fresh media with neomycin was added every 2-3 days for three weeks. To prepare a stock of HBV, Hep-ED19 cells were used because these cells have the HBV genome integrated into their DNA. These cells were cultured in 3% fetal bovine serum (FBS) media until they reached 100% confluency. The media was collected every 48 hours for three weeks. Then the media was concentrated via the polyethylene glycol (PEG) precipitation approach.

Results: Three weeks after transfection of Huh7 cells with the NTCP + neomycin plasmid, only the cells expressing NTCP and containing the neomycin resistance gene survived. The NTCP expression was confirmed via immunofluorescence (IF) assay using NTCP monoclonal antibody (mAb), which revealed that >90% of transfected cells were highly expressed NTCP. Through quantitative real time PCR, it was determined that the titer of our HBV stock came out to be $5x10^6$/uL. We are in process of infecting the NTCP-Huh7 cells with HBV stock and infectivity will be measured via IF staining of HBV-core protein mAb using ImageXpress.

Future direction: This cell-based infectious system will be used to investigate the anti-HBV activities of several biological materials, including scorpion, snake and bee venoms, and DNA binding compounds obtained through a collaboration with Aussit University, Egypt and Georgia University.

Title: Testing of the BRCA2 Protein in Repairing Double Stranded Breaks in *rad52* Mutated Cells

Authors:

Nancy Le (presenter), College of Health Sciences, CNSU, nancy.le3193@cnsu.edu

Husni Abdul-Rahman, College of Medicine, CNSU, husni.abdul-Rahman4444@cnsu.edu

Advisor: Dr. Damon Meyer, College of Health Sciences, CNSU, damon.meyer@cnsu.edu

Abstract: Breast cancer affects approximately 1 in 8 women in the United States, which underscores the need to identify risk factors associated with developing this disease. Mutations within the breast cancer susceptibility gene 2 (BRCA2) have been identified as a genetic risk factor that is correlated with a 70% lifetime risk of developing breast cancer. However, study of these BRCA2 mutations and their molecular defects in human cells has been challenging. As an alternative to human cells, Saccharomyces cerevisiae yeast cells can be used as a model organism to observe the effects of BRCA2 mutations on DSB repair. In yeast cells, the Rad52 protein recruits Rad51 during DSB repair; and in humans, this same recruiting function is carried out by BRCA2. Despite their functional similarities, there is insufficient research determining their complementation ability, although BRCA2 is hypothesized to partially complement the function of Rad52. To test this relationship, DSBs were initiated in WT and rad52 mutant cells, and the ability to repair the DSB via homologous recombination was determined in the presence or absence of BRCA2 on a plasmid vector. It was observed that the rad52 mutants displayed a significantly lower recombination frequency than that of the WT cells, which contain the empty vector without BRCA2. From these results, future exploration of BRCA2's complementation ability can be tested against these controls to consider the use of Saccharomyces cerevisiae as a model organism in investigating BRCA2 mutations to understand more about the various cancers and illnesses affected by the mutated BRCA2 gene.

Title: Evaluating 30-day Surgical Site Infection (SSI) Rates Using Protocol-guided Timing and Dosage of Perioperative Antibiotics

Authors:
Gordon C. Sproul, Pharm.D. Sutter Medical Center Sacramento (sproulg@sutterhealth.org)

Advisor: Andrea Brizee, Pharm.D., BCPS. Sutter Medical Center Sacramento (brizeea@sutterhealth.org)

Introduction: According to Surgical Care Improvement Project, appropriate antimicrobial dose selection and timing of administration of antibiotics prior to a surgical procedure are two key measures to control infection postoperatively. Individuals who are incorrectly administered antibiotics before a procedure are found to be at increased risk of dose-dependent adverse events, infusion related reactions, and overall mortality resulting from complications after surgery. This retrospective study evaluates the impact of a standard dose and timing protocol for pre-procedural antibiotics consistent with their pharmacokinetic profile on the 30-day incidence of readmissions resulting from surgical site infection.

Methods: This retrospective cohort study will be submitted to the Institutional Review Board for approval. Approximately 100-400 adult patients will be identified in the electronic medical record who were admitted for elective or emergent surgical care and administered a dose of antibiotic prior to surgery specified by a standard institutional dosing protocol. Primarily, a patient MRN, gender, weight, indication for procedure, antibiotic dose, formulation, frequency, administration time, procedure start time, and procedure end time will be recorded. Documentation will be reviewed to determine if patients received the correct dose of antibiotic, and if the antibiotic was given within 60 minutes prior to incision, or within 120 minutes for vancomycin and levofloxacin doses. Incidence rates for surgical site infection 30 days following discharge will be evaluated. The primary author will rate the patient's antibiotic dose, administration time prior to incision, and re-dose interval as appropriate or inappropriate using descriptive statistics in reference to the standard dosing protocol.

Results: Pending IRB data collection and retrieval 01/2020

Implications: This is a retrospective study designed to evaluate the effectiveness of a standard dosing protocol for surgical site infection control. The information learned from this study may provide evidence for improving patient outcomes by identifying accurate dosing, timing of administration, and re-dose intervals for various antibiotics utilized in surgery for SSI prophylaxis.

Title: The Dual Role of the PARK2 gene: a Cross-talk between Neurological Disorders and Cancer

Authors:

Kyle M. Cartier, Master of Pharmaceutical Sciences, CNSU, Kyle.Cartier6198@cnsu.edu

Advisor: Simeon O. Kotchoni, Master of Pharmaceutical Sciences, CNSU, simeon.kotchoni@cnsu.edu

Abstract: PARK2 gene mutations are a significant factor in both neurological disorders and cancer. PARK2 mutations have a role in Parkinson's disease (PD) (notably Juvenile Parkinsonism (i.e. AR-JP) and paralysis agitans (PA) (Classical Parkinson's Disease)) and are contributing factors in a range of cancers.

The PARK2 gene is located on the Q end of chromosome 6, and functions as a tumor suppressor gene through its protein product parkin. The recent rise of rapid genotyping methods has led to genotyping of AR-JP (and classical PD) cancer and patients. Common PARK2 mutations include single nucleotide polymorphism or mutations yielding fragments or the complete absence of the gene or gene product. PARK2 also involves the tumor-suppressor protein p53, which has been implicated in more than half of all cancers to date. These findings make this gene intriguing for the fields of clinical neuroscience, neuropharmacology and oncology. We review the aspects of this gene and its effects, with the hope that solutions can be made to protect this gene and limit the mechanism behind mutation of this gene, leading to the biochemical cross-talk that either can lead to Parkinson's or one of several types of cancer. As this gene affects the central nervous system when mutated, there may be other disease states, in addition to Parkinson's disease, that involve brain and spinal cord functioning, with some speculation that related disorders such as Alzheimer's disease, dementia, and others. For example, peripheral nerves that enter into the spinal cord via the dorsal root and its dorsal root ganglion may also be affected by this mutated gene; the impact for treatment of diseases such as neuropathy, muscular dystrophy, shingles, also may benefit from an intact PARK2 gene. While no drug or commercially available product is available to stabilize this gene, there are many potential solutions that could have a positive health impact to society.

Title: Dysregulation of Nrdp1 expression levels and cellular localization occurs in prostate cancer patients and is associated with worse patient outcomes

Authors: Elizabeth Ann Browning, College of Pharmacy, CNSU
elizabeth.browning3699@cnsu.edu

Advisor: Ruth Vinal, PhD, Department of Pharmaceutical & Biomedical Sciences, College of Pharmacy, CNSU,
ruth.vinal@cnsu.ed

Background: Nrdp1, an E3 ubiquitin ligase, can regulate levels of ErbB3, an EGF receptor family member which drives proliferation of prostate cancer (CaP) cells. We have shown that Nrdp1 is expressed in both the cytoplasm and the nucleus of CaP cells, this has not previously been reported. In addition, we have shown that African American (AA) CaP cells express lower levels of nuclear Nrdp1 compared to Caucasian American (CA) CaP cells and that this is associated with worse patient outcomes. The goal of the current study was to further elucidate the mechanisms which regulate Nrdp1 levels and cellular localization.

Methods: Subcellular fractionation, western blot, immunofluorescence, and confocal microscopy were used to assess cellular localization and expression levels of Nrdp1 in two cell lines (LNCaP (CA) and MDAPCa2b (AA)) following treatment with MG132, a proteasome inhibitor, or cyclohexamide, an inhibitor of translation.

Results: Treatment with MG132 caused a greater level of Nrdp1 accumulation in LNCaP compared to MDAPCa2b indicating that post-translational regulation of Nrdp1 via proteasomal degradation occurs to a greater extent in LNCaP cells. Time course treatments with cyclohexamide determined that cytoplasmic Nrdp1 half-life is longer in MDAPCa2b compared to LNCaP (24 versus 8 hours, respectively). Subcellular fractionation and confocal microscopy confirmed that Nrdp1 is located in the nucleus and cytoplasm of both cell lines, however, MDAPCa2b cells express much lower levels of nuclear Nrdp1 and levels do not appear to alter in response to cyclohexamide treatment.

Conclusions: Our combined data indicate that Nrdp1 levels can be regulated by different mechanisms in CA CaP versus AA CaP cells, and that restriction of nuclear translocation of Nrdp1 is a key mechanism which determines nuclear Nrdp1 in AA CaP cells.

Title: Low Levels of HIV-1 Envelope-mediated Fusion Are Associated with Long-term Survival of an Infected CCR5-/- Patient

Author: Ghalib Alkhatib, College of Medicine, CNSU
Ghalib.Alkhatib@cnsu.edu

Objectives: This study investigated whether Env-mediated fusion levels of R5X4 viruses are associated with long-term survival of an infected CCR5-/- patient.

Design: Four R5X4 Envs were cloned from each of two infected homosexual individuals (DR and C2) homozygous for the CCR5Δ32 allele. DR is a long-term survivor chronically infected with HIV-1 and his Envs were cloned 12 years after testing HIV-infected, whereas C2 Envs were isolated 1 year after primary infection.

Methods: The current study sequenced the gp41 subunits and created hybrid Envs that contained exchanged gp41 subunits or V3 loops. The Env-mediated fusion activity of Envs was examined in cell fusion and virus infection assays.

Results: Sequence analysis indicated novel polymorphisms in the gp41 subunits of C2 and DR, and revealed sequence homology between DR and certain long-term nonprogressors. The DR Envs consistently showed lower Env-mediated fusion, smaller size, and delayed onset of syncytia formation. Envs containing swapped gp41 regions resulted in the transfer of most of the fusion phenotype and in the shift of the inhibition concentration 50 (IC50) of the inhibitory T20 peptide. In contrast, Envs with swapped V3 domains resulted in the partial transfer of the fusion phenotype and no significant change in the IC50 of the fusion inhibitor Fuzeon (T20).

Conclusions: Env sequence polymorphisms identified two distinct fusion phenotypes isolated from infected CCR5-/- patients. Swapping experiments confirmed DR's low fusion phenotype. Env-mediated fusion is a critical factor among others contributing to long-term survival.

POSTERS

(Alphabetical by first name)

Title: Decrease Use of Opioid with Vibration Anesthesia Device in Upper Lid CO2 Laser Blepharoplasty

Authors: Aarin Thuan Pham Hoang, Barkha Tiwana Advisor: Randal Pham, MD, MS, FACS, FASOPRS

Introduction: CO2 laser blepharoplasty has several advantages compared to conventional blepharoplasty. The laser provides more effective hemostasis during surgery, causes less swelling, erythema and bruising during the post-operative period, and considerably shortens the recovery time. The laser also shows superior results when compared to cold-steel blepharoplasty in patients who are on anticoagulants. The vibration anesthesia device (VAD) utilizes neuromodulation as a means to lessen pain during surgery. The Gate Control Theory of Pain, first proposed by Melzack and Wall in 1965, states that non-noxious (vibrating) stimulation of the spinal cord closes the "gate," inhibiting the transmission of pain sensation to the brain. Fentanyl, an opioid used to provide anesthesia during surgery, is also the number one cause of opioid overdose death in the U.S. The purpose of this study is to evaluate the effectiveness of the VAD in decreasing the use of fentanyl in upper lid CO2 laser blepharoplasty.

Methods This retrospective study used chart review as the source of data. The VAD was used in upper lid CO2 blepharoplasty starting on 2/22/2017. Data was collected from all bilateral upper eyelid blepharoplasty surgery charts from 12/15/2014 to 12/31/19. The subjects and controls were matched for age and sex. The dose of fentanyl (50 mcg given each time), the number of times fentanyl was administered intravenously (IV) at the start of the surgery, and the number of times fentanyl was given intravenously throughout surgery were recorded. If the fentanyl was injected within 15 minutes of the first dose, it was recorded as two administrations. At the start of surgery, the VAD was placed over the upper lid superior to the injection site. The vibration was engaged and a 30 gauge needle was used to inject 3 mL of 2% lidocaine with 1:100,000 epinephrine mixed with 0.75% bupivacaine, in a 50-50 volume ratio, into each upper lid. The VAD was then used to distribute the anesthesia across the upper lid. The same procedure was performed bilaterally.

Results: There was a total of 52 patients (subjects) who received local anesthetics and intravenously administered fentanyl at the start of blepharoplasty with the VAD, of which 26 were male and 26 were female. The average age was 72.73 years (SD 8.20) and the median age was 71 years. The average number of times fentanyl was given intravenously at the start of the surgery was 1.00 (SD 0). The average number of times fentanyl was given intravenously throughout the surgery was 1.19 (SD 0.44). A total of 56 patients (controls) received local anesthesia and intravenously administered fentanyl at the start of blepharoplasty without the VAD, of which 22 were male and 35 were female. The average age was 72.82 years (SD 6.79) and the median age was 71 years. The average number of times fentanyl was given at the start of the surgery was 1.10 (SD 0.35). The average number of times fentanyl was given throughout the surgery was 1.32 (SD 0.51). A 2-tailed t-test showed a statistically significant difference between the number of doses given at the start of surgery ($p=0.039$). The difference between the total number of doses given throughout surgery for subjects and controls was not statistically significant ($p=0.178$).

Conclusion: The result showed that there was a statistically significant decrease in the amount of intravenously administered fentanyl given with the VAD at the start of surgery compared to cases in which VAD were not used. These data supported the hypothesis that the VAD helped decrease the amount of opioid use for CO2 blepharoplasty.

Title: Case Study of a Cadaver with an Azygous Lobe: Anatomy and Significance

Authors:

Aaron Downs, M.D. Candidate, California Northstate University College of Medicine, aaron.downs4122@cnsu.edu

Sailabala Vanguri M.D., Assistant Professor of Anatomy
California Northstate University College of Medicine,
sailabala.vanguri@cnsu.edu.

Introduction: The Azygos Lobe is an accessory lung lobe which is considered to be an uncommon anatomical variant. It is most often seen in the right lung. It is usually found accidentally during routine imaging, surgery, or cadaveric dissection. In this case, the azygos lobe, was found during cadaveric dissection. Though the lobe by itself does not cause clinical symptoms, it should be discussed in the context of surgical procedures, imaging, and spread of infection.
Methods: Data was collected during routine cadaveric dissection.

Conclusion/Implications:

- The azygos lobe is an uncommon anomaly that is found in 1% of anatomic specimens, on about 0.4% of chest radiographs and 1.2% of high resolution CT.
- In a chest x-ray, azygos lobe can result in a paratracheal opacity which can be mistaken for a pathological process.
- The azygos lobe may mimic an enlarged thymus, a substernal goiter, a localised pneumothorax, bulla, lung abscess, or neoplasm
- This anomaly poses a significant risk during the procedure of endoscopic thoracic sympathectomy.
- Mesoazygos, which is the pleural fold attaching to the arch of azygos vein acts like a barrier controlling the spread of certain pathological processes from azygos lobe to the rest of the lung tissue and vice versa.
- Azygos lobe may be prone to atelectasis and bronchiectasis particularly when there is a deep azygos fissure which may alter the bronchial wall and the quality of bronchial drainage in the Azygos Lobe.

Title: Modifications of σ–Hole Type DNA Minor Groove Binders Structure Effects in Binding Specificity and Affinity

Authors:
Dr. Abdelbasset A. Farahat (presenter), Master of Pharmaceutical Sciences program, CNSU, Abdelbasset.Farahat@cnsu.edu

Pu Guo**,** Department of Chemistry, Georgia State University

David W. Boykin, Department of Chemistry, Georgia State University David Wilson, Department of Chemistry, Georgia State University

Abstract: AT specific heterocyclic cations that bind in the DNA duplex minor groove have had major successes as cell and nuclear stains and as therapeutic agents which can effectively enter human cells. Expanding the DNA sequence recognition capability of the minor groove compounds could also expand their therapeutic targets and have an impact in many areas, such as modulation of transcription factor biological activity. Success in the design of mixed sequence binding compounds has been achieved with *N*-methylbenzimidazole (*N*-MeBI) thiophenes which are preorganized by a σ-hole interaction to fit the shape of the DNA minor groove and H-bond to the –NH of G·C base pairs that projects into the minor groove. Initial compounds bind strongly to a single G·C base pair in an AT context with a specificity ratio of 50 (K_d AT-GC/K_d AT) or less and this is somewhat low for biological use. We felt that modifications of compound shape could be used to probe local DNA microstructure in target mixed base pair sequences of DNA and potentially improve the compound binding selectivity. Modifications were made by increasing the size of the benzimidazole *N*-substituent, for example, by using *N*-isobutyl instead of *N*-methyl, and by changing the molecular twist by introducing substitutions at specific positions on the aromatic core of the compounds. In both cases we have been able to achieve a dramatic increase in binding specificity, including no detectible binding to pure AT sequences, without a significant loss in affinity to mixed base pair target sequences.

Title: Autoinflammation of Human Retinal Endothelial Cells: HMGB1 Expression in Hyperglycemic Conditions

Authors: Aiza Anwar (presenter), BS, CNSUCOM
aiza.anwar7088@cnsu.edu

Janet Lee-Coomes (presenter), MS, CNSU COM,
janet.leecoomes8583@cnsu.edu

Advisors: Ishwarlal Jialal, MD, PhD, formerly CNSUCOM, Elk Grove, CA, kjialal@gmail.com

Hongbin Wang PharmBS, MS, PhD, CNSUCOP,
hongbin.wang@cnsu.edu

Introduction: Diabetic Retinopathy (DR) is a feared complication of diabetes. Studies suggest that glycemic control and inflammation play pivotal roles in the pathogenesis of DR. Previously, it was shown that hyperglycemia (HG) increases the activities of toll-like receptors (TLR) 2&4 and receptors for advanced glycation end products (RAGE) in human microvascular retinal endothelial cells (HMVREC). Damage-associated molecular molecules (DAMPs) are associated with promoting pathological inflammatory responses and act as ligands for TLRs and RAGEs. However, the role of HG in inducing auto-inflammation by triggering DAMPs is poorly studied. We tested the effect of HG on the HMVREC expression of high mobility group box 1 protein (HMGB1), a DAMP which acts as a ligand for TLRs and RAGE. We assessed for both time course and dose response effects and expected that higher concentrations of glucose and longer incubation periods would induce higher levels of HMGB1 expression.

Methods: HMVRECs were grown to confluence in 12-well plates then subjected to hyperglycemia versus euglycemia (5.5mM glucose) conditions for 8 and 24 hour incubation periods. The supernatant was collected and HMGB1 levels were assayed by enzyme-linked immunosorbent assay (ELISA). We tested four hyperglycemic conditions: 15mM, 20mM, 25mM, and 30mM glucose. Based on initial results, the experiment was optimized to a 24 hour incubation period with 25mM glucose. Results and statistical significance were analyzed by Wilcoxon matched-pairs signed rank test.

Results: Incubation of HMVREC for 24 hours with 25mM glucose (n=8 experiments) led to an increased expression of HMGB1 compared to euglycemia. There was an 11% augmentation that was statistically significant (p=0.008).

Conclusion: There was a significant increase in HMGB1 levels when HMVRECs were subjected to 25mM glucose, suggesting an auto-inflammatory response to hyperglycemia via induced activation of TLRs and RAGEs. HMGB1 may be a potential target for anti-inflammatory therapies in DR and warrants further research.

Title: Antiproliferative effects of Carfilzomib on Human HT-29 Adenocarcinoma Colon Cancer Cells

Authors:
Alexander Nguyen, COP, CNSU, Alexander.Nguyen3924@cnsu.edu

Victor Changcoco, COP, CNSU, Victor.Changcoco8745@cnsu.edu

Hang Nguyen, COP, CNSU, Hang.Nguyen2562@cnsu.edu

Dinesh Vyas, MD, Dept of Surgery-SJGH and College of Medicine, CNSU, DineshVyas@yahoo.com

Simeon Kotchoni, Ph.D. Dept of Pharmaceutical & Biomedical Sciences-College of Pharmacy, California Northstate University, Simeon.Kotchoni@cnsu.edu
Melanie Rose, COP, CNSU, Melanie.rose@cnsu.edu
Lakshmi Shankar Chaturvedi, Ph.D. Dept of Pharmaceutical & Biomedical Sciences-College of Pharmacy; Dept of Basic Sciences and Surgery-College of Medicine, California Northstate University, Dept of Surgery-SJGH, Lakshmi.Chaturved@cnsu.edu.

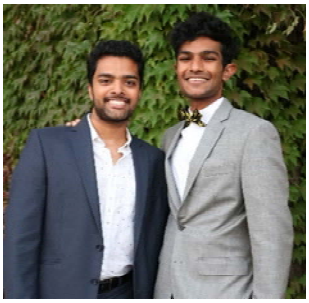
Introduction: Colorectal cancer (CRC) is the third most common cancer worldwide and a leading cause of cancer related death in the United States. Surgery, Chemotherapy and radiation is the most common way to treat the patients. These patients have a high risk of recurrence. The second generation proteasome inhibitor has been clinically shown to be effective for hematological cancers. However, role of proteasome inhibition as anti-tumorogenic potential and molecular mechanism has not been fully investigated in the solid tumors such as colon cancer. Present study investigated and compared the antiproliferative and cytotoxic effects of second generation irreversible proteasome inhibitor Carfilzomib (CFZ) alone and in a combination well known chemotherapeutic drug doxorubicin (DOX) on human colon HT-29 cells.

Methods: HT-29 cells were cultured in MyCoy's 5a medium with FBS at 37C with humidified conditions. Cell viability was assessed using CCK-8 kit. Cells were treated with vehicle control (DMSO) or various concentrations CFZ (0-500nM), DOX (0-1.5µM) and a combination of both to measure the cell proliferation and cytotoxicity. Genes involved in cell cycle regulation will be determined using CFZ, and a combination of DOX to determine the molecular targets involved in the regulation of growth of HT-29 cancer cells.

Results: We observed that CFZ as well as DOX dose dependently inhibit cell proliferation of HT-29 cells. Furthermore, a combination of both drugs found to have further additive effect at high concentration. We are exploring the molecular mechanism of anticancer potential of CFZ alone and in a combination of DOX in human HT-29 adenocarcinoma cells.

Conclusion: The current study revealed that irreversible second generation proteasome inhibitor Carfilzomib (CFZ) alone has a promising anticancer therapeutic potential in treating adenocarcinoma patients. However, further molecular mechanisms need to be delineated to understand its tumorigenic potential.

Title: Asian Clam Adaptations in Response to Environmental Pollutants



Authors:
Anand Singh, College of Health Sciences, CNSU, anand.singh9825@cnsu.edu
Ishaq Aslam, College of Health Sciences, CNSU, ishaq.muhammad8842@cnsu.edu.

Advisor: Dr. Damon Meyer, Science and Math Department Chair, CNSU College of Health Sciences, damon.meyer@cnsu.edu

Introduction: *Corbicula fluminea* is an invasive species of clam which occupies the American River. This clam species has different physical features, such as a larger cirri spacing, which allows the *C. fluminea* to outcompete the native clams for resources. The purpose is to see how *C. fluminea* copes with various environmental pollutants to thrive in the American River ecosystem. *C. fluminea* is able to alter its behavior and biochemical pathways in response to phosphate, Escherichia coli, heavy metals, and hard water in its environment.

Methods:

Phosphate

- Initial concentration of phosphate in American River was determined using a phosphate ion test kit (5x10-4M).
- Various concentrations of phosphate ions were placed in water and the pH was measured before and after to observe the production of phosphoric acid.
- Clam shells were placed in environmentally relevant concentrations of phosphate solutions and clam shell hardness was measured using a Shore D durometer before and after 14 days.

Bacteria Feeding

- E.coli broth was placed clam's beaker and three water samples were taken every 15 minutes for 120 minutes.
- Absorbance of water samples were measured to determine change in E.Coli concentration over time.

P-gp Expression

- A Western Blot analysis was conducted on gill tissue by using P-gp primary and secondary antibodies to determine P-gp expression in heavy metal and hard water.
- Image-J analysis semi-quantified amount of P-gp expressed.

Results:

- Higher concentrations of phosphate solution had a greater percent difference in clam shell hardness.
- *C. fluminea* fed on *E. coli* depicted through the decrease in *E. coli* concentration over time.
- P-gp was expressed most greatly in heavy metal of 2.5mM FeSO4.

Conclusion/Implications:

- Understanding how invasive species cope with environmental factors outside of their native habitat is imperative in knowing how to regulate their populations and protecting the native ecosystem.

Title: Dysregulation of the AR-Nrdp1-ErbB3 axis occurs in African American prostate cancer patients and is associated with worse outcomes

Authors:

Anhao Sam (presenter), Thomas Steele, Elizabeth Browning, Shawna Evans, Sheryl Krig, Neelu Batra, Salma Siddiqui, Paramita Ghosh, College of Pharmacy, CNSU

Advisor: Ruth Vinall, College of Pharmacy, CNSU, rvinall@cnsu.edu

Introduction: We previously showed that Nrdp1 is transcriptionally regulated by the androgen receptor (AR) in prostate cancer (CaP) cells and that Nrdp1 can post-translationally regulate ErbB3 levels. Increased levels of ErbB3 are associated with worse CaP patient outcome. The goal of the current study was to determine whether dysregulation of the AR-Nrdp1-ErbB3 axis contributes to prostate cancer health disparities for African American men, and to identify the underlying mechanisms involved.

Methods: Expression levels and localization of AR, Nrdp1, and ErbB3 were assessed (50 African American (AA) and 158 Caucasian (CA) CaP patients; immunohistochemistry) and two cell lines (LNCaP and MDAPCa2b; immunofluorescence/confocal microscopy, subcellular fractionation, western blot). Knockdown, forced overexpression, immunoprecipitation, and/or treatment with enzalutamide or synthetic androgen experiments were employed to investigate the relationship between AR, Nrdp1, and ErbB3 expression levels and localization.

Results: A statistically significant negative association between cytoplasmic levels of AR and nuclear Nrdp1 exists in both CA and AA CaP patients (Spearman correlation coefficient of -0.62 and -0.36, respectively). Reduced nuclear Nrdp1 expression levels predicted biochemical recurrence (AUC 0.63). AA CaP cells expressed significantly lower levels of both total and nuclear Nrdp1 compared to their CA CaP counterparts. Enzalutamide treatment had a lesser impact on Nrdp1 expression levels and localization in AA versus CA CaP cells. Immunoprecipitation studies demonstrated that Nrdp1 can bind to AR in CA CaP cells but not AA CaP cells.

Conclusions: Our combined data indicate that dysregulation of the AR-Nrdp1-ErbB3 axis occurs to a larger extent in AA than CA CaP cells and that this can contribute to worse patient outcomes. Lack of binding between AR and Nrdp1 in AA CaP cells may account for the lower levels of nuclear Nrdp1 observed in AA CaP cells.

Title: Genetic Variations & Clinical Effectiveness of Anti-PCSK9 Medication; a Clinical Case report Study

Authors: Arianne Dagdag (Presenter), Doctor of Pharmacy Candidate, Class of 2021, CNSU, College of Pharmacy, arianne.dagdag9568@cnsu.edu

Parwinder Purewal, Doctor of Pharmacy Candidate, Class of 2020, CNSU, College of Pharmacy, parwinder.purewal5909@cnsu.edu

Tony Joseph Eid, PharmD, REHS, BCACP, APH, CHC, AACC, Director of Experiential Education, CNSUCOP, tony.eid@cnsu.edu

Islam Mohamed B.Pharm, MS, PhD, Department of Pharmaceutical and Biomedical Sciences, CNSU College of Pharmacy, islam.mohamed@cnsu.edu.

Introduction: hyperlipidemia is a well-established risk factor for atherosclerotic cardiovascular disease (ASCVD). Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors are FDA-approved class for treatment of hyperlipidemia, which result in increased levels of low-density lipoprotein (LDL) receptors, and hence removal of LDL-cholesterol (LDL-C) from circulation.

Methods: An outpatient 55-year-old morbidly obese Caucasian male presented for further evaluation. His past medical history includes a long-standing history of hyperlipidemia, but no known ASCVD. Myocardial perfusion imaging study was positive for a small moderate posterior lateral ischemia with an ejection fraction of 63%. Family history was positive of early coronary heart disease (CHD). Medication history revealed initial use of atorvastatin 80mg as well as aspirin 81mg by mouth daily. His LDL-C goal was intended to be less than 70mg/dL. Since the patient's goal was not met, he was then transitioned to evolocumab at 140mg SQ twice monthly and his atorvastatin was discontinued.

Results: Despite the immediate decrease of LDL-C to undetected levels, the patient's LDL-C rebound to increased levels while on evolocumab 140mg SQ twice monthly. Adherence was assessed during each patient encounter with evidence of injection welts across his abdomen. A genetic study for a panel of 11 lipid genes were tested and results demonstrated a heterozygous genetic variation of the LPL gene (C.106G>A; p.Asp36Asn). The patient was then transitioned off of evolocumab to rosuvastatin 40mg daily along with ezetimibe 10mg daily.

Conclusion / Implications: Despite the clinical feasibility for anti-PCSK9 class for treatment of hyperlipidemia, clinical literature and guidelines are lacking in defining the eligibility and response rates of patients with different genetic variations. The current case provides insight for the interaction between patients' genetic variations and effectiveness of anti-PCSK9 class. In addition, it further justifies the implementation of genetic testing as a cost-effective procedure before initiating expensive anti-PCSK9 treatments.

Title: A Comparison of Skin Thickness and Hair Quality in Patients with Scarring Versus Non-Scarring Alopecia

Authors:

Arya Asghari (presenter), College of Graduate Studies, CNSU, arya.asghari6812@cnsu.edu.

Dorsa Heydarlou, College of Graduate Studies, CNSU, dorsa.heydarlou6809@cnsu.edu.

Advisor: Dr. Natasha Mesinkovska, MD, PhD, Department of Dermatology, UC Irvine, School of Medicine, nmesinko@uci.edu.

Introduction: The continuous enhancements in cosmetic research have increased the demand for advanced non-invasive methods of diagnosis and monitoring dermatological disease progression. A unique non-invasive optical imaging technique, optical coherence tomography (OCT), was studied for its capability of comparing skin thickness and hair quality in patients with scarring alopecia versus patients with non-scarring alopecia.

Methods: In order to test these parameters using OCT imaging, twenty male and female patients ranging from 26 to 65 years of age with clinically diagnosed alopecias of varying subtypes participated. Two different scalp regions were imaged and analyzed using ImageJ software. Upon determining normal data distribution, a Student's *t*-test was conducted for the three variables, including epidermal thickness, follicle quantity and diameter.

Results: The difference in average skin thickness for scarring versus non-scarring alopecia was found to be significant ($P<0.05$), whereas the differences in average follicle quantity and diameter were not found to be significant ($P>0.05$).

Conclusion/Implications: Although OCT imaging was unable to distinguish underlying microstructures such as active and inactive follicles, as demonstrated by finding no significant differences in average follicular quantity and diameter, it is inferred that OCT may be effective in diagnosing and monitoring hair loss diseases via differentiating between the epidermal thicknesses of scarring versus non-scarring alopecia.

Title: Implementing and Assessing a Faculty Development Workshop in Online and Hybrid Course Design

Authors:
Ashim Malhotra, Pharm.BS, M.S., Ph.D. (Presenter), Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, CNSU. Email: ashim.malhotra@cnsu.edu

Tracy Yarbrough, M.D., Ph.D., Department of Basic Science, College of Medicine, CNSU. Tracy.Yarbrough@cnsu.edu

Catherine Yang, Ph.D., College of Medicine, CNSU
Catherine.Yang@cnsu.edu

Introduction: Faculty Learning Communities (FLCs) are voluntary faculty communes facilitating life-long learning and constitute an interactive faculty development mechanism.

Methods: We implemented and assessed an FLC to promote technology use in healthcare education across the five CNU colleges of Pharmacy, Medicine, Psychology, Dental Medicine and Health Sciences. Our six-week-long FLC engaged the 30 participating faculty in implementing course design principles for creating hybrid and online classes. There were six two-hour-long training sessions each week led by experts in topics such as "elements of hybrid course design", "use of Active Presenter for interactive lecture videos", "assessment strategies for online and hybrid courses", and "communication strategies for hybrid and online courses". Each session included an hour-long lecture followed by working "hands-on" with experts to incorporate the discussed strategies into their courses. The FLC itself was a hybrid course and online follow-up time was provided to help attendees complete "homework" assignments, which typically consisted of completing the next phase of their developing course. A final session was reserved for participants to present courses in their respective disciplines that incorporated learning from the FLC.

Results: We adapted the SALG instrument with 45 questions to survey the perception of the FLC. The response rate was 41%, with 80% respondents indicating that the FLC enabled 1) examination of the design, potential usage and steps for the implementation of online and hybrid technology platforms in their teaching, and 2) identification of an area of technology-assisted or distance learning to incorporate into their teaching, while 90% felt that the session facilitators 3) demonstrated expertise in their subject matter and 4) were responsive to questions, comments, and opinions. Suggested areas of improvement included time and resource allocation.

Conclusion: The technology FLC was well received by CNU faculty and was valuable in advancing the educational mission of California Northstate University.

Title: High-Fidelity Simulation as a Novel Integration Tool for the CNUCOP Pharm.D. Curriculum

Authors:
Ashim Malhotra, PharmBS, M.S., Ph.D. (Presenter), Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, CNSU. Email: ashim.malhotra@cnsu.edu

Song Oh, Pharm.D, Department of Clinical and Administrative Sciences. College of Pharmacy, CNSU Song.Oh@cnsu.edu

Zhuqiu Jin, Ph.D., Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, CNSU. Email: zhuqiu.jin@cnsu.edu

Introduction: The 1910 "Flexner Report" placed foundational sciences early in medical and pharmacy education, followed by clinical sciences. However, assessment, anecdotal, and student perception data suggest that integration and the transition from didactic learning to clinical application remain difficult to achieve and measure.

Methods: To bridge this gap, we designed an Integrated Cardiovascular Simulation (ICS) and placed it in the Second Professional Year (P2) of the 4-year Pharm.D. curriculum. ICS was developed with input from Ph.D. and Pharm.D. faculty focused on congestive heart failure (CHF) complicated by preexisting arrhythmias and was staged through ER presentation (phase 1), admission to the ICU (phase 2), and hospital stay and discharge (phase 3). A Laerdal SimMan 3G manikin presented CHF symptoms and student teams were assessed on accurate identification of symptoms and the underlying pathophysiology. Laboratory values were integrated during Phase 2, while the manikin presented atrial and ventricular fibrillation, Torsades de Pointes, and asystole, allowing students to learn rhythm identification. P2 teams practiced the SBAR communication technique and patient counseling skills, and recommended therapy, elaborating MOA and adverse effects. ICS was assessed through pre- and post-session quizzes and perception data.

Results: Respondents indicated that ICS helped them learn: 1) arrhythmia pathophysiology (85%), 2) EKG interpretation of arrhythmias (89%), 3) adverse effects of antiarrhythmic medications (93%), 4) clinical decision making (92%), and 5) communication skills between team members (85%). Ninety-one percent felt that ICS made the content more clinically relevant than lecture, while student perception of their interaction with the simulated patient was rated at 74%. Student performance improved on a post-test (80.2%) compared to the pre-test (66.9%), with an increase in symptom and arrhythmia pattern recognition (41.2% and 36.7% increase in the post-test).

Conclusion: The high-fidelity ICS is a novel tool to achieve and assess the integration of foundational and clinical knowledge in a pharmacy program.

Title: A Review on the Integration of Cannabidiol into Pharmaceutical Care

Authors:
Ayeh Barekat M.S.(presenter), Elizabeth Ann Browning B.A.(presenter), James Alexander Lugtu B.S., Vivian Nguyen B.S., Sabrina Rai B.S., Julia Tryhorn B.S., Pa Nhia Vang B.S. Kyle Wong B.S., Eugene Kreys Pharm.D., Ph.D., BCPS, Tiffany Kreys Pharm.D., BCPP

Introduction: *Cannabis* has been evaluated as a therapeutic agent for a variety of diseases, but the mind-altering properties provided by the delta-9-tetrahydrocannabinol (THC) component have been a barrier to the adoption of its use by patients and medical professionals, and remains classified as Schedule I hallucinogens. On the other hand the cannabidiol (CBD) component is ubiquitous, and can be found in the form of capsules, tinctures, and oils to gummies, lemonade, and bath bombs.

Methodology: To elucidate the safety and efficacy of CBD for various therapeutic uses as well as its legal status an extensive review of literature was conducted.

Results: Currently, thirty-three states and the District of Columbia allow the use of cannabis for therapeutic uses, eleven states and the District of Columbia allow the recreational use of cannabis, while seventeen states restrict the use of cannabis to products that are high in CBD and low in THC. Unlike THC, CBD is a non-psychoactive cannabinoid and has many promising potential therapeutic uses. The Food and Drug Administration (FDA) approved a CBD oil product, Epidiolex, to treat seizures associated with Lennox-Gastaut or Dravat syndrome in pediatric patients over two years of age. Available evidence suggests that CBD may benefit patients with diseases including inflammatory diseases, chronic and neuropathic pain, rheumatoid arthritis, Crohn's disease, inflammatory bowel disease, cardiovascular disease, diabetic complications, Huntington's disease, anxiety, depression, psychosis, schizophrenia, cancer, nausea, infection, epilepsy, multiple sclerosis, Parkinson's disease, hypoxia-ischemia injury, and Alzheimer's disease. Additionally, studies in patients have shown that CBD is generally well tolerated with the most common adverse reactions including sedation, somnolence, fatigue, insomnia, sleep disorders, poor sleep quality, decreased appetite, rash, malaise, infections, and asthenia. It is important to note the capacity of CBD to cause hepatocellular injury and elevated serum transaminase levels, and that this risk is increased at higher doses of CBD and during concomitant use of CBD with valproate or acetaminophen. Additionally, CBD is metabolized by CYP3A4 and CYP2C19, CBD inhibits UGT1A9 and UGT2B7, and dose adjustments are recommended for substrates of CYP2C8, CYP 2C9, CYP2C19, CYP1A2, and CYP2B6 during CBD use, which allows for many potential drug-drug interactions. Drug-drug interactions involving CBD vary considerably in their clinical significance due to the wide variability in doses, products, route of administration, and many other factors making the role of pharmacists essential.

Conclusion: With the availability of a wide variety of CBD products and the growing knowledge of the harmful and beneficial effects of CBD, pharmacists play an important role in assessing if a patient is a candidate for the safe use of CBD. Pharmacists should be able to provide clinical advice on the administration and use of CBD products including proper dosing, counseling, and information about adverse effects.

Title: Aqueous Extract of Ocimum Sanctum L Inhibit Cell Proliferation and Modulate Cell Cycle Regulatory Cyclin Genes in Human Triple-Negative Breast Cancer Cells

Authors:
Ajay M. Patel, B.S. CNSUCOM Ajay.Patel9812@cnsu.edu
Tibebe Woldemariam, COP, CNSU, TWoldemariam@cnsu.edu
Dinesh Vyas, MD, Surgery-SJGH, CNSUCOM, DineshVyas@yahoo.com
Advisor: Lakshmi Chaturvedi, COP, CNSU, Lakshmi.Chaturvedi@cnsu.edu

Introduction: Breast cancer is the most frequently diagnosed cancer in women around the world. Triple-negative breast cancer (TNBC) is a subclass that does not express an estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth receptor (HER-2) which makes TNBC more aggressive and metastatic. Chemotherapy is the first-line therapy for the treatment but there are off-target effects and life-limit dose. Tulsi, also known as Holy Basil (Ocimum Sanctum Linn), is often used for various herbal remedies. Aqueous extracts of O. sanctum leaves (AEOS) have been shown to be anti-cancerous in other types of cancers but has not yet been evaluated in human TNBC. The aim of this study was to investigate the anti-proliferative effect and molecular targets of AEOS on human TNBC cells.

Methods: The dried leaves of Ocimum sanctum was obtained from a commercial suppliers (Sacramento, CA) and reduced to fine powders and percolated with distilled water. Evaporation of the solvent at 37ºC using Chefman-5 tray round food dehydrator. The residue was then dissolved with water at desired concentration required for bioassay. Human TNBC cell lines MDA-MB-231, MDA-MB-453, HCC70 and HCC1187 were obtained from ATCC and cultured in DMEM or RPMI with 10% fetal bovine serum. Cells were treated with various concentrations of AEOS (0-500µg/mL), doxorubicin (DOX, 0-500nM) or in a combination of both. Cell viability was measured at various time-points using cell counting kit (CCK-8) assay and cell proliferation was performed using BrdU assay kit. Gene expression was performed by using quantitative real-time PCR for cell-cycle regulatory genes.

Results: The AEOS exhibited significant cytotoxic effect against human TNBC cells (MDA-MB-231, MDA-MB-453, HCC70 and HCC1187) in a time and dose dependent manner. Furthermore, we identified the pure bioactive compounds from AEOS and confirmed their antiproliferative properties and molecular targets in human TNBC cells. We observed that O. Sanctum significantly inhibited Cyclin D1, B1 and A1 gene expression without affecting Cyclin E1 gene expression. Furthermore, a combination with a low dose of doxorubicin with the AEOS further decreased Cyclin D1 and A1 expression in comparison to each agent alone confirming an additive effect. The AEOS (500µg/mL) was found to be non-toxic to human fibroblast cell line (CCD-Co18) in comparison untreated control cells.

Conclusion: This study for the first time reports that AEOS have anti-carcinogenic potential through enhancing anti-proliferation in human TNBC cells with an additive effect by further decreasing Cyclin D1 and A1 when combined with low dose chemotherapeutic agent DOX. Collectively, this data provided evidence for the efficacy of AEOS as well as novel purified bioactive compound alone and/or in a combination may have potential in the treatment of drug resistant TNBC patients.

Title: Ependymal Cell Response after Acute Neutralization of C1q in Spinal Cord Injured *Foxj1*^{CreERT2}-tdTomato Reporter Mice

Authors:
Bahaar Muhar (presenter), CNSU, College of Graduate Studies, MPS student, Bahaar.muhar6811@cnsu.edu.

Advisor: Aileen Anderson, Physical Medicine and Rehabilitation, University of California, Irvine, aja@uci.edu

Abstract:

The pathogenesis of spinal cord injury (SCI) is highly regulated by inflammatory responses including complement. This study focus on a key component of classical complement pathway, C1q, which is known to have beneficial and detrimental roles in lesion pathogenesis after injury. In addition, our group has recently discovered that C1q can directly interact with human neural stem cells (NSC) through transmembrane receptors. In this study, I have used C1q neutralizing antibody (C1q nAb) to investigate the effect of C1q on cell proliferation and differentiation of endogenous spinal cord glial progenitor populations in a tamoxifen inducible Foxj1CreERT2-tdTomato mouse model that allows tracking of ependymal cell lineage after thoracic vertebrae (T9) contusion SCI. In parallel, I have assessed the effect of acute C1q neutralization on lesion expansion and locomotor function post-SCI. Unbiased stereological analysis was used for quantifying histological changes and number of ependymal cell derived cells. Locomotor analysis consisted of an open field BMS test and catwalk gait analysis. A single injection of C1q nAb into injury epicenter immediately after injury reduced lesion volume, increased spared tissue volume, and improved recovery of locomotor function. Administration of C1q nAb had also an impact on total numbers and astroglial differentiation of ependymal cell progeny. These data suggest that a single injection of C1q nAb can alleviate pathophysiological detriments after SCI and supports our previous studies by providing evidence that complement modulates spinal cord endogenous progenitor responses.

Title: Comparing Fall Risk Among Antiepileptic Drugs in the Elderly: A Nested, Case-Control Study of a Medicare Database

Authors:
Eugene Kreys (presenter), PharmD, PhD, BCPS
Suzanne Clark, R.Ph., Ph.D.
Tiffany-Jade Kreys, PharmD, BCPP

Background: Falls are the most common cause of death from injury, non-fatal injuries, and hospital admissions for trauma in the elderly. Numerous studies have demonstrated the increased fall risk as a result of treatment with antiepileptic drugs.

Objective: To compare the association between antiepileptic drugs and fall risk requiring inpatient hospitalization in the elderly.

Methods: This nested, case-control study used claims data from the Medicare database and included all patients ≥ 65 years of age with an epilepsy diagnosis and an inpatient admission in 2014. Patients with an inpatient admission for a fall (ICD-9: E880-E888) were matched to controls, those admitted for any other diagnosis aside from fall, fracture, or trauma, in a 1:3 ratio based on age, sex, and osteoporosis diagnosis. Initially, the increased fall risk with antiepileptic use was reestablished by comparing the odds of filling a prescription for an antiepileptic drug prior to admission, based on Part D claims data, to the controls. To compare fall risk among antiepileptic drugs, a second cohort, limited only to patients receiving antidepressants, was subsequently re-matched in a 1:1 ratio based on the same characteristics. Multivariate logistic regression analysis was used to control for concomitant medications and comorbidities that may increase fall risk.

Results: The first cohort consisted of 15,345 cases and 46,035 controls. The mean age was 77.9± 8.6 years, 63.3% were female, and 27.1% had osteoporosis. Fifty-four percent of cases were diagnosed with a fracture or trauma, with the most common being a femur or traumatic brain injury. Antiepileptic was low with only use was associated with a higher risk of falls with odds ratio (OR) of 3.24 (95% confidence interval [CI]: 2.76 – 3.80, p <0.001). The second cohort consisted of 197 cases and 197 controls. Combination of more than two antiepileptic drugs accounted for 27.2% of all antiepileptic use, followed by gabapentin monotherapy (23.9%), and levetiracetam monotherapy (15.7%). Phenytoin, levetiracetam, and gabapentin were the most common medications used in combination treatment. As compared to gabapentin, the risk of falls was higher for patients receiving carbamazepine (OR 7.86, 95% CI: 2.01 – 30.73, p <0.001), levetiracetam (OR 6.77, 95% CI: 3.30 – 13.93, p <0.001), phenytoin (OR 5.76, 95% CI 2.36 – 14.07, p <0.001), and combination antiepileptic treatment (OR 2.69, 95% CI 1.5 – 4.81, p <0.001).

Conclusion: The use of antiepileptics in an elderly population with a chronic diagnosis of epilepsy is associated with increased risk of falls. Carbamazepine, levetiracetam, phenytoin, and combination antiepileptic treatment was found to have an increased risk falls relative to gabapentin, the most commonly utilized antiepileptic medication in this patient population.

Title: Synthesis and Evaluation of Stimuli-Responsive Nanogels for the Treatment of Diabetic Retinopathy

Authors:

Fitsum Feleke Sahle (presenter), PhD, College of Pharmacy, CNSU, Fitsum.Sahle@cnsu.edu

Sangyoon Kim, Jingzhao Tang, Tao L. Lowe, Department of Pharmaceutical Sciences, University of Tennessee Health Science Center

Cameron V. Fili, David J. Hamilton, Department of Comparative Medicine, University of Tennessee Health Science Center

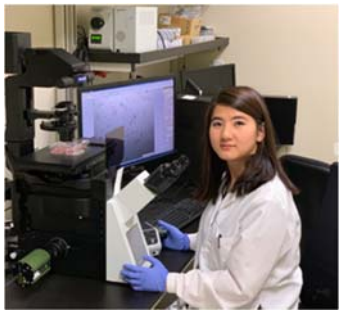
Purpose: Diabetic retinopathy (DR) affects about one third of the estimated 422 million people with diabetes mellitus and is a leading cause of vision-loss worldwide. It is associated with retinal neurovascular degeneration and studies indicated that subconjunctival insulin delivery may reduce the risk of DR onset and progression. However, the existences of the blood retinal barrier (BRB), and conjunctival and choroidal vasculature clearances limit the passage of drugs from sclera to retina. Therefore, the purpose of this project is to develop thermoresponsive and biodegradable nanogels for aqueous loading and sustained release of insulin after subconjunctival injection.

Methods: Insulin-loaded, thermoresponsive, biodegradable nanogels, containing different ratios of dextran-lactate- HEMA macromer and N-isopropylacrylamide (NIPAAM) monomer were synthesized at 45 °C, using Irgacure® 2959 as an UV initiator. The nanogels were rendered negatively charged by adding 10 mol% of acrylic acid with respect to NIPAAM. The nanoparticles were characterized with respect to size, zeta- potential, yield, and insulin loading efficiency. Insulin release kinetics from the nanogels was investigated by using the dialysis bag method. The toxicity of the nanoparticles and their degradation products in ARPE-19 cells was assessed by an MTT assay. The distribution of the nanogels in different ocular tissues following subconjunctival administration was determined in SD rats after tissue isolation, nanogel extraction and quantification.

Results: Negatively charged, 70 – 200 nm, insulin-loaded, thermoresponsive, and biodegradable nanogels with insulin loading efficiency of > 98% and yield > 80% were obtained. Insulin release from the nanogels was highly dependent on nanogel composition and drug release for more than 9 days was attained in vitro. The nanogels as well as their degradation products showed no sign of toxicity in ARPE-19 cells. The nanogels penetrated the BRB and stayed in the retina for at least 24 h after subconjunctival injection in SD rats.

Conclusions: The obtained thermoresponsive, biodegradable nanogels showed no sign of toxicity and released the loaded insulin for more than 9 days, in vitro. The nanogels could also bypass the BRB.

Title: Carfilzomib is a more potent anticancerous drug than Doxorubicin in human non-small cell lung cells



Authors:

Hang Nguyen (Presenter): College of Pharmacy, CNSU
Hang.Nguyen2562@cnsu.edu

Dinesh Vyas, MD, Dept of Surgery-SJGH and College of Medicine, CNSU, DineshVyas@yahoo.com

Advisor: Lakshmi Chaturvedi, College of Pharmacy, CNSU, Lakshmi.Chaturvedi@cnsu.edu

Introduction: Second generation proteasome inhibitor has been approved to treat refractory multiple myeloma patient. However, its anticancerous potential has not been fully elucidated in non-small cell lung cancer (NSCLC). In the current investigation, we aimed to determine the anticancer efficacy and molecular targets of Carfilzomib, a second generation irreversible proteasome inhibitor in.

Methods: Three human non-small cell lung cancerous (A549, Calu-1 and H1355) cells were cultured in RPMI-1640 medium with FBS at 37C at humidified atmosphere. Cell viability was determined using cell counting kit (CCK-8). NSCLC cells were treated with vehicle control (DMSO) or various concentrations CFZ (0-1000nM), DOX (0-3.0μM) and a combination of both to measure the cytotoxicity and anticancer potential. The molecular targets of CFZ will be determined by quantitative real-time PCR for cell-cycle regulatory genes in human NSCLC cells.

Results: We observed that CFZ significantly dose dependently inhibited cell proliferation of all three NSCLC (A549, Calu-1, and H1355) cells at 72 hour time-point. We further observed that CFZ found to more sensitive to H1355 than Calu-1 and A549 cells. Nonetheless, DOX also significantly inhibited proliferation of only H1355 cells but had very minimal effect on other two NSCLC cells. A combination of both CFZ and DOX did not further enhanced the rate of growth inhibition of any NSCLC cells.

Conclusion: The current study revealed Carfilzomib (CFZ) might have a promising anticancer therapeutic potential in treating human non-small lung cancer patients.

Title: A Review of Synthetic Lethality and Cancer Therapy

Author:

Hannah Neiger (presenter), College of Medicine, CNSU

Shymaa Bilasy, Ph.D., College of Medicine, CNSU

Catherine Yang, Ph.D., College of Medicine, CNSU

Yihui Shi, M.D., Ph.D., College of Medicine, CNSU

Abstract:

BRCA1 (breast cancer type 1) and *BRCA2* (breast cancer type 2) are tumor suppressor genes with pivotal roles in the development of breast and ovarian cancers. *BRCA1* and *BRCA2* are essential for the DNA double-stranded break (DSB) repair via homologous recombination (HR), which is the only known virtually error-free DNA repair mechanism. Following *BRCA1* or *BRCA2* mutations, HR is directly compromised thereby; forcing cells to adopt alternative error-prone repair pathways that will ultimately result in tumorigenesis. Synthetic lethality denotes the process of cell death following the simultaneous inactivation of two synthetic lethal genes. Whereas, the inactivation of one gene alone does not affect cell viability. Therefore, the fundamental idea of synthetic lethality can be instrumental in identifying new therapeutic targets for the *BRCA1* or *BRCA2* mutations. The poly(ADP-ribose) polymerase A (PARP) is the synthetic lethal partner of the *BRCA* genes. Its role is imperative in the single-strand break (SSB) DNA repair system. Recently, Olaparib (a PARP inhibitor) was approved for treatment of BRCA1/2 breast and ovarian cancer as the first successful synthetic lethality-based therapy, showing considerable success in the pursuit of effective targeted cancer therapeutics. Nevertheless, the possibility of drug resistance to cancer targeted therapy based on synthetic lethality necessitates the development of additional therapeutic options. Therefore, current research focuses on developing other synthetic lethal partners for *BRCA1* and *BRCA2* as well as other targeted treatments for clinical use. This literature review will address cancer predisposition genes, including *BRCA1*, *BRCA2*, and *PALB2*; synthetic lethality in the context of DNA repair machinery as well as available treatment options.

Title: Selective S1P3 Receptor Antagonism inhibits S1P3 Agonist-induced Cell Proliferation of Fibroblast Cells, as a Drug Target Approach for Intestinal Fibrotic Crohn's Disease

Authors:

Hannah Tran (Presenter), College of Pharmacy, CNSU, Hannah.Tran4836@cnsu.edu

Ruthy Tran, College of Pharmacy, CNSU, Ruthy.Tran1965@cnsu.edu

Leo Fitzpatrick, College of Pharmacy, CNSU, lfitzpatrick@cnsu.edu

Tibebe Woldemariam, College of Pharmacy, CNSU, TWoldemariam@cnsu.edu

Advisor: Lakshmi Shankar Chaturvedi, College of Pharmacy, CNSU, Lakshmi.Chaturvedi@cnsu.edu

Introduction: Inflammatory bowel diseases (IBD), that includes Crohn's disease (CD) and ulcerative colitis (UC), affect as many as 1.6 million Americans. Severe fibrosis is seen in up to 30% of patients with Crohn's Disease (CD), and currently, there is no effective therapy for CD patients with fibrosis. Sphingosine 1-phosphate (S1P), a bioactive, small lipid molecule, plays essential roles in cellular processes, including angiogenesis, migration, cytoskeleton rearrangement, proliferation, and cell survival by acting through five G protein-coupled receptors ($S1P_1$-$S1P_5$). These results suggest that molecule targeting S1P3 have potential to be developed into drugs against intestinal fibrosis associated with CD. However, role of S1P3 receptor in the modulation of fibrotic-CD has not been fully elucidated. In current study, we investigated Role of Sphingosine-1-phosphate receptor (S1P3) agonist, and the efficacy of S1P3 antagonists on the proliferation of mouse-3T3 and human colonic fibroblast (CCD-18Co) cells.

Methods: Cell Counting Kit-8 (CCK-8) and BrdU incorporation assays were used to determine the efficacy of S1P3 agonist on the induction of cell proliferation in both fibroblast cells and various inhibitors were used to determine the S1P3 agonist-induced proliferation of 3T3 and CCD-18Co cells.

Results: We observed that S1P3 agonist peptide induces proliferation of both mouse-3T3 and human CCD-Co-18 fibroblast ells and it was inhibited by pan S1P3 inhibitor-TY-52156. Furthermore, an antagonist of S1P3 peptide blocked S1P3 agonist-induced proliferation of 3T3 and CCD-Co-18 cells. In fact, bioactive natural plant product extract also blocked the S1P3 agonist-induced cell proliferation of mouse 3T3 cells.

Conclusion: Our data suggest that S1P3 receptor antagonist might have role in the modulation of S1P3 agonist-induced in intestinal fibrotic Crohn's disease. However, studies need to be conducted in vivo to confirm these findings.

Title: Targeted miR-146a: an Innovative Treatment Modality for Shear Stress-induced Vascular Inflammation

Authors: Hassan Alshiyab, PharmD (presenter), MPS, CNSU, hassan.al-shiyab6803@cnsu.edu.
Sheena Thomas BS, Division of Cardiology, Emory University School of Medicine and Atlanta VA Medical Center, sheena.ann.thomas@emory.edu.
Kim Rooney BS, Division of Cardiology, Emory University School of Medicine and Atlanta VA Medical Center, kimberly.rooney@emory.edu.
Katherine Ferrara PhD, Department of Radiology & Molecular Imaging Program, Stanford University, kwferrar@stanford.edu.
Advisor: Islam Mohamed B.Pharm, MS, PhD, PBS Dept., CNSUCOP islam.mohamed@cnsu.edu.
Charles D. Searles MD, Division of Cardiology, Emory University School of Medicine and Atlanta VA Medical Center, csearle@emory.edu.

Introduction: Atherosclerotic lesions preferentially localize to areas exposed to low magnitude oscillatory shear stress (OSS) forces. MicroRNA-146a (miR-146a) is known to be shear-responsive and can potentially modulate vascular inflammation through suppression of toll-like receptor (TLR) inflammatory pathway. Nevertheless, little is known about the interplay between miR-146a and TLR pathway in response to acute OSS in vivo. Therefore, we tested the hypotheses that acute induction of OSS in vivo results in vascular inflammation through dysregulation of miR-146a and activation of the TLR inflammatory pathway and whether targeted miR-146a can prevent OSS-induced vascular inflammation.

Methods: 11-13 weeks old male wild type (WT) mice were subjected to abdominal aortic coarctation (AAC); a unique model of acute induction of OSS in mouse abdominal aorta, for 3-7 days. miR-146a expression was enhanced by targeted delivery of miR-146a using tail vein injections (200□g/mouse/day for 2 days) of nano-coated cationic lipoparticles (CCLs+miR-146a), compared with non-targeted CCLs+miR-146a, targeted CCLs+scrambled miR or vehicle respectively as controls. Downstream acute OSS segments were compared to upstream unidirectional shear stress (USS) segments using total RNA deep sequencing, RT-PCR, western blot and ANOVA.

Results: in WT mice, total RNA deep sequencing revealed a significant upregulation of the TLR pro-inflammatory pathway in OSS versus USS segments that was associated with decreased miR-146a expression. Targeted CCLs+miR-146a treatment resulted in significant inhibition of VCAM-1, MCP-1 and MMP-9 expression in OSS compared with USS segments versus corresponding segments in non-targeted CCLs+miR-146a, targeted CCLs+scrambled miR or vehicle control groups.

Conclusion / Implications: our findings support a key shear-sensitive signature response of miR-146a to acute OSS in vivo & its direct role as a negative regulator of the pro-inflammatory TLR pathway. Combining the state of the art AAC model with the targeted CCL delivery vehicles will lay the foundation for developing innovative and specific miR-based therapeutic modalities for atherosclerosis.

Title: Complement Activation Fragment C4a Inhibits LPS-induced Signaling in Human Moncytes and Endothelial Cells

Authors:

Hongbin Wang, Department of Pharmaceutical and Biomedical Sciences, California Northstate University College of Pharmacy, CA 95757, USA

John D. Lambris, Department of Pathology & Laboratory Medicine, Perelman School of Medicine University of Pennsylvania, Philadelphia, PA 19104, USA

Abstract: Activation of the complement cascade is one of the major effectors of the inflammatory responses. Cleavage of complement components in the course of complement activation produces low-molecular-weight peptides, including C3a, C4a, and C5a. Complement activation fragments C3a and C5a have been extensively studied and demonstarted potent anaphylatoxic properties. Our recent study idnetified that C4a, fragmented from C4 activation, mediates effector functions through binding to protease-activated receptor (PAR) 1 and PAR4. Early studies demonstrated that animals with the deficiency of complement C4 were reported to be more susceptable to endotoxin-induced shock, suggesting that C4 protects animals from endotoxic effects. However, the molecular mechanism for C4 protective effect on endotoxic shock in animals is poorly understood. Methods: We propose that C4 activation fragment, C4a, possiblly through binding to PAR1/4 on platelets, monocytes, and endothelial cells, inhibits LPS-induced platelet aggregation, IL-1□ and TNF□ cytokine production from monocytes, and endothelium permeability to achieve C4 protective effects in endotoxic shock animal models. Results: In the present study, we found that pretreatment with C4a to human primary monocytes can significantly inhibit LPS-induced IL-1beta and TNFalpha production. Moreover, LPS-induced the phosphorylation of extracellular signal-regulated kinases (ERK) and [Ca2+] influx were significantly inhibited by the pretreatment of C4a. Our experiments also revealed that C4a significantly decreased endothelium permeability when human endothelial cells were cultured in the presence of LPS, indicating under endotoxemia condition, C4a prevents LPS-induced endothelium disruption. Implications: Our data provide the insight into the mechanism of C4's protective effect on endotoxic shock and would provide a valuable resource for the scientific community to generate future therapeutic interventions for the treatment of clinical endotoxemia. Future direction: We will use the mouse model to elucidate the role of C4a-PAR1/4 interaction on LPS-induced endotoxic effects.

Title: Identifying Risk Factors for Hydrocodone and Illicit Drug Abuse in the U.S. to Facilitate Prevention Planning

Authors:
James A. Lugtu, BS, Pharm.D. Student, Class of 2022, College of Pharmacy, CNSU. JamesAlexander.Lugtu8822@cnsu.edu

Amy Ferrarotti, BS, Pharm.D. Student, Class of 2021, College of Pharmacy, CNSU. amy.ferraroti4907@cnsu.edu

Craig Wetterer, Ph.D., J.D., College of Psychology, CNSU. craig.wettrer@cnsu.edu

Jose Puglisi, Ph.D. College of Medicine, CNSU. Jose.Puglisi@cnsu.edu

Ashim Malhotra, PharmBS, MS, PhD, Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, CNSU. ashim.malhotra@cnsu.edu

Introduction: The U.S. opioid epidemic is at a crisis point with 279,065 overdose-related deaths reported in 2017. Our goal was to determine risk factors for prescription and illicit drug use in the U.S.

Methods: Using the U.S. Substance Abuse & Mental Health Data Archive (SAMHDA) and the 2017 National Survey on Drug Use and Health (NSDUH), we analyzed the effect of 1) race, 2) age, 3) gender, 4) total family income, and 5) education on self-reported drug use from 56,276 individuals across 15 categories. The prescription drugs included in our study were hydrocodone, oxycodone, tramadol, codeine, morphine, fentanyl, buprenorphine, meperidine, hydromorphone, and methadone.

Results: Hydrocodone was the most abused prescription drug (2.6%), while ecstasy was the most abused illegal substance (1.3%), with hydrocodone abuse equal to that of ecstasy, marijuana, crack, cocaine, and heroin combined. Hydrocodone abuse was highest in the Native American population (4.8%), four times greater than ecstasy use (1%), two-fold greater than ecstasy use in Caucasians (3% vs. 1.4%) and Black/African Americans (2% vs 1%), while it was the least in Asians (1%). The most likely age of abuse was between 18 to 30 years. Hydrocodone abuse in the older population was 25-fold greater than ecstasy. Use was higher for individuals with college/associate's degree (3.7%) than graduates (1.8%) and higher where total family incomes were less than $20,000 (3.2%) compared to $75,000 or more (2.2%), $p < 0.01$. Logistic regression showed that the variable most strongly correlated with drug abuse was education with a weight factor of 37.6%, followed by age-26%, gender-22.7%, and race-11%, while net family income only contributed 3.7%.

Conclusion: Our study revealed that opioid prescription rather than illegal substance abuse was higher, hydrocodone was the most abused prescription drug in 2017, and the overall education level and total family income were poorly correlated risk factors for drug abuse.

Title: PBPK and its Virtual Populations: Prediction of Pediatric Furosemide Dose Using SimCyp®

Authors:

Janie Yu (presenter), P3, CNUCOP, Janie.yu1236@cnsu.edu.

Dr. Rania Elkeeb, PhD.relkeeb@gmail.com.

Advisor: Dr. Eman Atef, PhD., Department: Pharmaceutical and Biomedical Sciences, CNUCOP, eatef@cnsu.edu.

Introduction: Dosing regimens in pediatrics are commonly and empirically derived from adult clinical trial data. However, extrapolating pediatric dose from adult regimen could potentially result in over or under dosing due to the changing physiology in the pediatric population. Hence, substantially impacting the pharmacokinetics of the drug. The aim of this study is to simulate pediatric clinical studies to show the potential applications of mechanistic physiologically based pharmacokinetic modeling software (PBPK) in pediatric furosemide dose calculation.

Methods: In our study, we performed a series of literature search to collect data on current furosemide dosing of pediatric patients. We simulated the furosemide pharmacokinetics in the pediatric population; age 0-6 months in both fed and fasted states using the Simcyp® simulator (version 18). The Advanced Dissolution Absorption and Metabolism Model (ADAM) was used. Analysis of simulated data were compared to published clinical values.

Results: The developed PBPK model reasonably predicted the C_{max}, T_{max} and AUC across age groups of 0-6 months old. The predicted C_{max}, T_{max}, and AUC are within a two-fold range of the observed data for each individual patient, which indicates that the PBPK model is useful in predicting furosemide PK and dose in pediatric population.

Conclusion/Implications: A PBPK Simcyp ® model of furosemide in infants correlates well with published clinical data. However, our limitation of clinical data from one patient will require additional clinical data involving the effect of food in the pediatric population in order to optimize validation of our pediatric model. Implications of this study conclude that a PBPK model developed with SimCyp® may be used to simulate pediatric doses of different drugs.

Title: Implementation and evolution of a student-driven mentorship program in the CSHP-Sacramento Valley chapter

Authors:

Jeffrey Nehira, BS, PharmD, FCSHP (presenter), CAS/EE, College of Pharmacy, CNSU, Jeffrey.nehira@cnsu.edu.

Hae Ji Shin, College of Pharmacy, CNSU
Lucas Harjono, College of Pharmacy, UOP
Jaqueline Saechao, College of Pharmacy, CNSU
Jordan Yee, College of Pharmacy, UOP

Introduction: The CSHP-Sacramento Valley Chapter (CSHP-SV) launched its mentorship program in 2012 with the innovation of promoting professional growth of student members through mutual support and networking. This Mentorship Program developed into a student-centered program involving students from both University of the Pacific (UOP) and California Northstate University (CNU). Between September 2018 and May 2019, there were 47 total participants (29 mentees and 18 mentors). This poster describes the structure of the CSHP-SV Mentorship Program and analyzes improvements made in the past year based on survey results from mentor and mentee participants.

Methods: The Mentorship Committee consists of the Mentorship Chair from CSHP-SV, and a Student Chair from each school. They coordinate recruitment, mentor-mentee matching, program activities, and monitor feedback. Prospective mentees and pharmacist mentors were asked to complete respective applications between September and December. Mentors were taken from a survey of CSHP-SV pharmacist volunteers who wished to take a more active role in furthering the development of the next generation of pharmacists. Mentees were chosen from an applicant pool of both UOP and CNU students who sought expertise and support from experienced, active pharmacists. Participants' application response preferences were used to match mentees to their respective mentors with consideration of various factors such as goals of the mentee, expertise of the mentor, and shared interests. Mentors and mentees are expected to develop their own professional relationships. The program chairs plan regular group activities, such as an appreciation dinner and an end-of-the-year picnic. Since 2013, an annual Mentor-Mentee "Meet and Greet" session is coordinated at CSHP Seminar. Measures of success and areas for improvement of the program are determined through surveys sent to participants at the end of each school year. Baseline figures from 2018 show mentorship program satisfaction score of 9.4 out of a scale of 10 for mentees and 8.75 for mentors. These results showed increased scores from 8.9 for mentees and 8.0 for mentors in 2017.

Conclusion/Implications: This continually evolving Mentorship Program strives to promote professional growth among its members through developing mutually beneficial relationships between pharmacist mentors and student mentees. For the purpose of its continuing improvement to increase membership involvement, the program plans to implement a requirement for the mentee to contact his or her mentor and establish additional events throughout the year to strengthen the network between members and support further improvement in members' careers. These events include but are not limited to: Health-System Pharmacy Roundtable and Mock Job Interviews. Our structure can potentially influence other chapters to implement similar programs for its students to reach their professional goals.

Title: Sirt3 regulates Insulin Signaling Pathway in Adipocytes


Authors:
Jennifer Huang (presenter)*, Jennifer Magness (presenter)*, Jake Castroreale, Tin Le, George Talbot, Melanie Rose, Linh Ho#
CNSU College of Pharmacy
* J.H. and J.M. contributed equally to this work
Advisor: Dr. Linh Ho, Pharmaceutical & Biomedical Sciences
Corresponding author: California Northstate University College of Pharmacy, Elk Grove, CA 95757, USA. Tel.: +1 916 686 7370. Email: linh.ho@cnsu.edu

Introduction: The sirtuin family of proteins are integral in various physiological processes related to aging, metabolism, cancer, inflammation, neurodegeneration and cardiovascular diseases. Sirtuin-3 (Sirt3) has been determined the major mitochondrial deacetylase playing an essential role in various metabolic pathways including fatty acid breakdown, tricarboxylic acid cycle, and oxidative phosphorylation. The purpose of this research is to investigate effects of Sirt3 on insulin signaling pathway in adipocytes.

Methods: We utilized knockout model using siRNA or Sirt3 inhibitor (3-TYP) to inhibit Sirt3 expression. We induced Sirt3 expression using Sirt3 plasmid versus plasmid without gene insertion as control or Sirt3 activator (Honokiol) in 3T3-L1 cells. Quantitative PCR and western blots were used to quantify amounts of target genes and evaluate protein expression levels. Oil Red O staining was also performed to visualize and quantify stored lipid amounts in treated cells compared to controls.

Results: Sirt3 inhibition decreased adipogenesis and lipid accumulation in differentiated adipocytes from 3T3-L1. Inhibition was associated with stimulated adipokines TNF-α and IL-6 released from adipocytes; however, suppressed adiponectin and perilipin-1. Sirt3 modulated insulin signaling pathway in adipocytes via regulating glycogen synthase kinase-3β (GSK-3β). Induction of Sirt3 resulted in increased GSK-3β protein expression and decreased insulin-mediated phosphorylation of GSK-3β at Ser9. Sirt3 induction stimulated lipolysis in maturing adipocytes including hormone sensitive lipase (HSL), lipoprotein lipase (LPL), and adipose triglyceride lipase (ATGL). Inhibition of Sirt3 resulted in decreased GSK protein expression and increased insulin-mediated phosphorylation of GSK-3β at Ser9.

Conclusion/Implications: In summary, Sirt3 inhibition induced inflammatory response TNF-α and IL-6 released from adipocytes. Sirt3 induction reversed inflammation-related changes in adipokines, facilitated insulin signaling transduction pathway by increased GSK-3β expression and decreased phosphorylation modification of GSK-3β at serine residue 9 and improved insulin sensitivity in adipocytes. These findings contribute to the effort of targeting Sirt3 for treatment of obesity and type 2 diabetes.

Title: Efficacy and Safety of Transitioning From Clonidine to Dexmedetomidine in Mechanical Ventilation

Authors:

Jinjing Cheng, PGY-1 Resident, College of Pharmacy, CNSU, jinjing.cheng@cnsu.edu

Introduction: Critically ill patients requiring mechanical ventilation usually require sedation to minimize discomfort, and to treat agitation along its negative consequences. The 2013 Society of Critical Care Medicine guidelines for Pain, Agitation and Delirium suggest the use of non-benzodiazepine sedatives such as dexmedetomidine and propofol because they are associated with a reduced duration of mechanical ventilation, shorter ICU length of stay, and lower incidence of delirium.

Dexmedetomidine is a selective α2-receptor agonist with sedative, analgesic, and sympatholytic properties. Patients on dexmedetomidine are more arousable and interactive and has minimal respiratory depression. Dexmedetomidine is only available in IV formulation and requires cardiovascular monitoring due to the risk of hypotension and bradycardia. Clonidine is also a α2-receptor agonist with sedative, analgesic and anxiolytic properties.

ICU patients who require dexmedetomidine for sedation are required to receive the medication in the ICU. The high cost of dexmedetomidine and ICU stay may be mitigated by the use of enteral clonidine immediate release (IR). The purpose of this study is to assess the efficacy and safety of patient's transition from dexmedetomidine to clonidine at Alta Bates Summit Medical Center and Eden Medical Center.

Methods: This retrospective observational cohort study will be conducted at Eden Medical Center and Alta Bates Summit Medical Center between August 1, 2018 and August 31, 2019. The research data will be collected utilizing the Sutter EHR system (EPIC) and research analysis shall be descriptive.

Title: Disease Ecology and Diversity of Native Bees in Sacramento

Authors:
Lauren Hisatomi (presenter), California Northstate University, College of Health Sciences, Lauren.Hisatomi5946@cnsu.edu.

Patrick Reed (presenter), California Northstate University, College of Health Sciences, Patrick.Reed2894@cnsu.edu

Advisor: Dr. Kit Keane, Department of Math and Science, California Northstate University, College of Health Sciences, Kristopher.Keane@cnsu.edu

Introduction: Bees are ubiquitous inhabitants of most environments, even ones that have been highly altered such as cities. However, little study has quantified the effects of urbanization on this group. The European Honeybee, *Apis Mellifera*, which is well-studied due to its importance in commercial agriculture and the recent characterization of colony collapse disorder, provides us with effective tools to assess the disease ecology of thousands of lesser-known native species which inhabit California. While surveys indicate that urban bee assemblages are able to maintain relatively high diversity by relying on hotspots of floral resources and nesting habitat (ex. gardens and wild spaces), we have no knowledge directly measuring the health of these populations. Here we study the presence and disease/parasite loads across species and sites in human altered landscapes.

Methods: We used a GIS-based approach to test for patterns in abundance and diversity of bees collected passively via blue-vane traps. Parasite screening was conducted via DNA extraction and PCR to assess the relative prevalence and distribution of fungal parasites in native bees (*Nosema* spp.).

Results: We have identified several specimens that have tested positive for *Nosema* spp. No correlations have been identified between environmental variables and presence/disease data.

Conclusion/Implications: The results indicate that *Nosema* is present in native carpenter and bumble bees (*Xylocopa* and *Bombus* spp.) in the Sacramento area. Interestingly, we have not yet found any correlations between disease, diversity, or abundance with regards to environmental variables. We are currently working to increase the number of specimens screened and expanding to additional collection sites, additional environmental variables, and additional diseases such as RNA viruses.

Title: Removal of Early Senescent Cells to Protect Retinal Ganglion Cells in Glaucoma

Authors:

Mary Jabari (presenter), California NorthState University, College of Graduate Studies, MPS student, Mary.Jabari6725@cnsu.edu.

Dr. Viet Anh Nguyen Huu, Field Application Scientist at Precision NanoSystems, nhva78@gmail.com.

Advisor: Dr. Dorota Skowronska- Krawczyk, Ophthalmology Department, University of California, San Diego, DorotaSK@health.ucsd.edu.

Abstract: Glaucoma is a group of diseases with diverse molecular mechanisms of pathogenesis, all of which converge on a common pathway leading to typical optic nerve damage and consequent characteristic patterns of visual field loss, what may ultimately progress to blindness. Of all the glaucoma-associated risk factors, patient's age is by far the strongest and consistently reported. Concurrent with the age-related increase in the prevalence of glaucoma is the age-related decreased population of retinal ganglion cells (RGCs) in the retina. Pathological studies have shown a steady decrease of RGC number during normal aging, starting at a young age and continuing at a rate of approximately 5000 cells per year. Glaucomatous loss of RGCs can be therefore viewed as a premature aging effect. In our recent work, we observed that the expression of p16Ink4a, a gene whose expression levels increase during normal aging, is strongly up-regulated upon increased IOP, leading to enhanced senescence in the RGCs, and, most likely as a direct consequence, to RGC death. Importantly, senescent cells contribute to aging and age-related diseases by altering tissue microenvironments via their senescence-associated secretory phenotype (SASP) molecules, which are largely composed of inflammatory chemokines and cytokines, matrix-remodeling proteases and growth factors. We thus theorize that glaucoma progression is accelerated due to prolonged exposure to microenvironment alterations caused by naturally aging senescent cells.

Title: Role of the SIX6 transcription factor in the pathogenesis of glaucoma

Authors:

Mary Jabari (presenter), California NorthState University, College of Graduate Studies, MPS student, Mary.Jabari6725@cnsu.edu.

Dr. Viet Anh Nguyen Huu, Field Application Scientist at Precision NanoSystems, nhva78@gmail.com.

Advisor: Dr. Dorota Skowronska- Krawczyk, Ophthalmology Department, University of California, San Diego, DorotaSK@health.ucsd.edu.

Abstract: Glaucoma is a group of diseases with diverse molecular mechanisms of pathogenesis, all of which converge on a common pathway leading to typical optic nerve damage and consequent characteristic patterns of visual field loss, what may ultimately progress to blindness. Of all the glaucoma-associated risk factors, patient's age is by far the strongest and consistently reported. Concurrent with the age-related increase in the prevalence of glaucoma is the age-related decreased population of retinal ganglion cells (RGCs) in the retina. Pathological studies have shown a steady decrease of RGC number during normal aging, starting at a young age and continuing at a rate of approximately 5000 cells per year. Glaucomatous loss of RGCs can be therefore viewed as a premature aging effect. Several studies have identified nonsynonymous coding variant SIX6-rs33912345 His141Asn as strongly associated with glaucoma. A murine model of glaucoma was established by raising intraocular pressure (IOP) to induce RGC injury. To directly assess the functional relevance of SIX6-His versus SIX6-Asn variants in eye function, transcriptomic and epigenetic changes in RGC isolated from mouse strains expressing the "protective" and "risk" SIX6 allele were assessed. We concluded that the SIX6-His mice are more vulnerable to RGC cell loss post IOP and have potentially a more pronounced loss of functionality in these surviving RGC's. The SIX6 gene is a target for further studies and treatment for age related eye diseases.

Title: Understanding the mechanism of age-related macular degeneration

Authors:

Mary Jabari (presenter), California NorthState University, College of Graduate Studies, MPS student, Mary.Jabari6725@cnsu.edu.

Daniel Chen, Scientist at Spring Discovery, ddanielchen0@gmail.com

Advisor: Dr. Dorota Skowronska- Krawczyk, Ophthalmology Department, University of California, San Diego, DorotaSK@health.ucsd.edu.

Abstract: Methylation of the regulatory region of the Elongation Of Very Long Chain Fatty Acids-Like 2 (ELOVL2) gene, an enzyme involved in elongation of long-chain polyunsaturated fatty acids, is one of the most robust biomarkers of human age, but the critical question of whether ELOVL2 plays a functional role in molecular aging has not been resolved. Here, we report that Elovl2 regulates age- associated functional and anatomical aging in the mouse retina in vivo, which has direct relevance to age-related eye diseases such as age-related macular degeneration (AMD), a leading cause of blindness worldwide. We show that an age-related decrease in Elovl2 expression is associated with increased DNA methylation of its promoter. In vivo reversal of this Elovl2 promoter hypermethylation through intravitreal injection of a demethylating agent, 5-Aza- 2'-deoxycytidine (5-aza-dc), leads to increased Elovl2 expression, and concomitant rescue of age-related decline in visual function as measured by electroretinography (ERG) in vivo. Mice carrying a point mutation C234W that disrupts Elovl2-specific enzymatic activity display electrophysiological characteristics of premature visual decline, as well as the early appearance of autofluorescent deposits, well-established functional and structural markers of aging in the mouse retina. Finally, we find drusen-like deposits underneath the retinal pigment epithelium in Elovl2 mutant mice, a pathological hallmark of AMD. These findings indicate that ELOVL2 activity regulates aging in the retina, provide a molecular link between polyunsaturated fatty acids elongation and drusen biogenesis, and suggest novel therapeutic strategies for treatment of AMD and other age-related eye diseases.

Title: Klebsiella Pneumoniae Carbapenemase (KPC)-producing *Escherichia Coli* Shield *Staphylococcus aureus* and *Enterococcus Faecalis* from Beta–lactam Exposure

Authors:
Michael Kent (Presenter), PharmD Candidate 2020, CNSU, Michael.Kent3017@cnsu.edu

Mohammadamin Asadirad, PharmD Candidate 2020, CNSU, Mohammadamin.Asadirad4346@cnsu.edu

Ayeh Barekat, PharmD Candidate 2021, CNSU, ayeh.barekat6108@cnsu.edu

Fantasia Rodriguez, PharmD Candidate 2020, CNSU, Fantasia.Rodriguez2760@cnsu.edu

Advisor: Dr. Justin Lenhard, PharmD, Department of Clinical and Administrative Sciences, College of Pharmacy, CNSU, Justin.lenhard@cnsu.edu

Introduction: The spread of carbapenem-resistant Enterobacteriacea (CRE) threatens public health. The present study's aim was to quantify the in vitro killing of β-lactams against methicillin-sensitive *S. aureus* (MSSA) or ampicillin-susceptible *E. faecalis* during co-culture with CRE.

Methods: Two ampicillin-susceptible *E. faecalis* isolates (AR Bank#0573 and AR Bank#0671), two cefazolin-susceptible MSSA isolates (ATCC#25923 and AR Bank#0484), and one KPC-producing *E. coli* isolate (AR Bank#0114) were utilized in 24-hour static time-killing studies. The pharmacodynamics of ampicillin (for experiments utilizing *E. faecalis*) or cefazolin (for experiments utilizing MSSA) were assessed against each Gram-positive organism alone or during co-culture with the *E. coli*. Pharmacodynamics were quantified using a Hill-type mathematical model that described the log ratio change of bacterial counts after 24 hours of antimicrobial exposure.

Results: In the time-killing analysis, 96 mg/L of ampicillin achieved a 4.1 log CFU/ml reduction against *E. faecalis* AR Bank#0573 in monoculture, whereas the same concentration only achieved a 1.8 log CFU/ml reduction against the organism during co-culture. Against MSSA, cefazolin concentration 16 mg/L achieved a 2.3 log CFU/ml reduction and a 2.5 log CFU/ml reduction against MSSA ATCC#25923 and MSSA AR Bank#0484 in monoculture, respectively, whereas the same concentration killed 1.4 log CFU/ml of MSSA ATCC#25923 and achieved a 0.6 log CFU/ml reduction against MSSA AR Bank#0484 during *E. coli* co-culture. In the Hill Function analysis, maximal killing was significantly lower in co-culture in comparison to monoculture for *E. faecalis* AR Bank#0573 [Emax 1.14 (95% CI 0.80 – 1.49) versus 7.08 (95% CI 6.70 – 7.46)], *E. faecalis* AR Bank#0671 [Emax 1.16 (95% CI 0.86 – 1.46) versus 7.29 (95% CI 6.84 – 7.74)], MSSA ATCC#25923 [Emax 2.26 (95% CI 1.09 – 3.43) versus 4.62 (95% CI 3.69 – 5.55)] and MSSA AR Bank#0484 [Emax 2.17 (95% CI 1.07 – 3.27) versus 4.89 (95% CI 4.12 – 5.66)].

Conclusions: KPC-producing *E. coli* protected MSSA and ampicillin-susceptible *E. faecalis* from β-lactam exposure.

Title: Therapeutic Effects of Glatiramer Acetate and Grafted CD115+ Monocytes in a Mouse Model of Alzheimer's Disease

Authors:

Michelle Moyseyev Senderovich (presenter), Yosef Koronyo, Brenda C. Salumbides, Julia Sheyn, Lindsey Pelissier, Songlin Li, Vladimir Ljubimov, David Daley, Dieu-Trang Fuchs, Michael Pham, Keith L. Black, Altan Rentsendorj, Maya Koronyo-Hamaoui

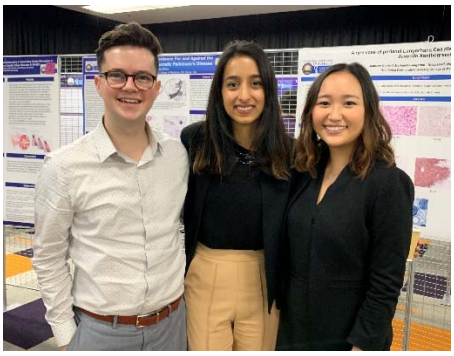
Introduction: The role of monocytes in repair and regeneration of Alzheimer's disease (AD) is still controversial. A T cell-based immunization was found to be effective in attenuating AD-like neuropathology and to induce infiltration of bone marrow-derived cells into the brain, involved in b-Amyloid (Ab) phagocytosis.

Methods: Here, we vaccinated APPSWE/PS1dE9 double-transgenic mice model of AD, using T cell-based vaccinations as glatiramer acetate (GA) copolymer or an altered myelin- derived (MOG45D) peptide loaded on dendritic cells (DC-45D), and investigated neuropathological consequences as well as molecular and cellular milieu modifications, with and without systemic blood-enrichment with Gr-1+ monocytes.

Results: We found that both GA and DC-45D vaccinations were extremely effective in limiting b-Amyloid (Ab) insoluble and soluble burden and the neuroinflammation, as well as in reviving hippocampal neurogenesis and halting cognitive decline in APP/PS1-Tg mice. Furthermore, a combination therapy of GA vaccination and systemic blood-enrichment with Gr-1+ monocytes were found to be superior in ameliorating AD pathology and especially in improving learning performance. We attribute this benefit to the observed shift in phenotype of local cell population surrounding active amyloid lesions, especially the recruitment of monocyte-derived macrophages directly involved in Ab clearance and displaying an anti-inflammatory phenotype (TNF allow/IL-10high). Following vaccination, we also detected a significant increase in brain neurotrophic support (IGF-1 and TGFb) and availability of MMP-9, an enzyme capable to degrade Ab and chondroitin sulfate proteoglycan (CSPG) scar tissue and growth-inhibiting protein.

Conclusion/Implications: Altogether, these results identify infiltrating monocytes and a local cellular and molecular immunoregulation, as key features pivotal for fighting against AD-like neuropathology. Furthermore, it identifies infiltrating monocytes and CD4 T cells as modulators of local immune-regulation and their pivotal roles in fighting AD-like neuropathology.

Title: A Surveillance, Epidemiology, and End Results Analysis of Long Term Patient Outcomes with External Beam Radiation Therapy ± High-Dose Brachytherapy for Squamous Cell Carcinoma of the Vulva



Authors:
Mollee Chu (presenter), College of Medicine, CNSU, mollee.chu5563@cnsu.edu
Mariam Soni (presenter), College of Medicine, CNSU, mariam.soni1481@cnsu.edu
Austin Thompson (presenter), College of Medicine, CNSU, austin.thompson2703@cnsu.edu
Advisor: Jose Puglisi PhD, College of Medicine, CNSU, jose.puglisi@cnsu.edu
Advisor: Tracy Yarbrough MD PhD, College of Medicine, CNSU, tracy.yarbrough@cnsu.edu

Introduction: Little is known whether combined brachytherapy (BT) with external beam radiation therapy (EBRT) has better outcomes than EBRT alone, with recent evaluation showing no significant improvement in survival. The goal of this study was to reevaluate patient outcomes for vulvar cancer and compare outcomes for individual subtypes to see if there is an improvement when BT is added to EBRT.

Methods: Data between 2000 and 2016 from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database was analyzed. Patients with EBRT+BT or EBRT treatment alone were analyzed with the exclusion of patients with prior surgical resection. Overall survival (OS) and disease-specific survival (DSS) were assessed using the Kaplan- Meier method and significance denoted with the Log Rank (Mantel-Cox) method.

Results: A total of 1,188 patients were analyzed, with 1,135 receiving EBRT alone and 53 receiving EBRT+BT. A combination of EBRT+BT was significantly associated with better overall ($p = 0.014$) and disease-specific survival ($p = 0.028$) compared to EBRT alone. EBRT+BT treatment was associated with better outcomes for patients receiving treatment between 2010-2016 ($p = 0.008$) compared to EBRT alone, while there was no significant benefit for patients receiving treatment between 2000-2009. Better overall survival ($p = 0.046$) and disease-specific survival ($p = 0.032$) outcomes were seen in patients under 70 receiving combination therapy rather than EBRT alone. There was no significant association between treatment methods for certain subgroups, including race and year of diagnosis.

Conclusion: EBRT+BT is associated with improved survival compared with EBRT alone in the overall group of patients. Certain subgroups may not receive significant survival benefit from EBRT+BT, and should consider this when deciding on radiation therapy; however, this may require further analysis in the future with a greater cohort of patients.

Title: A Retrospective, Observational Study Evaluating Cost Efficacy, Safety and Use of Single Dose Vials versus Prefilled Syringes

Author: Muhamod Saied, PharmD.

Abstract: Anesthesiologists prepare prior to each case by drawing up medications from a vial/ampule into a syringe which require proper labeling and storage. Some medications drawn are either not used or only a small dose is needed per case. The market currently has prefilled anesthesia syringes available that would minimize waste and accountability but can be costly. Additionally, medication error is elevated due to improper labeling and storage safety concerns. The purpose of this study is to assess if prefilled syringes are more cost effective and would improve patient safety compared to self-drawn syringes. We will discover in this project if transitioning to prefilled syringes of anesthesia medications be more cost effective than using single dose vials/ampules?

Anesthesiologists work in high stress environments where they must often procure, draw and administer medication themselves. Transitioning to prefilled syringes may be a step in the right direction to reduce the number of steps in administering a medication and prevent unnecessary medication errors that can occur in the OR.

While prefilled syringes have been endorsed by the Anesthesia Patient Safety Foundation it still has not been fully adopted by practitioners. In a study that directly compared the use of self-drawn syringes and prefilled syringes, the author's goal was to identify the vulnerabilities present in each method. For example, when using self-drawn syringes anesthesiologists would sometimes be required to draw up medication during surgery while completing other tasks simultaneously. This sort of complexity does not exist when using prefilled syringes. The authors identified 8 potential vulnerabilities in the use of prefilled syringes compared to 21 potential vulnerabilities found when medications were drawn from vial into a syringe.

There could the potential of cost savings for a variety of reasons by using prefilled medication. Anesthesiologists often draw their medications from vials/ampules into syringes prior to procedures which leads to medications not being used at all or partially wasted. In a study completed by the Icahn School of Medicine at Mount Sinai, the authors estimated that the total cost of preventable drug waste by anesthesiologist totaled up to $185,250 yearly in just their facility.

This will be a retrospective observational study to be conducted at Eden Medical Center from 7/23/19 to 8/26/19.Research Data will be gathered utilizing the Sutter electronic health record (HER) and Pyxis machines. Research analysis shall be descriptive.

The methods used in this project is descriptive statistics (mean, frequency, percentage, standard deviation) will be used for data analysis. Continuous data will be described as a mean and standard deviation if normally distributed. If non-normal distribution, continuous data will be described as medians and interquartile ranges. Advanced data analysis may be conducted using Statistical Analysis System (SAS) or Microsoft Excel.

Title: Using Novel Mitogenome Capture To Analyze Genetic Diversity Of The Endangered Southern River Otter

Authors:

Natalí Chávez (presenter), College of Graduate Studies, CNSU and * Natali.Chavez6766@cnsu.edu

Lillian D. Parker* ParkerLD@si.edu

Aurora G. Trejo* TrejoA2@si.edu

Margad-Erdene Ochirbat* OchirbatME@si.edu

Jessica D. Quinta* QuintaJ@si.edu

(Principal Investigator): Jesús E. Maldonado* MaldonadoJ@si.edu

Maximiliano A. Sepúlveda, Departamento de Conservación de la Diversidad Biológica, Gerencia de Áreas Silvestres Protegidas del Estado, Corporación Nacional Forestal, Santiago, Chile

maximiliano.sepulveda@gmail.com

* Center for Conservation Genomics, Smithsonian Institution, Washington, D.C.

Abstract: The Southern River Otter, *Lontra provocax*, is an endangered mustelid with a limited distribution in southern Chile and Argentina. The region we focus on in this study is the Valdivian Coastal Reserve in southern Chile, where the otters share habitat with the invasive American mink, *Neovison vison*. The mink population was established from individuals that escaped from fur farms in the 1970s. The terrestrial movement of the minks means that there is potential for them to transmit diseases from domesticated dogs to the otters, including canine distemper virus (CDV). This threat, in addition to predation from dogs and habitat destruction, makes the river otters susceptible to local extinction. This goal of this research is to use non-invasively collected samples to assess the genetic diversity and structure of the otter and mink populations. We use 8 microsatellite loci to identify unique individuals from DNA derived from 47 mink and 37 otter scat samples. We then use a novel set of in-solution hybridization probes to enrich and sequence mitochondrial genomes from fecal DNA derived from each individual. Our preliminary analysis of mitogenomes reveals greater genetic diversity in the otters than in the minks, and a genetic signature of population expansion in the minks. Future analysis will investigate population structure and gene flow. This research provides data critical for assessing and maintaining the genetic health of the endangered Southern River Otter, and applies novel methodology that enables the use of non-invasively collected samples for conservation genetics.

Title: Bioengineering MicroRNA-298 and Anti-miR-126 Agents for Cancer Therapy Research

Authors:

Neelu Batra (presenter), nbatra@ucdavis.edu. Ravina Sidhu, Pui Yan Ho, Ai-Ming Yu

Abstract: In the past decades, research has led to the discovery of functional noncoding RNAs (ncRNAs) such as microRNAs (miRs or miRNAs) in cells. This discovery has brought light to the crucial role that ncRNAs play in regulating target gene expression and controlling tumor growth and metastasis, which makes ncRNAs critical to the field of cancer therapeutics. In recent years, scientists have conducted in vitro studies using synthetic miRNA agents that falter in RNA function, structure, and stability due to extensive artificial modifications. In this current study, Escherichia coli is used as a faster, more cost effective alternative to produce large quantities of natural ncRNAs with no or some posttranscriptional modifications. We were able to produce 15-20 mg of chimeric miRNA agents using this novel method. Two RNAs were chosen for this study, a siRNA against miR-126-3p (simiR-126-3p) and miR-298-5p, and were fused into a tRNA/pre-miR-34a molecule. An anion exchange fast protein liquid chromatography (FPLC) method was used to purify the two desired ncRNA agents, which yielded 20 mg of simiR-126-3p and 15.6 mg of miR-298-5p from a 1 L bacterial culture. Purity was confirmed by a high-performance liquid chromatography (HPLC) assay; simiR-126-3p was >99% pure and miR-298-5p was >97% pure. These highly purified biologic siRNA/miRNA agents are viable candidates for cancer therapy research in vitro and in vivo. Acknowledgment: This study is supported by grant R01GM133888 from NIH/NIGMS.

Title: Using the CRISPR Cas 9 System to benefit CAR-T Cell Immunotherapy in Acute Lymphoblastic Leukemia (ALL)

Author: Neha Khatter

Abstract: Acute lymphoblastic leukemia, (ALL) is one of the most prominent types of cancers that are among children and adolescents in the US. The disease is seen in children but can be seen in individuals of any age. The first line of treatment for ALL is chemotherapy. Chemotherapy has showed promising results in tumor reduction, however, the cytotoxicity effects pose to be much greater. Chemotherapy is designed to target and remove cancer cells, however, there have been many cases where it kills healthy cells and thus further weakens the immune system. Relapse in individuals with ALL have also been noted. Due to these side effects, the advancements in immunotherapy have been further studied, and more specifically CAR-T Cell immunotherapy (Chimeric Antigen Receptor). This form of treatment utilizes the patient's own immune system, specifically their T cells, to target and treat the cancer. The benefits to this form of treatment in comparison to chemotherapy is that CAR-T therapy uses the body's own immune system to specifically target the cancer with little affect to healthy cells. Although, there have been cases of CAR-T damaging healthy cells, as well as cytokine storms within the body. To alleviate these toxic effects, the help of the CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) Cas 9 system can be useful. CRISPRs technology allows scientists to specifically edit DNA to their gene of their choice. By taking a CAR and introducing it to the TRAC T-cell receptor α constant locus, CRISPR will be able to edit this in order to promote specificity in targeting ALL.

Title: Aqueous Astragalus Extract Inhibits Proliferation and Differentiation of 3T3-L1 Adipocytes

Authors:

Nhi Duong, Melanie Rose, Tibebe Woldemariam, Linh Ho#

Corresponding author: California Northstate University College of Pharmacy, Elk Grove, CA 95757, USA. Tel.: +1 916 686 7370. Email: linh.ho@cnsu.edu

Introduction: Sirtuins are a family of proteins that act as nicotinamide adenine dinucleotide (NAD)-dependent deacetylases, causing post-translational modifications in target proteins to regulate their function. Out of 7 Sirtuins, Sirtuin-3 (Sirt3) has an important role in controlling metabolic balances as well as metabolic diseases. *Astragalus membranaceus*, commonly known as Huang Qi or astragalus, is used in Chinese herbalism for stimulating the immune system and many organs of the body, while lowering blood pressure and blood sugar levels. The objective of this study was to assess the effect of aqueous astragalus extract on proliferation and differentiation of 3T3-L1 pre-adipocytes into adipocytes and underlying molecular mechanism.

Methods: Pre-adipocytes cells (3T3-L1) were used to assess the effect of astragalus extract on Sirt3 activity linked to adipogenesis and signaling pathway at different concentrations compared to untreated cells. BrdU assay was used to assess effect of astragalus extract on cell proliferation. Adipogenesis, oil red o (ORO) staining, and ORO elution quantification were also performed to evaluate the lipid droplets accumulation of 3T3-L1 adipocytes. Quantitative PCR and western blots were used to quantify expression of target genes and evaluate protein expression levels.

Results: Astragalus extract inhibited proliferation of 3T3-L1 cells compared to the untreated cells (controls). Cells treated with higher concentration of astragalus extract (500µg/ml and 250µg/ml) exhibited lower cell proliferation compared to control. Interestingly, with lower concentrations of astragalus extract (125µg/ml, 62.5µg/ml, and 31.25µg/ml), proliferation of 3T3-L1 cells were higher compared to control. It meant at the concentration of 125µg/ml of astragalus extract or lower, the proliferations of 3T3-L1 were not affected and even increased. Thereafter, we used astragalus extract at concentration of 125µg/ml or lower for experiments. Astragalus decreased adipogenesis by ORO elution quantification compared to controls at concentration of 100, 50, and 10µg/ml. Sirt3 expression levels decreased when increased concentration of astragalus by qPCR and Western Blots. Interestingly, protein kinase B (AKT) and phosphorylated AKT expression levels were also suppressed when increased concentration of astragalus.

Conclusion: Astragalus extract inhibited adipogenesis of 3T3-L1 pre-adipocytes by inhibiting enzyme Sirt3 protein expression as well as AKT and phosphorylated AKT. Further experiments will be performed to identify whether astragalus suppressed adipogenesis via AKT pathway and any linear relationship between Sirt3 and AKT pathway for this effect of astragalus.

Title: Bilateral Incomplete Duplicated Ureters in a Male Cadaver- a Case Study

Authors:
*Peter Alexieff, M2, College of Medicine, Peter.Alexieff3351@cnsu.edu
*Tiffani Angelica Barham, M2, College of Medicine, tiffani.barham9398@cnsu.edu
*Mollee Iff Chu, M2, College of Medicine, Mollee.Chu5563@cnsu.edu
*Sarah Mudite Fetterolf, M2, College of Medicine, Sarah.Fetterolf4695@cnsu.edu
*Matthew Elliott Golden, M2, College of Medicine, Matthew.Golden5606@cnsu.edu
Advisor: Sailabala Vanguri, Assistant professor of Anatomy, CNU-COM, Sailabala.vanguri@cnsu.edu
*All authors contributed equally with cadaver dissection and writing.

Introduction: During the routine cadaver dissection in the Anatomy lab of California Northstate University College of Medicine, an adult male cadaver was found with bilateral incomplete duplication of ureters. Duplication of ureters is one of the most common anomalies of the collecting system, affecting approximately 0.1-3% of the population. It is a congenital anomaly and can be associated with other developmental abnormalities. It can be associated with clinical conditions such as hydrocele, ureterocele, urinary tract infections, and vesicoureteral reflux. Further details of the case will be discussed during the presentation.

Methods: We performed a retroperitoneal abdominal dissection, following the ureters from the kidneys into the pelvis bilaterally. The ureters were followed into the bladder.

Results: Ureter duplication was seen bilaterally extending from the pelvis of the ureter and downwards. The duplex ureters join before entering the bladder at the vesicoureteral junction, and thus are incomplete duplex ureters.

Conclusion: Bilateral incomplete duplex ureters are associated with a number of potential complications. Observing this anatomy prepares students for cases they may see clinically.

Title: Evaluation of Gene Oct4 Expression in Pancreatic Cells and Human Pancreas Tumor

Authors:

Dr. Seyed Saeid Zamanieh Shahri, MD, College of Health, CNSU, Saeid.zamanieh@cnsu.edu

Dr. Sonia Sayyedalhosseini, MD, College of Health, CNSU, Sonia.sayyedalhosseini@cnsu.edu

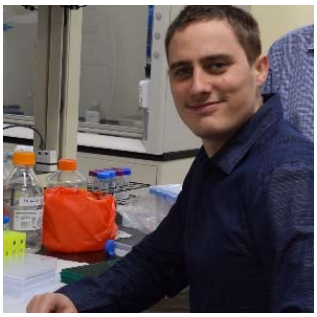
Introduction: The Oct4 gene is one of the important genes involved in stem cell self-renewal control. Recently, this gene has been proposed as a novel molecular marker for cancer detection. Therefore, in this study we examined the expression of Oct4 gene in MIA Paca-2, PA-TU-8902 and AsPC-1 cell lines as well as pancreatic cancer.

Methods: : In this experimental study, MIA Paca-2, PA-TU-8902 and AsPC-1 cell lines were cultured in DMEM and RPMI-1640 medium containing 10% fetal bovine serum (FBS) in a 37-degree centigrade , incubator containing 5% CO2 and 90% moisture were cultivated. Pancreatic tumor and non-tumor specimens were purchased from Tumor Bank of Iran. RNA extraction and cDNA synthesis were then performed. Oct4 expression levels were determined using Real-time PCR. Protein expression levels of target genes in cell lines were evaluated using flow cytometry and immunocytochemistry.

Results: The expression level of Oct4 was higher in cancer cell lines than in control (normal tissue) samples. The protein expression levels of the target genes in the target cell lines were confirmed by lysitometry and immunocytochemistry.

Conclusion/Implications: Oct4 can be considered as a molecular marker of cancer in pancreatic cells. This gene may play an important role in the uncontrolled proliferation of cancer cells.

Title: Lemongrass Essential Oil and its Major Constituent Citral and Citral Derivatives Modulate Adipogenic Gene Expression in 3T3-L1 Preadipocytes



Authors:

Steven Sprenger, B.S. College of Medicine, CNSU, steven.sprenger3881@cnsu.edu
Tibebe Woldemariam, College of Pharmacy, CNSU, TWoldemariam@cnsu.edu
Dinesh Vyas, MD, Dept of Surgery-SJGH and COM, CNSU, DineshVyas@yahoo.com
Simeon Kotchoni, Ph.D. College of Pharmacy, CNSU, Simeon.Kotchoni@cnsu.edu
Advisor: Lakshmi Shankar Chaturvedi, COP, CNSU, Lakshmi.Chaturvedi@cnsu.edu

Introduction: Lemongrass essential oil (LO) from Cymbopogon flexuosus possess numerous therapeutic properties. Despite efficacy in vivo, the mechanism for the modulation of obesity has not been elucidated. Obesity results in elevated risk for metabolic diseases, including type 2 diabetes, liver and kidney disease, hypertension, osteoarthritis, and coronary heart disease. We investigated the role of Lemongrass essential oil (LEO) and its major components citral (3,7-dimethyl-2,6-octadienal), citral dimethyl acetal (1,1-Dimethoxy-3,7-dimethylocta-2,6-diene), citral diethyl acetal (1,1-Diethoxy-3,7-dimethylocta-2,6-diene), and mixed citral cis/trans isomers in the modulation of adipogenesis and the molecular targets in preadipocyte 3T3-L1 murine fibroblast cell culture system.

Methods: 3T3-L1 cells were maintained in DMEM supplemented with fetal calf serum (FCS). Adipogenesis was induced using Dexamethasone 0.25µM, 3-isobutyl-methylxanthine (IBMX) 0.5mM, and insulin 10mg/mL (DMI) for 2 days after reaching 70% confluency followed by insulin 10mg/mL for additional 5 days. Treatment for 48 hours with $2.5x10^{-3}$ % essential oils started on day 5. Intracellular lipid droplets were stained using Oil Red O and photographed under 10x magnification. Cell viability was performed using CCK-8 kit. Non-toxic concentrations of LEO and its major constituents were then used for modulation of adipogenesis. Total RNA was extracted and expression of genes involved in regulation of adipogenesis, including cluster of differentiation 36/fatty acid translocase (CD36/FAT), fatty acid binding protein 4 (FABP4) also known as adipocyte Protein 2 (aP2) and Peripilin, or lipid droplet-associated protein (Peripilin 1, PLIN), were quantitated using real-time PCR. RPLP0 (Ribosomal Protein Lateral Stalk Subunit P0) was used as housekeeping gene.

Results: We observed that LEO attenuates induction of adipogenesis by down-regulating FAA content. Furthermore, LEO and its major constituents significantly inhibit expression of CD36/FAT, FABP4/aP2, and PLIN genes involved in fatty acid metabolism.

Conclusion: LEO modulates adipogenesis through attenuation of several adipogenic genes, but further research is necessary to understand the complete mechanism.
Title: Using Non-Invasive Cardiac Output Monitoring System To Evaluate Net Fluid Balance Compared To Usual Care In Sepsis Patients

Title: Using a Non-Invasive Cardiac Output Monitoring System to Evaluate Net Fluid Balance Compared To Usual Care in Sepsis Patients

Authors:
Summer Faria (presenter), PharmD, Sutter Medical Center, Sacramento
Tina Dinh, PharmD, BCPS, Sutter Medical Center, Sacramento
Seumsack Somtakoune, PharmD, BCPS, Sutter Medical Center, Sacramento
Leah Hatfield, PharmD, BCPS, Sutter Medical Center, Sacramento
Meyng Cho, PharmD, BCPS, Sutter Medical Center, Sacramento

Introduction: Early detection of sepsis and fluid resuscitation has been associated with decreased mortality in sepsis patients. However, a sustained positive fluid balance is associated with an increased risk of death per the Surviving Sepsis Campaign (2018). Targeted volume resuscitation using non-invasive cardiac output monitoring (NICOM) is aimed to optimize a stroke volume that would result in decreased fluid balance and improved outcomes in patients with sepsis and septic shock. This study evaluates fluid status managed with NICOM compared to usual standard of care without the use of NICOM.

Methods: This is a quality improvement, retrospective cohort study that has been approved by Sutter's international review board. Identification of patients in this study is through a code sepsis alert that is triggered by a patient with a lactate level of 4 mmol/L or more and a suspected or confirmed infection to identify patients with sepsis or septic shock. Pre-existing dialysis patients, obstetrics, code sepsis alerts outside of the emergency room or intensive care unit, and bleeding patients will be excluded from this study. Approximately 400 adult patients will be identified using data collected by the electronic intensive care unit (eICU). Statistical analysis will be performed to identify the significant differences between the usual standard of care and the NICOM group using Chi-square and unpaired t-test. Chi-square test will be used for requirement for vasopressors, mechanical ventilation, and acute renal replacement therapy. Unpaired t-test will be used for net fluid balance, length of stay, duration of vasopressors and mechanical ventilation.

Title: Implementing Discharge Pharmacy Services for Reducing Readmission Rates and Patient Harm

Authors:

Tiffany On, College of Pharmacy, CNSU, tiffany.on@cnsu.edu

Introduction: Patients may experience difficulty in transitioning from the hospital upon discharge due to various factors, which can include medication changes and administration times. As such, medication discrepancies can result in hospital readmissions and adverse events. Therefore, the implementation of a discharge pharmacist role can facilitate the patient care process via reconciliation of the discharge orders and delivery of counseling services prior to hospital discharge. The purpose of this study is to determine the impact of developing a discharge pharmacist position in reducing admission rates and preventing patient harm.

Methods: Prospective study assessing the impact of discharge pharmacist services for inpatients. Inclusion criteria include adults admitted and discharged. Exclusion criteria include pediatric patients, pregnant patients, patients who are discharged with hospice care, left against medical advice, transferred out, discharged prior intervention, and who died before discharge.

Title: Mapping the Co-Curriculum to C.A.P.E. Outcomes and ACPE Standards 3 and 4

Authors:
Tiffany-Jade Kreys, Pharm.D.(presenter), Department of Clinical and Administrative Sciences, College of Pharmacy, CNSU. Email: TKreys@cnsu.edu

Eugene Kreys, Pharm.D., Department of Clinical and Administrative Sciences, College of Pharmacy, CNSU. Email: EKreys@cnsu.edu

Ashim Malhotra, Pharm.BS, M.S., Ph.D., Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, CNSU. Email: ashim.malhotra@cnsu.edu

Introduction: ACPE requires students to participate in co-curricular activities that allow them to apply and refine skills learned in the classroom. To meet this requirement, CNUCOP developed, implemented, and mapped co-curricular learning outcomes (CoCuLOs) to six areas of the C.A.P.E domains and ACPE Standards 3 and 4.

Methods: CNUCOP developed a co-curriculum encompassing 1) social awareness and cultural sensitivity, 2) professionalism and advocacy, 3) self-awareness, 4) innovation and entrepreneurship, 5) public health and education, and 6) service and leadership. P1 to P3 students are required to participate in two CoCuLO events each year, to fulfill a total of 6 CoCuLOs by the end of the P3 year. Upon completion of an event, students submit a self-reflection detailing how the event satisfied a specific CoCuLO. Advisors evaluate the self-reflection using a rubric to determine the students' level of proficiency in the CoCuLO. Aggregate data from the CoCuLO evaluations were mapped to programmatic learning outcomes.

Results: For AY 2017 to 2018, 18 students completed 10 events for CoCuLo 1, 11 for 2, 17 for 3, 1 for 4, 28 for 5, and 1 for 6. On average, CoCuLO 4 (innovation) essays were graded the highest, while CoCuLo 2 (professionalism) essays received the lowest rubric scores, though no significant difference in scores occurred.

Conclusion: CNUCOP's novel approach to assessing the co-curriculum provides a mapping tool to easily gauge the fulfillment of CoCuLOs, which are difficult to assess. Our approach to establishing and assessing the co-curriculum will be shared with other programs.

Title: Barberry Inhibits Prostate and Breast Cancers via Inhibiting Sirt3 and AKT Pathway

Authors: Tin Le, Jenny Nguyen*, Thanh Truc Do Nguyen*, Trung Ky Pham, Melanie Rose, Tibebe Woldemariam, Linh Ho#

* J.N. and T.T.D.N. contributed equally to this work.
# Corresponding author: California Northstate University College of Pharmacy, Elk Grove, CA 95757, USA. Tel.: +1 916 686 7370. Email: linh.ho@cnsu.edu

Introduction: Sirtuin-3 (Sirt3), a member of Sirtuins (1-7) family of NAD^+ dependent deacetylase proteins, has important roles in regulation of cellular homeostasis and cell death, metabolic diseases, and cancers. *Berberis vulgaris*, commonly known as barberry, is herbal plant that has shown to have health benefits including anti-inflammatory, lowering blood sugar, and help with digestions. The objective of this study was to assess whether the effect of aqueous barberry extract on modulating Sirt3 to regulate cell proliferation and apoptosis leading to inhibit cancer cells.

Methods: Effect of aqueous barberry extract on Sirt3 activity was tested using fluorometric assay. BrdU assay was performed to assess effect of the barberry extract on cell proliferation. Prostate (PC3 and LNCaP) and breast (MCF-7) cancer cell lines were used to assess relevant biological effects of the barberry extract at concentrations of 1µg/ml, 10µg/ml, 100µg/ml, and 500µg/ml or at different concentration where indicated on cancer cells compared to untreated cells (controls).

Results: Aqueous barberry extract at different concentrations added yielded lower Sirt3 activity *in vitro* compared to control of a putative 100% Sirt3 activity. Treatment with barberry at concentrations of 500, 100, 10, and 1 µg/ml inhibited cell proliferation and this effect was concentration dependence. In line with the inhibiting results of the barberry extract on Sirt3 activity *in vitro*, Sirt3 expression levels in PC3 cells were decreased with increasing barberry concentrations by Western Blot (WB). Interestingly, the phosphorylation levels of protein kinase B (P-AKT) yielded similar result with decreasing when barberry concentrations increase. In sharp contrast, Sirt3 expression levels in LNCaP cells were increased with increasing barberry concentrations by WB. The P-AKT density levels yielded similar result with increasing levels when barberry concentrations increase. This result may be due to LNCaP cells owning androgen-sensitive receptors, unlike PC3 cells. However, further studies are needed to investigate the mechanism. In MCF-7 cells, both AKT and phosphorylated AKT levels induced, meanwhile the Sirt3 expression decreased when barberry concentrations increase compared to controls. Gene expression levels of Sirt3 and other Sirtuins were not changed in treated samples compared to the controls.

Conclusion: Barberry extract inhibited proliferation of cancer cells with concentration dependence. It shown reduced Sirt3 activity and Sirt3 protein expression in MCF-7 and PC3 when increased concentrations of barberry. The reduction of Sirt3 protein was linear with P-AKT protein in PC3 cells, however, in opposite manner in MCF-7 cells. Sirt3 protein expression and P-AKT both were decreased when increased concentrations of barberry in LNCaP cells. Further studies are needed to strengthen these results for the effect of aqueous barberry extract as a Sirt3 inhibitor to suppress cancers via AKT pathway for an ultimate goal of a cancer treatment.

Title: Topical Lidocaine Patches May Induce QTc Prolongation in a Patient with Cardiac Ischemia

Authors:
Tony Joseph Eid, Pharm.D. (presenter), Department of Clinical and Administrative Sciences, College of Pharmacy, CNSU. Email: Tony.Eid@cnsu.edu

Ashim Malhotra, Pharm.BS, M.S., Ph.D., Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, CNSU. ashim.malhotra@cnsu.edu

Introduction: Lidocaine has long been used for the treatment of arrhythmia, with intravenous lidocaine shown to improve calculated QT (QTc). However, the effect of continuous lidocaine delivery through topical patches in patients with underlying cardiac ischemia has not been evaluated.

Methods: We present a case of a 59-year-old Filipina female with a history of poorly controlled hypertension and neuropathic non-cancerous pain. She was prescribed a lidocaine patch, with the direction of using a patch every 12 hours within a 24-hour period. The patient presented to the clinic with severely elevated blood pressure and an electrocardiogram was ordered. Cardiac ischemia was suspected based on the presentation of atypical chest pain. The patient was monitored during her first visit while she was on the lidocaine patch and was advised to stop usage, which was implemented within a week. Subsequent, electrocardiographic monitoring was carried out after 91 days of lidocaine discontinuation. A review of the patient's medication history during medication reconciliation did not indicate medications associated with QTc prolongation.

Results: Electrocardiographic recording with the patient on the lidocaine patch demonstrated a QT calculated using the Bazett formula (QTcb) of 511 msec, a heart rate of 71 bpm, and a QT interval of 470 msec. Subsequent electrocardiographic monitoring in the absence of the lidocaine patch demonstrated a QTcb of 459 msec, an improvement of 50 msec, a heart rate of 66 bpm, and a QT interval of 438 msec, a reduction of 38 msec.

Conclusion: Since QTc is considered to be prolonged if it is greater than 440 ms for men or 460 ms for women, and a QTc of more than 500 is associated with increased risk of Torsades de Pointes, we concluded that discontinuation of lidocaine prevented the development of deleterious rhythm for this patient. However, the sample size needs improvement for conclusive analysis.

Title: Sirt3 Regulates Adipogenesis and Adipokine Secretion via Its Enzymatic Activity

Authors:
Tram Hoang Thao Nguyen, Oanh Ma* and Truc Le*, George Talbott, Dorothy Ha, Linh Ho#
CNSU, College of Pharmacy, Elk Grove, CA 95757, USA
* O.M. and T.L. contributed equally to this work.
#Corresponding author: California Northstate University College of Pharmacy, Elk Grove, CA 95757, USA. Tel.: +1 916 686 7370. Email: linh.ho@cnsu.edu

Introduction: Sirt3 is a critical factor in multiple metabolic and aging disorders including cardiovascular disease, age-related hearing loss, cancer, obesity and type 2 diabetes. The purpose of this research was to identify if Sirt3 plays a role in marrow adipogenesis and adipokines secretion, especially adiponectin using bone marrow-derived stroma (ST2) cell model. The underlying mechanism of Sirt3 in regulation of adipogenesis that linked to its enzymatic activity was identified by Mass Spectrometry analysis.

Methods: We used Sirt3 induction by overexpressing using Sirt3 plasmid and Sirt3 inhibition by Sirt3 inhibitor 3-TYP in ST2 cells to assess the role of Sirt3 in adipogenesis and regulation of adipokine secretion.

Results: Sirt3 overexpression leads to a significant increase in adipogenesis compared to controls. The induction of adipogenesis by Sirt3 is associated with increased gene expression of adipocyte markers as well as adiponectin/adipokines. In sharp contrast, the inhibition of Sirt3 exhibited significantly decreased adipogenesis, adipocyte markers and adiponectin/adipokines compared to the controls. Interestingly, perilipin 1 (Plin 1) expression was decreased in Sirt3 induction, however, increased in Sirt3 inhibition. The increase of adipogenesis by Sirt3 was associated with its enzymatic deacetylase activity by Mass Spectrometry analysis. 115 mitochondrial acetylated peptides from 67 mitochondrial proteins had lower levels of acetylation in adipocytes induced by Sirt3 overexpression (Sirt3OE) compared to the control. Of the 67 proteins less enriched in acetylation, 22 acetylated proteins were decreased by more than 2-fold. These proteins are considered potential Sirt3 substrates in adipogenesis.

Conclusion: Sirt3 has a novel, important role in modulating adipogenesis and adiponectin/adipokine expression. The connection axis among Sirt3-adipogenesis-adipokines was linked to its substrates by mass spectrometry analysis. Perilipin 1 is a good candidate for further study the coordination between Sirt3 and perilipin 1 in regulation of systemic metabolism. We hope our study contributes to the efforts of revealing Sirt3 functions in metabolic homeostasis and diseases.

Title: Machine Learning Based Method for Accurate Prediction of Breast Cancer

Authors:

Tuan Tran, Department of Clinical and Administrative Sciences, College of Pharmacy, California Northstate University, tuan.tran@cnsu.edu.

Uyen Le, Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, California Northstate University, uyen.le@cnsu.edu

Hieu Tran, Dean, College of Pharmacy, California Northstate University, hieu.tran@cnsu.edu.

Introduction. Main objective of this study is to utilize advanced computing methods for accurate prediction of breast cancer based on preliminary clinical data.

Methods. We used a well-known dataset provided by the Wisconsin Breast Cancer Database. First, we performed data preprocessing to identify missing values, outliers and potential predictors. Next, we used the advanced machine learning method, Random Forest, for modeling. To construct our model, data is randomly divided into 70% for training and 30% testing. Performance is measured by accuracy, sensitivity (true positive) and specificity (true negative).

Results. The dataset included 698 cases with 11 attributes. We identified 16 missing values and removed these associated observations. Analysis revealed that 64.96% and 35.04% of cases were benign and malignant, respectively. In addition, correlation analysis showed that CellSize and CellShape are highly correlated with coefficient of 0.91 (*p-value* = 0.001). This finding helps to eliminate one of the attributes in our model to avoid multicollinearity. Our constructed model achieved very high prediction accuracy of 97.63% with 95% confident interval of (94.56% - 0.99.23%). The result is higher than our previously published accuracy of 96.63%. Additionally, the model also achieved very high sensitivity and specificity of 98.55% and 95.89%, respectively. Finally, CellShape and ClumpThickness were identified as the two most important predictors for detecting breast cancer.

Implications. The study provided an accurate and effective method for predicting breast cancer. It opened up new avenue for early breast cancer detection and treatments. Our future work will perform parameter fine-tuning to achieve higher accuracy.

Title: Revealing Trends of Overdose Deaths and Opioid Prescriptions via Google Keyword Search

Authors:

Tuan Tran, Department of Clinical and Administrative Sciences, College of Pharmacy, California Northstate University, tuan.tran@cnsu.edu.

Uyen Le, Department of Pharmaceutical and Biomedical Sciences, College of Pharmacy, California Northstate University, uyen.le@cnsu.edu

Erika Titus-Lay, Department of Clinical and Administrative Sciences, College of Pharmacy, California Northstate University, erika.Titus-Lay@cnsu.edu.

Introduction. The objective of this study was to reveal trends of overdose deaths and filled opioid prescriptions in the U.S. via Google keyword search.

Methods. Data was collected from the Centers for Disease Control and Prevention (CDC), National Institute on Drug Abuse (NIDA), and Google Trends including opioid prescription rates from 2013 - 2017, number of overdose deaths per 100,000 persons in 2016 and frequencies of "opioid" keyword searches associated with geographical locations from years 2013 - 2016. Correlation analysis was used to identify trends of overdose deaths and opioid prescriptions of different states. Keyword search ranking identified the top 10 states with the most overdose deaths.

Results. Pearson correlation analysis showed strong correlation of filled prescriptions from 2013 - 2017 with coefficients greater than 0.96, p-values <= 0.001. Findings showed consistent prescription filling trends across the states over time. Analysis of Google keyword searches from 2013 - 2016 showed strong correlation with overdose deaths in 2016 with coefficients from 0.56 - 0.78, p-values <= 0.01. Additionally, high correlations of monthly keyword searches and overdose deaths in 2016 were identified, ranging from 0.61 - 0.78, p-values <= 0.01. Finally, keyword search ranking correctly identified 80% of the top 10 states having the most overdose deaths in 2016.

Implications. The study proposes a novel way for estimating trends of overdose cases and opioid prescriptions in the U.S. Policy makers can use it for public health surveillance. Our future work includes refining keyword combinations and collecting more data for predictive modeling.

Title: Time to Benefit for Stroke Reduction after More Intensive Blood Pressure Control in Older Adults

Authors:
Vanessa Ho (presenter), MS, College of Medicine, CNSU
Irena Stijacic-Cenzer, MS, Division of Geriatrics, UCSF
Sei J Lee, MD, MAS, San Francisco Veterans Affairs Medical Center

Background: Although hypertension treatment in older adults decreases stroke risk, it may also lead to immediate harms such as dizziness, orthostatic hypotension, and falls. Guidelines recommend targeting preventive interventions with immediate harms and delayed benefits to those older adults whose life expectancy exceeds the time to benefit. The time to benefit for hypertension treatment to prevent strokes is unknown; our objective was to estimate a meta-analyzed time to benefit for stroke prevention after initiation of more intensive hypertension treatment.

Methods: Using two Cochrane systemic reviews, we identified randomized controlled trials comparing standard blood pressure control (placebo or usual treatment) versus more intensive blood pressure control that reported time to stroke outcomes. We focused on studies of older adults (mean age >65 years). We fit Weibull survival curves and used a random-effects model to estimate the pooled annual absolute risk reduction (ARR) between control and intervention groups. We applied Markov Chains Monte Carlo methods to determine the time to ARR thresholds (ARR = 0.002, 0.005, and 0.01).

Results: Seven eligible trials (n = 20918) were included in our survival meta-analysis with mean age ranging from 69-84 years and study follow-up times ranging from 2.0-5.8 years. We found that it took 2.6 years (95% CI: 1.3-3.9) to avoid 1 stroke for 100 persons receiving more intensive hypertension treatment (ARR = 0.01). It took 1.4 years (95% CI: 0.6-2.1) to avoid 1 stroke for 200 persons (ARR = 0.005) and 0.6 years (95% CI: 0.2-1.1) to avoid 1 stroke for 500 persons (ARR = 0.002).

Conclusions: More intensive hypertension treatment for 100 persons prevents 1 stroke in 2.6 years (95% CI: 1.3-3.9). The rates of harms from more intensive hypertension treatment ranges from 1-7%. Our results suggest that more intensive hypertension treatment is most beneficial for older adults with life expectancy >2.6 years.

Title: Anticancer Potential of Carfilzomib, a Proteasome inhibitor on Human Caco-2 Colon Cancer Cells

Authors:

Victor Cuyugan Changcoco, College of Pharmacy, CNSU, Victor.Changcoco8745@cnsu.edu

Alexander Nguyen, COP, CNSU, Alexander.Nguyen3924@cnsu.edu

Hang Nguyen, College of Pharmacy, CNSU, Hang.Nguyen2562@cnsu.edu

Dinesh Vyas, MD, Dept of Surgery-SJGH and COM CNSU, DineshVyas@yahoo.com

Simeon Kotchoni, Ph.D. Dept of Pharmaceutical & Biomedical Sciences-College of Pharmacy, California Northstate University, Simeon.Kotchoni@cnsu.edu

Melanie Rose, COP, CNSU, Melanie.rose@cnsu.edu

Advisor: Lakshmi Shankar Chaturvedi, Ph.D. Dept of Pharmaceutical & Biomedical Sciences-College of Pharmacy; Dept of Basic Sciences and Surgery-College of Medicine, California Northstate University Lakshmi.Chaturved@cnsu.edu.

Background: Colorectal cancer (CRC) is the third most common cancer and the third leading cause of cancer related death in the United States. Surgery is the primary form of treatment followed by chemotherapeutic interventions. About 50% patient have high recurrence rate. Second generation Proteasome inhibitor has been clinically shown to be effective as anticancer therapeutic for hematological cancers like multiple Myeloma. However, despite the proven efficacy of these drugs in hematologic malignancies, their anticancer potential and molecular mechanism has not been fully elucidated in solid tumors such as colon adenocarcinoma. In current study, we investigate and compare the antiproliferative and cytotoxic effects of novel irreversible second generation proteasome inhibitor Carfilzomib (CFZ) alone in a combination with chemotherapeutic drug doxorubicin (DOX) on human colon adenocarcinoma Caco2 cells.

Methods: Caco2 cells were cultured in DMEM with FBS. Cell viability was assessed CCK-8 kit. Cells were treated with various concentrations CFZ (0-500nM) alone, DOX (0-1.5µM) alone and a combination of both to assess the cell viability and cytotoxicity. Genes involved in cell cycle regulation will be determined using CFZ, and a combination of DOX to determine the molecular targets involved in the regulation of growth of colon cancer cells.

Results: We observed that both CFZ and DOX significantly inhibit the cell proliferation in a dose dependent manner of Caco-2 cells at 24 hour treatment. Furthermore, a combination of both drugs found to not have further additive effect on the rate of growth inhibition. We are exploring the molecular mechanism of anticancer potential of CFZ alone and in a combination of DOX in Caco-2 cells.

Conclusions: The current study revealed that a novel irreversible second generation proteasome inhibitor Carfilzomib (CFZ) alone might have a great anticancer therapeutic potential in treating colon cancer patients. However, further in vivo studies are needed to be conducted.

Title: Phorbol 12-myristate 13-acetate Dedifferentiates Human Cardiac Myofibroblasts to Fibroblasts

Authors:

Vy Tran Luu (Presenter): P2, College of Pharmacy, CNSU, Vy.TranLuu4045@cnsu.edu
Sang Phan: P2, College of Pharmacy, CNSU, Sang.Phan5876@cnsu.edu
Advisor: Zhuqiu Jin: College of Pharmacy, CNSU, zhuqiu.jin@cnsu.edu

Introduction: The differentiation of fibroblast to myofibroblast is generally considered as an irreversible conversion which represents a critical step in pathogenesis of fibrosis. The mechanisms of myofibroblast differentiation from fibroblasts have been studied extensively. Reversal of myofibroblast differentiation to fibroblasts remains incompletely understood. Phorbol 12-myristate 13 acetate (PMA) is involved in multiple cellular functions via PKC signaling pathways. The effects of PMA to dedifferentiate formed myofibroblasts is unknown.

Methods: To investigate whether PMA dedifferentiates the formed myofibroblasts, NIH 3T3 fibroblasts and human cardiac fibroblast (HCF), cultured in DMEM and fibroblast medium (FM)-2 respectively, were induced to convert into myofibroblasts in the presence of 2 ng/ml of TGF-β1 for 24- or 48-hour incubations. Expression of α-SMA, the biomarker of myofibroblasts, and FSP-1, the biomarker of fibroblasts, in both cell lines was detected by using western blotting and immunofluorescence. Collagen gel contraction induced by cardiac fibroblasts was determined as well.

Results: After incubation with TGF-β1, morphology changes in the shape and the size of NIH 3T3 and HCF cells were observed by the presence of large nuclei and cytoplasm. The levels of expression of α-SMA were increased whereas expression of FSP-1 was reduced after 48-hour incubation with TGF-β1. NIH 3T3 and HCF cells were then treated with PMA concentrations (10 ng/ml, 50 ng/ml and 100 ng/ml) or DMSO control for additional 24- and 48- hour incubations. Western blot confirmed the reduction in expression of α-SMA in cells treated with PMA. As PMA concentration increased, the expression of α-SMA remarkably decreased. PMA also reduced TGF-β1-induced collagen gel contraction.

Conclusion: TGF-β1 induces differentiation of fibroblasts to myofibroblast. PMA dedifferentiates the formed myofibroblast back into fibroblasts. Although the mechanism of PMA-induced reversal differentiation remains to be identified, the novel findings of this study shed light on future development of novel agents to treat fibrotic diseases.
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Title: Impact of Decoding Medication Tradenames on Students' Performance; a Feasibility Study

Authors:

Yasmin Elsobky, B. Pharm, BCPS, Drug information specialist & Adjunct Lecturer of Drug Information, College of pharmacy, Alexandria University, Egypt, yasminelsobky@alexu.edu.eg

Welly Mente, PharmD, FCSHP, Department of Clinical & Administrative Sciences, College of Pharmacy, California Northstate University, College of Pharmacy, welly.mente@cnsu.edu

Eugene Kreys, PharmD, PhD, BCPS, Assistant Professor, Clinical & Administrative Sciences & Director of Assessment, College of Pharmacy, California Northstate University, College of Pharmacy, eugene.kreys@cnsu.edu

Islam Mohamed B.Pharm, MS, PhD (presenter), Department of Pharmaceutical and Biomedical Sciences, California Northstate University College of Pharmacy, islam.mohamed@cnsu.edu.

Introduction: Learning medication tradenames can be a memorization challenge for pharmacy & healthcare students. Academic communication often utilizes generic names. In contrast, interactions with patients mostly utilize tradenames. In parallel, healthcare practitioners' self-confidence in their knowledgebase can possibly impact their dispensing patterns. The purpose of the current study is to assess whether the introduction of decoding of medication tradenames (explanation of techniques, or expressions used in medication tradenames) of the Top 200 medications in USA & internationally, can result in improved pharmacy students' performance, long-term retention, self-perception of competency & quality of learning experience.

Methods: (a) Baseline performance of students in formative assessment questions before implementing the educational intervention of decoding international medication tradenames, will be compared versus their performance on final summative assessment questions after the intervention. (b) the average performance of students who received the educational intervention in questions specific to the Top 200 medications in cumulative Milestone assessment will be compared versus the average students' performance in similar questions from previous academic years without the education intervention. (c) survey questions will be used to evaluate students' self-perception of competency & quality of learning experience.

Results: according to preliminary analysis as compared to formative assessments, overall aggregate averages of students' performance on summative assessment questions decreased by 23.6% (from 77.5% to 53.9%) on the year prior to the intervention, whereas, it was increased by 5.7% (from 78.5% to 84.1%) on the year the education intervention was implemented.

Conclusion / Implications: Supplementing Pharmacy curricula with the art & science of formulating the Top 200 medication tradenames can possibly improve students' academic performance, long-term retention & learning experience. Furthermore, decoding the hidden messages in tradenames can help to improve future pharmacists' self-perception & confidence in their healthcare education, which can ultimately enhance their clinical services in different fields of practice.