



TRANSLATIONAL RESEARCH SYMPOSIUM

CNU RESEARCH DAY PROGRAM

January 19, 2018 9:00am - 5:00pm

LOCATION: CNUCOM CLASSROOMS 1A & 1B

**CALIFORNIA NORTHSTATE UNIVERSITY
9700 W. TARON DRIVE
ELK GROVE, CA 95757**

Program at a glance

Time	Sessions Overview
8:00am - 9:00am	Registration
9:00am - 9:15am	Dr. Alvin Cheung, PharmD, MHSA (CNU President - Opening Remarks)
9:15am - 9:20am	Dr. Hieu T. Tran (Dean & Professor, CNUCOP)
9:20am- 9:30am	Dr. Phil Mack (Vice President of Research, CNU)
9:30am - 10:15am	Keynote speech – Professor Ralph W. de Vere White, M.D. (UC Davis)
10:15am - 10:35am	Student Presentation – COP (Jessica Y. Dallalzadeh, P3; title: A novel mechanism underlies reversal of myofibroblast differentiation by phorbol 12-myristate 13-acetate) -
10:35am - 10:55am	Student Presentation – COM (Daniella Lent-Schochet, M2; title:)
10:55am - 11:15am	Faculty Presentation – COP – (Hatem Elshabrawy, Ph.D.; title: Novel roles of IL-11 in RA pathogenesis)
11:15am - 11:35am	Student Presentation – COP (Vinna Nam, P3; title: Trends of Hospitalizations as a Result of Infectious Causes in Patients with Autoimmune Diseases)
11:35pm - 11:55am	Faculty Presentation – COM (Hugo Arias, Ph.D.; title: Preclinical studies of novel positive allosteric modulators of $\alpha 7$ nicotinic receptors)
11:55am - 1:15pm	Poster Presentation – Lunch Break
1:15pm - 1:35pm	Faculty Presentation – CHS (Christopher Wostenberg, Ph.D.; title: Longitudinal Utilization of Molecular Modeling Projects Across the Chemistry Curriculum)
1:35pm - 1:55pm	Student Presentation – CHS (Anusri Yanumula, title: In silico Anti-Cancer Drug Development: Insights from Existing Pin1 Inhibitor Testing)
1:55pm - 2:10pm	Resident Presentation – COP (Cathy Liang, PharmD; title: Comparison and Evaluation of Appropriate Daptomycin (CUBICIN®) Usage across Four Sutter Health East Bay Hospitals: A Daptomycin Medication Use Evaluation)
2:10pm – 2:20pm	Resident Presentation – COP (Vincent Largo, PharmD; Retrospective, observational descriptive study of an Emergency Department-based Pharmacist)
2:20pm – 2:35pm	Resident Presentation – COP (Emily Medeiros, PharmD; title: Adherence to a Chemotherapy and Biologic Dose Rounding Protocol and Financial Implications)
2:35pm – 3:35pm	Poster Presentation - Coffee Break
3:35pm - 3:55pm	Student Presentation – COM (Rohaum Hamidi, M2; title: Concussion Education for High School Athletes)
3:55pm – 4:15pm	Student Presentation – COP (Viet Nguyen, P2; title: Don't Slack, TakeBack: A Long-Term Drug Take-Back Initiative)
4:15pm – 4:45pm	Awards for Students Poster and Oral Presentations & Awards for Grant Winners
5:00pm	Meeting Concludes – Depart or catch up with Poster Presentations

Keynote Speaker



RALPH dE VERE WHITE, M.D.

Emeritus Director, UC Davis Cancer Center



Dr. de Vere White received his medical degree from Dublin University, Ireland and completed his residency in surgery at St. Vincent's Hospital in Dublin and in urology at Duke University in Durham, N.C.

His research in prostate cancer started in evaluating the role of DNA ploidy and proceeded to molecular analysis showing that P53 mutations led to androgen independence. Presently, he is investigating the therapeutic roles of micro RNA's, notably miR-124, in overcoming castrate resistance. His lab was the first to publish a functional role from micro-RNA's in this disease. In urothelial cancer, he championed the role of neoadjuvant chemotherapy prior to cystectomy. His research focused on the 20% of patients presenting with muscle invasive disease who account for 80% of the mortality from this disease, through programs in microdosing, P53 pathway analysis and patient derived tumors (PDX), using NSG mice. He has a 30 year history of leading urological clinical trials. He has authored 325 peer- reviewed scientific articles. In 2014, as reported by the Blue Ridge Institute, he was the best funded urologist in the country.

He was chair of urology at UCD from 1984-2006 and the director of the UCD Cancer Center since 1996, leading it to NCI designation in 2002, and Comprehensive Designation in 2012.

Dr. de Vere White is the past chair of the DOD Prostate Cancer Integration group, past President of the Society of Urologic Oncology (SUO), and recipient of the Huggins medal by the SUO for lifetime achievement in Urological Oncology. At UCD, he received a prize for excellence in mentoring (2004) and for medical research (2011).

Keynote Speaker Abstract

Struggles To Improve Survival for Patients with Urothelial Bladder Cancer

Dr. Ralph de Vere White

The increasing mortality from cancer can only be defeated by a combination of basic clinical translation and disparities research. Bladder cancer is an ideal model of how to integrate these efforts; it is also a cautionary tale of how difficult cancer is to defeat. 75,000 Americans a year develop bladder cancer, 16,000 die of it, while 500,000 people are survivors. 80% of these cancers do not invade the bladder muscle [non muscle invasive disease,] 15% are muscle invasive, and 5% have metastasis when they are first seen. So at presentation 95% of patients have cancer that is confined to their bladder, this cancer can be accessed through a patients urethra without the need for incision, the cancer can be removed in this fashion using many instruments, and there is often a relatively large volume of disease available for all types of corollas studies. Yet, there has been no improvement in survival for patients with bladder cancer in the last 30 years. The keys to improving survival and quality life are to reduce recurrence of non-muscle invasive cancer by, A) better visualizing the disease so it can be more completely resected, Auto Florence Microscopy. After resection of non-muscle invasive bladder cancer, therapy is placed in the bladder endeavoring to reduce reoccurrence. To improve presently used treatment through molecularly targeted chemotherapy.

For patients with muscle invasive cancer clinical trials done over many years show that if chemotherapy was given before the bladder was removed it improves survival in 50% of patients who had responded to the chemotherapy. The issues that this raise are A) how to predict the response of a patient to this toxic chemotherapy before it is administered. We are utilizing Microdosing for this purpose. How do we develop new therapies that will be more effective and that utilize molecularly targeted therapy guided through sequencing a patient's tumors. We are pursuing two ways to accomplish this A) Patient derived xenographs [PDXs] B) micro chambers.

To help people who are treating bladder cancer governing bodies throughout the world produce practice guidelines. For non-muscle invasive bladder cancer three of these guidelines are fully supported by these bodies in America, Europe, and Asia. And yet presently 80 to 90% of patients are treated outside of these guidelines. Can this be improved as a relatively easy way of improving outcomes of patients with this disease. This talk will walk the audience through these efforts to improve outcomes for these patients.

A novel mechanism underlies reversal of myofibroblast differentiation by phorbol 12-myristate 13-acetate

Jessica Dallalzadeh¹, George Talbott², Helen Le¹, Paia Lor¹, Zhuqiu Jin²



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Fibrosis often results in organ dysfunction and failure in diseases, such as: chronic heart failure, hepatic cirrhosis, pulmonary fibrosis, and end-stage renal disease. The differentiation of fibroblasts into myofibroblasts results in the secretion of collagens and other extracellular matrix proteins that limit organ function and underlie the fundamental basis of fibrosis. TGF- β 1 induces the differentiation of α -SMA-expressing myofibroblasts from fibroblasts. However, the mechanism to induce reversal of myofibroblast differentiation remains elusive. Phorbol 12-myristate 13-acetate (PMA) has been used for the stimulation of lymphocytes and splenocytes. It is also involved in multiple cellular functions by potently activating protein kinase C (PKC). Nevertheless, the effect of PMA on the formation of myofibroblasts is unknown. To investigate whether PMA plays a role in myofibroblast differentiation, NIH 3T3 fibroblasts were cultured in DMEM medium for 48 hours in the presence of DMSO (vehicle control), PMA, or PKC inhibitors (calphostin C, chelerythrine, and staurosporine) alone or plus PMA. The expression of α -smooth muscle actin (SMA, a hallmark of the myofibroblastic phenotype), fibroblast-specific protein 1 (FSP1, a biomarker of fibroblasts), and TGF- β 1 in cultured fibroblasts was detected by western blotting and immunofluorescence. Expression of α -MARCK phosphorylation was also detected to examine the activity of PKC activation. Positive staining of α -SMA was observed in some cells in control culture conditions, and these α -SMA positive cells exhibited significant morphology changes with large nuclei and cytoplasm, compared with α -SMA negative fibroblasts. Treatment with PMA 50 ng/mL for 48 hours reduced the expression of α -SMA and TGF- β 1, and pretreatment with the three PKC inhibitors mentioned above could not abrogate PMA-induced reduction of α -SMA and TGF- β 1. These results indicate that some myofibroblasts are derived from fibroblasts under basic culture conditions. PMA induces reversal of myofibroblast differentiation via a PKC-independent mechanism.

An Exploratory Analysis of Biogenic Amine and Lipid Status in Nascent Metabolic Syndrome



Daniella Lent-Schochet¹, Ryan Silva¹, Matthew McLaughlin¹, Priya Reddy¹, Joseph Leong¹, Neeraj Ramakrishnan¹, Travis Hamilton Denna¹, Ishwarlal Jialal, MD, PhD¹

¹California Northstate University College of Medicine

Background: Metabolic syndrome (MetS), a cardio-metabolic cluster afflicting 35% of American adults, increases the risk for cardiovascular disease (CVD) and type-2 diabetes (T2DM). Increased level of Trimethylamine N-oxide (TMAO), a choline and L-carnitine derived metabolite, correlates with CVD and T2DM. Prior studies have also linked elevated branched chain amino acids (BCAA), aromatic amino acids (AAA), and lipids with T2DM and CVD. However, the precise role of biogenic amines and lipids remains unclear. This study evaluated the following amines: choline, L-carnitine, TMAO, glutamate, tyrosine, isoleucine, methionine, and leucine, as well as the following lipids: ceramide, acylcarnitine, and fatty acid (FA8 to FA26), and phosphatidylcholine 34:2 (PC34:2) in MetS patients without CVD or T2DM compared to match controls. We also characterize how these metabolites correlate with inflammatory markers.

Methods: MetS (n=30) and controls (n=20) was defined by the Adult Treatment Panel III criteria, with patients having 3 of the 5 characteristics of increased triglycerides, low HDL-cholesterol, plasma glucose of 100-125 mg/dl, increased waist circumference, and hypertension. All patients had normal renal function. Samples were prepared from patient's frozen urine samples at -70 degrees, separated using liquid chromatography, and quantified with mass spectrometry.

Results: There was a statistically significant increase in L-carnitine ($p=0.0002$) and a reduction in glutamate levels in MetS ($p=0.0001$) compared to controls. There was a trend of significant increase in TMAO levels ($p=0.08$), while choline was not significantly altered in MetS. Tyrosine ($p=0.0012$) and isoleucine ($p<0.0001$) levels were significantly elevated, while lysine ($p<0.0001$) and methionine ($p=0.0110$) levels were decreased in MetS subjects compared to the controls. PC34:2 was increased in MetS compared to controls ($p=0.03$). No significant differences between ceramide, acylcarnitine, and fatty acid (FA8 to FA26) levels in MetS and control were identified.

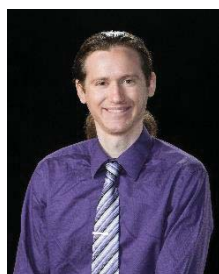
L-carnitine correlated significantly with sTNFR1 and leptin, and inversely to adiponectin. TMAO correlated with IL-6, endotoxin, and chemerin. Glutamate was inversely related to TMAO, L-carnitine, IL-6, and endotoxin. Furthermore, isoleucine significantly correlated with IL-6, lipopolysaccharide binding protein (LBP), endotoxin, nitrotyrosine, and leptin levels. Tyrosine levels did not correlate with any of the parameters. Methionine and lysine correlated inversely with toll-like receptor 4 (TLR4), while only lysine inversely correlated with IL-6 and endotoxin. PC34:2 significantly correlated with high sensitivity C-reactive protein, IL1b, IL8, free fatty acids, adipokine, leptin, and inversely with the adiponectin.

Conclusion: We show that L-carnitine, isoleucine, and PC34:2, are directly, while glutamate, lysine and methionine are inversely, correlated with markers of inflammation in nascent MetS. These metabolites could be direct biomediators or markers of inflammation in the pathogenesis of MetS, and the sequelae of CVD and T2DM.

Longitudinal Utilization of Molecular Modeling Projects Across the Chemistry Curriculum

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Christopher Wostenberg, Ph.D.

In recent years, an influx of chemical education studies have shown the educational benefits of molecular modeling projects at various levels within the chemistry curriculum. While these studies provide a framework for improving student learning, the molecular modeling projects and studies have generally been isolated to a one or two semester course. In order to monitor longer-term learning gains within and beyond chemistry, we have designed/modified existing molecular modeling projects for each chemistry course. In the general chemistry laboratory, students are tasked with utilizing molecular visualization software to determine molecular shapes, bond angles and bond lengths, which are compared to predictive models learned in the lecture. The curriculum builds upon the visualization skills from the general chemistry project with more robust molecular modeling projects delivered across the organic chemistry lecture and laboratory courses. Students perform calculations to become more familiar with concepts including chirality, reactivity, and spectroscopy. Finally, in biochemistry, students complete a semester-long inquiry based project incorporating bioinformatics, PDB visualization, and basic drug design. Each project is self-contained within its course, not requiring, but being enhanced by the experience and skills gained from previous projects. The projects build up from one atom centers in general chemistry, to multiple atom centers in organic chemistry, and finally, to complex protein structures in biochemistry. Engagement with the projects is expected to help students develop a stronger framework for a conceptual understanding of molecular geometries, properties, and reactivity. Initial development of the courses and the corresponding projects is complete and now the projects are being modified to more fully incorporate common themes, techniques and skills. Student gains in knowledge and confidence in both chemistry and software literacy due to the projects will be measured throughout the courses and beyond via surveys.

Trends of Hospitalizations as a Result of Infectious Causes in Patients with Autoimmune Diseases

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Vinna Nam

Background: The advent of biologics has led to a meaningful improvement of treatment of various autoimmune diseases. Unfortunately biologics may increase the risk of certain infections, which are one of the leading causes of death for patients with autoimmune diseases. It is critical to determine how the introduction of biologics has changed infection risk over time.

Objective: To evaluate trends of hospitalizations due to infections in autoimmune diseases.

Methods: Retrospective cohort study was performed with IBM® SPSS® Statistics 22. The data was derived from National Hospital Discharge Survey (NHDS) and from 1965 to 2010 Using ICD-9 diagnosis codes, this study identified subjects with the three autoimmune diseases which were chosen based on frequent use of biologic drugs as the treatment: multiple sclerosis (340.00), Crohn's disease (555.xx), and rheumatoid arthritis (714.0x). The infections of focus were candidiasis (112.xx), clostridium difficile (008.45), and pneumonia and influenza (480.xx-488.xx). Linear regression was performed to assess trends in the number of hospitalizations and logistic regression was performed to compare mortality before and after FDA approval of biologics. Multivariable analyses were used to adjust for age, gender, race, and primary source of payment.

Results: Overall, the number of hospitalizations statistically significantly ($p < 0.05$) increased over time in for patients with rheumatoid arthritis due to candidiasis, clostridium difficile, and pneumonia and influenza, for patients with Crohn's disease for candidiasis and pneumonia and influenza, and multiple sclerosis for clostridium difficile and pneumonia and influenza. Mortality after FDA approval of biologics significantly increased in rheumatoid arthritis patients that were hospitalized for candidiasis and clostridium difficile and in multiple sclerosis and Crohn's disease patients hospitalized for pneumonia and influenza ($p < 0.001$).

Conclusions: Among the national cohort of autoimmune patients, there is a significant increase in the number of hospitalization as well as mortality due to the infections over time. This suggests the need for closer monitoring for infections in these patient populations and a possible reevaluation of the risk/benefit profile of biologics for certain high risk subgroups.

Preclinical studies of novel positive allosteric modulators of $\alpha 7$ nicotinic receptors

Hugo R. Arias, Ph.D.

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Hugo Arias, Ph.D.

Positive allosteric modulators (PAMs) enhance the efficacy of agonists without directly acting on orthosteric, but allosteric, binding sites. We previously characterized the pharmacological activity of PAM-2 (3-furan-2-yl-N-p-tolyl-acrylamide) and two more derivatives at $\alpha 7$ nicotinic acetylcholine receptors (AChRs) (Arias et al., 2011, *Biochemistry* 50, 5263; Arias et al., 2016, *Int. J. Biochem. Cell Biol.* 76, 19). Since these highly selective compounds reactivate desensitized $\alpha 7$ AChRs, they were initially classified as type II PAMs (Targowska-Duda et al., 2014; *Neurosci. Lett.* 569, 126). This classification is supported by macroscopic current studies where the profile of PAM-2 resembles that of PNU-120596, the archetype of type II PAMs (Andersen et al., 2016; *Neuropharmacology* 107, 189).

Passive avoidance test results indicated that PAM-2 enhances memory acquisition (1.0 mg/kg) and memory consolidation (0.5-2 mg/kg), after acute and chronic (21 consecutive days) treatments (Targowska-Duda et al., 2016; *Behav. Brain Res.* 302, 142). Biochemical studies in parallel indicated that the chronic treatment (21 days) with PAM-2 increases Erk1/2 phosphorylation in the hippocampus and cortex. In addition, electrophysiological recordings of hippocampal neurons indicated that PAM-2 enhances choline-evoked $\alpha 7^*$ AChR currents.

Using the set-shifting task test, it was also demonstrated that PAM-2 enhances cognitive flexibility in an $\alpha 7$ -selective manner (i.e., 6 mg/kg methyllycaconitine inhibited the activity elicited by PAM-2 (Potasiewicz et al., 2015; *Br. J. Pharmacol.* 172, 5123). The results also showed that an inactive dose of selective $\alpha 7$ agonists such as DMXBA and A-582941 enhances the activity elicited by an inactive dose (0.1 mg/kg) of PAM-2, suggesting synergistic interactions. These results suggest that PAM-2 provokes a myriad of neurochemical effects that can be translated into the observed behavioral outcomes.

In conclusion, selective $\alpha 7$ PAMs might be used for the treatment of cognitive disorders (e.g., Alzheimer's disease and schizophrenia).

Novel roles of IL-11 in RA pathogenesis

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Hatem Elshabrawy, PhD

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disease affecting 1.5 millions of Americans. Several cytokines are involved in RA pathogenesis and may serve as potential therapeutic targets. Despite its overexpression in joints of RA patients, data from studies describing the role of IL-11 in RA are controversial. In phase I/II studies, treatment with IL-11 did not affect disease activity, while others established that patients in remission had lower serum IL-11 levels that correlated with disease activity score (DAS)28 improvement. To address these controversies, we sought to elucidate the expression pattern, and functional role of IL-11 and IL-11Ra in RA synovitis.

Methods: IL-11 and IL-11Ra expressions were determined in RA tissues and cells using immunohistochemistry, western blot, and ELISA. IL-11 effector functions, on RA fibroblasts and endothelial cells, were studied using scratch assay and endothelial cell migration and tube formation assays respectively.

Results: We found that IL-11 levels were significantly higher in RA synovial fluid (SF) compared to osteoarthritis (OA) SF (47 fold) and plasma from RA (19 fold), OA (75 fold) and normal (NL) (18 fold) volunteers. The expression of IL-11 was significantly elevated (2 fold) in the sublining endothelial cells of RA relative to NL synovial tissues (STs). In addition, the expression of IL-11 was higher (2.5 fold) in the lining fibroblasts of RA compared to OA STs. Both histology and Western blot analysis demonstrated that IL-11Ra is expressed in RA ST fibroblasts and endothelial cells but not in NL or RA macrophages. IL-11 expression was induced in RA ST fibroblasts primarily by IL-1 β ; however, expression in endothelial cells, RA monocytes, and macrophages was only promoted by RA SF. Employing RA fibroblasts based scratch assay, we observed that IL-11 could dose dependently promote RA fibroblast migration through IL-11Ra starting at 100 ng/ml, as the effect was abrogated in the presence of soluble IL-11Ra-Fc chimeric protein. In addition, IL-11 induced synovial fibroblasts to release IL-8 and VEGF which contributed to endothelial cell transmigration and tube formation. Furthermore, IL-11 induced endothelial cell migration and tube formation *in vitro* and *in vivo* at physiologically relevant concentration. The addition of the soluble IL-11Ra-Fc chimeric protein reduced the IL-11 induced endothelial cell migration by 50% and abrogated the tube formation driven by RA SF suggesting that the pro-angiogenic effect of IL-11 is mediated through IL-11Ra.

Conclusion: IL-11 promotes both RA fibroblast migration and angiogenesis. Therefore, our study suggests that IL-11 may be responsible for synovial fibroblast hyperplasia and it further potentiates disease severity by increasing the invasion of new blood vessels into the RA pannus.

In silico Anti-Cancer Drug Development: Insights from Existing Pin1 Inhibitor Testing

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Anusri Yanumula

Cancers arise from excessive unregulated cell division. A major protein involved in the regulation of cell division, whose overexpression has been linked to various cancers, is Peptidyl-prolyl cis-trans isomerase NIMA-interacting 1 (Pin1). Pin1 is a multiple domain protein, with most of the enzymatic activity occurring at the prolyl isomerase (PPIase) domain. The PPIase domain is responsible for catalyzing the interconversion of isomeric forms of other proteins involved in the cell division cycle through a phosphorylation-dependent manner. The active site in the PPIase domain that is responsible for this enzymatic activity is composed of two main areas – one composed of highly hydrophobic groups that bind well to prolyl moieties, and one composed of positively-charged side chains of amino acids that interact strongly with phosphate groups. Therefore, the PPIase domain of Pin1 has become a promising target for competitive inhibition, which then restores Pin1 activity back to equilibrium, and thus prevents the excessive cell division seen in a variety of cancers. In the effort to develop novel inhibitors of Pin1, an in-depth study of the specific residue interactions and binding structures with known inhibitors was undertaken. A set of existing Pin1 inhibitors, including Juglone, PiB, ATRA, and benzimidole, were tested in silico with Autodock Vina, a static docking and scoring program, implemented within UCSF Chimera's graphical user interface. Binding affinity scores were compared with experimental values from literature. Visualization of corresponding binding conformations will be used to generate an improved understanding of the protein-ligand interactions important for active site inhibition. The correlation between ligand molecular structure and the type and strength of interactions with Pin1 were analyzed; the insights gained from this analysis will be discussed. Future work will focus on developing novel inhibitors from the knowledge obtained.

Comparison and Evaluation of Appropriate Daptomycin (CUBICIN®) Usage across Four Sutter Health East Bay Hospitals: A Daptomycin Medication Use Evaluation

Cathy Yan-Fang Liang

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Cathy Yan-Fang Liang

Vancomycin remains one of the most widely used antibiotics for the treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) and other serious gram positive infections. Its use, however, is limited by the increasing prevalence of resistant organisms, the need for frequent monitoring, inconsistencies in complex pharmacokinetic/pharmacodynamics dosing, and known adverse complications of infusion-related reactions, nephrotoxicity, and possibly ototoxicity. Because of these issues, there is an increasing need for other agents that target resistant, gram positive infections. Daptomycin has been a potential option in patients not a candidate for vancomycin. It is currently FDA approved for gram positive, complicated skin and skin structure infections (cSSSI) and bloodstream infections (bacteremia) due to *S. aureus*. One limiting factor for daptomycin utilization, however, has been its cost. In 2016, daptomycin was the 17th highest expenditure medication for the Sutter Health System, totaling over \$5.1 million annually, and it remains one of the highest cost per utilization antibiotics at Sutter. Given the cost, this multi-center study aims to evaluate inappropriate use of daptomycin across four Sutter East Bay Hospitals: Eden Medical Center, Alta Bates Summit Medical Center (Ashby campus and Summit campus), and Delta Medical Center between the months of July 2016 to June 2017. Secondary assessments include identifying common off-labeled uses and presenting a financial analysis evaluation to potentially determine a system wide recommendation for use. Based on available data within the Sutter EMR system (EPIC), this study consists of retrospective chart reviews of subjects that received daptomycin within the prespecified facilities during the indicated time frame. Pre-defined aspects for each subject will be recorded and used in the analysis to determine what percentage of inpatient daptomycin orders were prescribed inappropriately. Data collection will be conducted between December 2017 to February 2018 and analyze will reported according through the month of March 2018.

Retrospective, observational descriptive study of an Emergency Department-based Pharmacist

Vincent Largo, Pharm.D.

Sutter Health East Bay Region PGY1 General Pharmacy Resident



Vincent Largo, Pharm.D.

The purpose of this retrospective observational study is to evaluate the potential cost savings based upon a review of the Emergency Department-based Pharmacist interventions between February 14, 2017 through September 14, 2017. This study will evaluate the impacts of associated costs of the pharmacist interventions in regards to both the patients and the healthcare system. In addition, this research will explore the perceptions of medication safety by the other healthcare personnel within the Emergency Department with the added presence of a Pharmacist.

Although JCAHO has changed its stance on prospective medication order reviews by the remote pharmacist for the Emergency Department, there may still be a significant impact from interventions made through placing a decentralized pharmacist within the Emergency Department. There are currently no prior or current studies regarding Emergency Department-based Pharmacist interventions resulting in potential cost savings for patients; the primary arm of this retrospective research study will be the first to analyze the cost savings from a patient-centric perspective. Through the implementation of an Emergency Department-based Pharmacist at Sutter Delta Medical Center on February 14, 2017, the associated costs to patients have been recorded via an excel spreadsheet. This study will retrospectively observe the types of interventions and the associated dollar amounts.

There have been several prior studies regarding Emergency-Department-based Pharmacist interventions resulting in potential associated costs for an institution; the secondary arm of this retrospective research study will analyze the associated costs from a healthcare system perspective. Prior research studies have found that medication-related issues have occurred in 11% of Emergency Department visits, which is one of the three main departments in a hospital wherein high medication error rates can have serious consequences, according to the hallmark publication *To Err is Human: Building a Safer Health System*. In addition, a significant portion of Emergency Department encounters are avoidable, stemming from patients seeking non-urgent care for medical conditions which could have been prevented or treated by a primary care physician, thus resulting in waste and inefficiency in the United States healthcare system. Based upon the prior studies, the average cost avoidance of interventions made by an Emergency Department-based Pharmacist averaged about \$1600.

There has been one prior study regarding the perceptions of medication safety when there was an implementation of an Emergency Department-based Pharmacist position; the tertiary arm of this research study will explore the perceptions of medication safety from the other Emergency Department personnel. With the fast pace and initial presentation of unstable patients, emotionally-charged family members and friends, the Emergency Department of a hospital can be a challenging environment for interdisciplinary healthcare teams. From the perspective of the various Emergency Department personnel, there are frequent interruptions and distractions due to the high volume of both new and familiar patient traffic, wide array of diseases and medical conditions, high number of verbal medication orders and dispensing machine overrides due to the emergent environment, and high-risk IV medications within designated time goals such as Alteplase.

Adherence to a Chemotherapy and Biologic Dose Rounding Protocol and Financial Implications

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Emily Medeiros, Pharm.D.

A chemotherapy and biologic dose rounding protocol was implemented at Alta Bates Summit Medical Center which allows the pharmacist to round the prescribed dose to the nearest vial size as long as the dose is within 5% of the original chemotherapy dose or within 10% of the original biotherapy dose. This protocol was implemented because dose rounding has the potential to provide the institution with significant cost savings. The purpose of this quality assurance study is to assess adherence to ABSMC's chemotherapy and biologic dose rounding protocol at the Summit and Herrick campuses, to evaluate areas for improvement, and opportunities to maximize cost savings. Data will be collected prospectively during the data collection period from January 1, 2017 through February 28, 2018. Any adult patient who received one of the selected biologic or chemotherapeutic infusions at the Summit or Herrick campus will be included in the study. The following agents were selected for evaluation because of their significant cost at ABSMC: azacitidine, bendamustine, bevacizumab, carfilzomib, cetuximab, cyclophosphamide, daunorubicin, daratumumab, decitabine, eribulin, infliximab, ifosfamide, nivolumab, paclitaxel, rituximab, and trastuzumab. Descriptive analyses will be conducted for lost financial opportunity, adherence to protocol, and data trends for process improvement. Categorical data will be reported in percentages or dollar amounts. Continuous data will be described as a mean and standard deviation. Data collection is still in progress at this time. The results of this research project will be presented in May of 2018 at the Western States Pharmacy Conference.

Evaluation of Teaching Methods in Concussion Education for High School Athletes

Aradhana Verma, Elizabeth Philips, Rohaum Hamidi, Alana Freifeld, Kamaljeet Khaira, Jose Puglisi



Rohaum Hamidi

Introduction: Nearly one-third of athletes have sustained previously undiagnosed concussions. Through discussions with high school athletic leadership in Sacramento, CA, we found that the majority of the schools have no established concussion education beyond distribution of an information sheet required by law. The purpose of this study is to assess awareness and to identify the most effective approaches of delivering concussion education to student athletes.

Methods: This is a prospective cohort study investigating the effectiveness of a “train-the-trainer” model to deliver concussion education to student athletes. Nine high schools of the San Juan Unified School District were enrolled in the study from the following sports: men’s football, men’s and women’s soccer, and men’s and women’s basketball. Schools were divided into three groups: 1) train-the-trainer intervention: coaches delivered education material to their athletes after attending a teaching workshop; 2) direct intervention: students received education via video and hand-outs; and 3) control. Teaching resources for the intervention groups were taken from the “Heads Up” program, a concussion awareness initiated by the Center for Disease Control. Schools were stratified by socioeconomic status based on free-and-reduced lunch statistics and then randomly assigned.

To determine baseline knowledge, a pre-intervention online survey was administered to all participating student athletes. The survey examined athlete knowledge of concussions, attitudes towards reporting concussions, and demographic information. An identical survey was administered at the end of each sport’s season to assess changes in knowledge and attitudes. For knowledge-based questions, the average survey score for each group before and after the intervention will be assessed with t-test and inter-group comparison with one-way ANOVA test.

Results: 221 football athletes completed the pre-intervention survey. 98 post-surveys have been received from the train-the-trainer and direct intervention cohorts, and collection is ongoing. Winter sport pre-intervention survey collection has also begun, with 143 surveys collected so far.

Preliminary results from the post-intervention survey indicate an improvement in knowledge-based and behavioral-based question responses in both the train-the-trainer and direct intervention group. The train-the-trainer group was associated with a larger degree of improvement in correct responses (72±2% pre vs. 87±2% post-intervention, $p < 0.001$) than the direct intervention group (70±2% pre vs. 78±4% post-intervention, $p < 0.03$). Values are expressed as mean±SEM.

The train-the-trainer group also showed a greater change in behavioral-based questions. For example, in the question “I know what a concussion is and I know what to do about it”, the train-the-trainer intervention group reported an increase from 31% to 78% ($\Delta = 47\%$), while the direct intervention group only increased from 38% to 56% ($\Delta = 18\%$).

Conclusion: Preliminary data suggests that the train-the-trainer model is an effective means of delivering concussion education, and is associated with larger improvements for both knowledge-based and behavioral-based questions than the direct intervention.

DON'T SLACK, TAKE-BACK: A LONG-TERM DRUG TAKE-BACK INITIATIVE

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Viet Nguyen

Objective:

This goal of this project is to provide residents of Sacramento county and surrounding areas with education and tools to properly dispose of unused and expired medications.

Background:

Medication misuse in the United States has increased at an alarming rate. One can argue this is due in part to an excess of unused medications in patients' home; these include prescription narcotics, a major cause of today's opioid epidemic. The lack of public awareness on drug disposal methods along with limited drug disposal options are contributing factors to this problem. To solve this problem, will need to work with professionals, government, local officials, and lawmakers to improve legislation.

Methods:

This will be a long term project comprised of multiple phases. Our initial phase consists of the establishment of a coalition for planning and financial procurement, education outreach, and legislative improvement.

Results:

Several studies to investigate the impact of the drug take-back initiative are planned.

We will: 1. Survey hospitals and local agencies to examine whether the current available drug collection receptacles (kiosk) have had any effect on the prevention of medication overdose. 2. Anonymously survey kiosk participants on the class of drugs that are being discarded to determine the effect on the opioid epidemic, if any. 3. Analyze drugs present in the water supply to impact of drug take back on water contamination.

Conclusion:

Current drug take-back efforts and data within the Sacramento County are limited. We intend Don't Slack, Take-Back to generate data and improve proper drug disposal. The benefits of pursuing a take-back program is multifold: improve public safety by removing the drugs from the community, educating the public about the importance of proper disposal, and increase the access to disposal programs through legislative addendums.

Poster # 1

POTENTIAL CELLULAR PROTECTIVE BENEFITS OF CAROTENOIDS EXTRACTED FROM LYCIUM BARBARUM USING NON-TOXIC SOLVENT SYSTEMS

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Katherine Le

Lycium barbarum, also known as Goji berries, is a commonly used medicinal plant in the traditional Chinese medicine and has grown its popularity as a health food product due to its high nutritional contents, including amino acids, vitamin C, and polysaccharides. In addition, Goji berries have an abundance of carotenoids, which give the Goji berries their vibrant, red color, and flavonoids, which act as antioxidants within the body to combat against cellular damage that result from the natural process of aging and chronic diseases.

The process of isolating the carotenoids from *Lycium barbarum* in liquid form involved the use of different non-toxic, biocompatible extraction solvent systems that are environmentally friendly and safe for human use, without the need for conventional toxic, organic solvents, such as ethanol, ethyl acetate, and acetone. The results produced were similar to those of the toxic, organic solvents. The individual carotenoids were further isolated using flash chromatography, which then underwent further analysis and were identified using the nuclear magnetic resonance and mass spectrometry. In addition to identifying the carotenoids in active fractions, flavonoids were also detected, and also show antioxidant activities. The chemical and physical data of the extraction and isolation procedure will be presented.

The results of the experiment could have important implications for future research regarding the effects of carotenoids and flavonoids on skin protection and the development of a natural sunscreen alternative. Additionally, further investigations should focus on the potential anti-inflammatory benefits of Goji berries in gastrointestinal disorders, such as inflammatory bowel diseases.

Poster # 2

Determination of Environmental Factors' Impact on Stress and Frequency of Stressed *C. fluminea* (n=30) within Lake Natoma

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Sujata Dahal

Corbicula fluminea (Asian clams) have presented a major problem to the United States, as they are invasive species, outcompeting the native clams for food, and imbalancing the ecosystem. The purpose of this study was to examine the environment of Lake Natoma, and the various environmental factors that can negatively affect *C. fluminea*, in order to further examine environments that have been invaded and contain this invasive species. This was done through analyzing the salinity and pH of the water, as well as the abundance of *E. coli* among the total amount of coliforms present. If the clams were found to be stressed (through evaluating the upregulation of HSP70 in the clam gill tissue), then it was hypothesized that sources of stress would be found in the environment. Thus, the environmental factors evaluated as potential sources of stress in Lake Natoma were: pH, salinity, and *E. coli* abundance. The pH of the water was 7.95, and the salinity was determined to be 1.005 ppt. The amounts of *E. coli* present in the water were consistently within a range of 0-20% of the total amount of coliforms present, with little variation; this is low enough to be considered a limited food supply that both *C. fluminea* and native clam species are competing for. The levels of HSP70 in the three clams collected indicated that 24 out of the 30 clams collected were under environmental stress in Lake Natoma. Because the pH and salinity were within the preferable range for *C. fluminea*, it can be concluded that a source of stress was due to the limited food supply, and not the other factors studied.

Poster # 3

The cellular localization of the Nrdp1, an E3 ubiquitin ligase, differs in African American versus Caucasian American prostate cancer cells

Anhao Sam^{*1}, Katelyn Macias^{*1}, Vu Nguyen¹, Kim Cao¹, Ying Ho¹, Phung Vuong¹, Hamidullab Abdul¹, Jamiee Ubhoff¹, Neelu Batra¹, Sheryl Krig¹, Blythe-Durbin Johnson², Paramita Ghosh^{2,3}, Ruth Vinall¹

**These authors contributed equally to this project. ¹California Northstate University, Elk Grove, CA, ²University of California Davis (UCD), School of Medicine, Sacramento, CA; ³VA Northern California Health Care System (VANCHCS), Mather, CA*



Anhao Sam



Katelyn Macias

Ubiquitination/proteasomal degradation is one of several post-translational control mechanisms that cells use to regulate protein levels. Dysregulation of this process is associated with the incidence and progression of several cancer types, including prostate cancer (CaP). There are several hundred different ubiquitin ligases and these have different target molecules. We have previously shown that Nrdp1, an E3 ubiquitin ligase, can mediate the ubiquitination/proteasomal degradation of ErbB3 in cell lines derived from Caucasian American (CA) CaP patients. ErbB3, a member of the EGFR family of tyrosine kinase receptors, plays a key role in promoting CaP progression; its activation causes CaP cell proliferation. Our recent immunohistochemistry (IHC) analyses revealed that Nrdp1 is predominantly localized in the cytoplasm in tumor biopsies from CA CaP patients. In contrast, Nrdp1 is predominantly localized in the nucleus of African American (AA) CaP patients. The goal of the current study was to determine why this difference exists.

IHC analysis of CaP patient diagnostic biopsies determined that nuclear Nrdp1 levels are significantly lower in AA CaP patients (n=19) versus CA CaP patients (n=121)(p=0.008). A similar association was observed in CaP cell lines; immunofluorescence (IF) analyses demonstrated MDAPCa2b and E006 (cell lines derived from AA CaP patients) express significantly lower levels of nuclear Nrdp1 compared to LNCaP, CWR22Rv1, C4-2, and C4-2B (cell lines derived from CA CaP patients). Altering androgen and/or AR levels affected Nrdp1 localization (IF analyses) in cells lines derived from CA CaP patients but not in cell lines derived from AA CaP patients. Our combined data indicate that androgen/AR-mediated translocation of Nrdp1 into the nucleus is dysregulated in AA CaP cells. On-going studies are focused on determining the functional and clinical significance of nuclear Nrdp1 expression in CaP cells as well as the potential of using nuclear Nrdp1 as a biomarker to predict patient outcome.

Poster # 4

Synthesis of a Known Binder of the GRB2 SH2 Domain from Naphthaldehyde

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Alyssa Bowsby

GRB2 (Human Growth Factor Receptor Bound Protein 2) is an adaptor protein whose overexpression has been linked to CML (chronic myeloid leukemia). Importantly, GRB2 binds its partners through its SH2 (Src Homology 2) domain and acts as a homodimer. Thus, to enhance GRB2 inhibition, we've set out to link two known monomeric binders of the GRB2 SH2 domain to yield novel dimeric antagonists. These synthesized dimeric antagonists are designed to mimic endogenous phosphotyrosine binding residues and simultaneously bind dual GRB2 SH2 domains, thus blocking the activity of the GRB2 homodimer. This method of GRB2 inhibition has not yet been studied despite the significant potential for increased binding affinity of the antagonists and subsequent enhanced biological activity. The motivation, design, and novel synthesis of our dimeric antagonists will be presented, along with a preliminary evaluation of biological activity.

Poster # 5

Sirt3, A Skinny Gene

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Dorothy Ha

Sirt3 is a major mitochondrial deacetylase which has important roles in regulation of metabolic homeostasis and metabolic diseases. The purpose of this research is to identify if Sirt3 plays a role in marrow adipogenesis to improve insulin sensitivity through increased adipokines, especially adiponectin using cell models. Particularly, we used the gainfunction of Sirt3 in mesenchymal stem cells (ST2 cells) model to assess the role of Sirt3 in adipogenesis. We were able to successfully overexpress Sirt3 and differentiate ST2 cells into adipocytes. We also found that the induction of Sirt3 leads to increased adipogenesis compared to controls. The increase in adipogenesis was in line with elevated triglyceride levels in Sirt3 overexpression compared to controls. This data is consistent with the number of differentiated adipocytes, which was highly significant in Sirt3 overexpression than in the controls using Oil Red O staining. We are working on testing if the induction of adipogenesis by Sirt3 is associated with increased gene expression of adipocyte markers as well as adiponectin/adipokines using quantitative PCR. We also will measure glucose uptake in insulin resistance model, free fatty acid uptake, and mitochondrial function of Sirt3 overexpression related adipogenesis model. Our next direction is to use the loss of function of Sirt3 in messenchymal stem cells (ST2 cells) and will assess the same parameters as gain of function of Sirt3. Therefore, we will be able to affirm the role of Sirt3 gene in modulating adipocytes via adiponectin/adipokines to regulate insulin resistance. We hope our study contributes to the efforts of revealing Sirt3 functions in metabolic diseases to ultimate goal of using Sirt3 as a potential anti-diabetogenic target in treating insulin resistance and other metabolic abnormalities.

Poster # 6

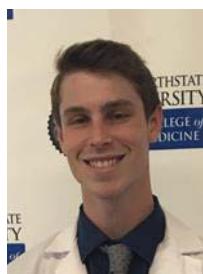
Selectivity of coronaridine congeners at nicotinic acetylcholine receptors and inhibitory activity on mouse medial habenula

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Gabriel E. Beaudoin

The inhibitory activity of coronaridine congeners on human (h) $\alpha 3\beta 4$, $\alpha 4\beta 2$, and $\alpha 7$ nicotinic acetylcholine receptors (AChRs) is determined by Ca^{2+} influx assays, whereas their effects on neurons in the ventral inferior (VI) aspect of the mouse medial habenula (MHb) are determined by patch-clamp recordings. The Ca^{2+} influx results clearly establish that coronaridine congeners inhibit h $\alpha 3\beta 4$ AChRs with higher selectivity compared to h $\alpha 4\beta 2$ and h $\alpha 7$ subtypes, and with the following potency sequence, for h $\alpha 3\beta 4$: (+)-catharanthine > (\pm)-18-methoxycoronaridine [(\pm)-18-MC] > (\pm)-18 methylaminocoronaridine [(\pm)-18-MAC] ~ (\pm)-18-hydroxycoronaridine [(\pm)-18-HC] for h $\alpha 4\beta 2$: (\pm)-18-MC > (+)-catharanthine > (\pm)-18-MAC ~ (\pm)-18-HC; and for h $\alpha 7$: (+)-catharanthine > (\pm)-18-MC > (\pm)-18-HC > (\pm)-18-MAC. Interestingly, the inhibitory potency of (+)-catharanthine ($27 \pm 4 \mu\text{M}$) and (\pm)-18-MC ($28 \pm 6 \mu\text{M}$) on MHb (VI) neurons was lower than that observed on h $\alpha 3\beta 4$ AChRs, (+)-catharanthine ($0.68 \pm 0.10 \mu\text{M}$) and (\pm)-18-MC ($1.47 \pm 0.21 \mu\text{M}$), suggesting that these compounds inhibit a variety of endogenous $\alpha 3\beta 4$ AChRs. In addition, the interaction of bupropion with (-)-ibogaine sites on h $\alpha 3\beta 4$ AChRs is tested by [^3H]ibogaine competition binding experiments. The results indicate that bupropion binds to ibogaine sites at desensitized h $\alpha 3\beta 4$ AChRs with 2-fold higher affinity than at resting receptors, suggesting that these compounds share the same binding sites. In conclusion, coronaridine congeners inhibit h $\alpha 3\beta 4$ AChRs with higher selectivity compared to other AChRs, by interacting with the bupropion (luminal) site. Coronaridine congeners also inhibit $\alpha 3\beta 4$ AChRs expressed in MHb (VI) neurons, supporting the notion that these receptors are important endogenous targets for their anti-addictive activities.

Poster # 7

Curing Cancer With Clams

Neha Prakash & Tania Nasrollahi

California Northstate University College of Health Sciences



Neha Prakash

Multidrug resistance in cancer cells results in the cells' ability to combat various anticancer treatments. In human cells this resistant behavior often leads to metastasized cancer. The overall purpose of our research is to understand the effects of multidrug resistance in cancer cells by using what we know about the HSP70 protein levels in *Corbicula fluminea*. The experiments done in regards to the HSP70 protein can be used as a model to study MXR/ABCG2 protein and its behaviors in cancer cells. Through prior research in Chemistry 110 and 120, dealing with the nutrient efficiency of the clams' environment, it was concluded that the ion concentration affects the function of biological systems of marine life. In Biology 110 and 120, the nutrient abundance and biological stress indicators were observed and analyzed to better comprehend the environment of these organisms. Through extensive research, it was determined that multidrug resistance in the invasive species promotes the induction of the MXR protein and is therefore a result of the presence of toxic metals in the gills of these freshwater clams. The expression of the MXR protein in these clams can be measured through means of the Western blot technique, as utilized in Biology 120. In order to compare the similar functions of the MXR protein in relation to humans, a protein-specific antibody must be used to target the P-Glycoprotein in human cells. Building off of past research on the environment of the *Corbicula fluminea*, it can be hypothesized that if the organisms possess the MXR/ABCG2 protein, the species will continue to obtain an advantage over the native clam species in the freshwater systems.

Poster # 8

***In Vitro* and *Ex Vivo* Effects of Silymarin Fractions on Pro-Inflammatory Cytokine Secretion**

Ella T. Mokrushin, George Talbott, Tibebe Woldermariam, Leo R. Fitzpatrick.

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Ella Mokrushin

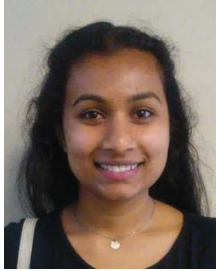
Our prior studies determined that certain extracted fractions of Silymarin inhibited pro-inflammatory cytokine secretion from macrophage and colonic epithelial cell lines. In these studies, we examined *in vitro* and *ex vivo* effects of silymarin fractions on pro-inflammatory cytokine secretion. **Methods:** Colitis was induced in male C57BL/6 mice (n=16) by giving 2 % Dextran Sulfate Sodium (DSS) drinking water for a six-day period. Control mice (n=8) were given untreated water. Employing a 24 hour colonic culture system, the *ex vivo* effects of crude silymarin extract, two different silymarin fractions, as well as commercially derived silybinin and isosilybinin (20 to 200 $\mu\text{g/ml}$) were examined. Colonic strips obtained from mice with/without DSS-induced colitis were used; and the secretion of MIP-2 and TNF- α in cell culture media was determined by ELISA. Further, the effects of silymarin compounds on IL-8 and TNF- α chemokine secretion induced by colitis supernatant (CS) was characterized with HT-29 colonic epithelial and RAW 264.7 macrophage cell lines, respectively. **Results:** Prominent inhibition of MIP-2 and TNF- α secretion from colonic strips of mice with/without DSS-induced colitis was observed with various silymarin treatments (crude extract, fractions 2 and 5, silybinin, isosilybinin). Further, dose dependent inhibition of dual cytokine (IL-23 and IL-1 β) stimulated secretion of IL-17 from colonic strips of mice with/without DSS-induced colitis was found with silymarin treatments. Finally, significant attenuation of TNF- α from CS-stimulated RAW 264.7 cells was found for crude silymarin extract and isosilybinin treatments. Inhibition of IL-8 secretion from CS-stimulated HT29 colonic epithelial cell line was observed for isosilybinin. **Conclusion:** These results additionally contribute to the identification of silymarin-derived flavonolignans with optimal anti-inflammatory properties, which can be employed for future *in vivo* testing in murine models of colitis.

Poster # 9

Stress Levels of *Corbicula fluminea* in the Presence of Phosphate

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Reshmika Ramesh

The purpose of our research is to study the effects of fertilizer runoff on an invasive species of clams known as *Corbicula fluminea*. This was accomplished using tribasic phosphate as a substitute for fertilizer and measuring the stress levels of the clams in response to various concentrations of this phosphate buffer. Stress levels were measured based on ammonia secretion. The expected result was that an increase of phosphate in clams' environment would lead to an increase in ammonia stress levels. The results showed the addition of phosphate to the environment influenced ammonia stress levels, but no direct correlation was found between concentration of phosphate and corresponding stress level.

POSTER # 10

Application of a First Order Absorption Model in Simulating Furosemide Pharmacokinetics in Adults Population Using Simcyp® Simulator

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Vu Nguyen

Objective: To validate the developed Furosemide profile in adult population using First Order Absorption Model in Simcyp® as a model for potential use in simulation in other populations

Background: Furosemide is a loop diuretic classified as class IV of the Biopharmaceutics Classification System (BCS). Furosemide is indicated in management of edema associated with heart failure and hypertension. Simcyp® simulator is a platform for modelling and simulation of the processes of absorption, distribution, metabolism and excretion of drugs in healthy and diseased populations such as healthy adults, pediatrics, geriatrics, patients with kidney failure or liver failure.

Methodology: The Furosemide compound profile was developed using extracted physicochemical properties and pharmacokinetic parameters of the drug from drug database and literature search. The simulated parameters were compared to published in vivo studies in human using the Simcyp® simulator. The adult pharmacokinetic behaviors of furosemide was studied at doses of 20 mg, 40 mg and 80 mg of furosemide.

Results: Simulated furosemide PK parameters using the Adult Population (Healthy Volunteers) were consistent with the published parameters across 2 independent studies. The studied parameters included tmax, Cmax, and AUC.

Conclusion: The Furosemide new compound profile is validated in Simcyp® Simulator and has a potential to be used in other populations such as pediatrics, geriatrics, pregnancy and patients with kidney dysfunction.

Poster # 11

Associations of Blood Glucose Monitoring Frequency and Glycemic Control in Youth with Type 1 Diabetes

Yasaman Pirahanchi, MS (California Northstate College of Medicine); Lisa Volkening, MA; Zijing Guo, MPH; Julia Cartaya, MD; Lori Laffel, MD, MPH; Joslin Diabetes Center, Boston, MA



Yasaman Pirahanchi

Blood glucose monitoring (BGM) is a fundamental component of type 1 diabetes (T1D) management and is used to make decisions about insulin administration, exercise management, and diet intake. More frequent daily BGM has been associated with lower A1c levels in persons with T1D. Our goals were to compare daily frequency of BGM ascertained by 3 different methods in youth with T1D, and to determine the relationship between BGM frequency and A1c. BGM frequency was assessed by 3 commonly used methods: BG meter download for the previous 2 weeks, clinician report (chart review), and self-report (interview). Only participants with BGM frequency data for all three methods were included in analyses. A1c was measured using standard procedures. The IRB approved the protocol and parents/youth provided written consent/assent. In the sample of 385 youth with T1D (50% female, age 13.6 ± 2.5 years, 74% pump users, A1c $8.2 \pm 0.9\%$), the 3 methods of assessing BGM frequency were significantly correlated ($r = .71$ to $.82$, $p < .0001$ for all) but BGM frequency by self-report (6.4 ± 2.3 x/day) was significantly higher than by both meter download (5.6 ± 2.4 x/day, $p < .0001$) and clinician report (5.7 ± 2.4 x/day, $p < .0001$). For all methods, more frequent BGM was associated with lower A1c overall ($r = -.31$ to $-.40$, $p < .0001$ for all) with similar associations shown across age (< 13 vs. ≥ 13 years), sex (male vs. female), diabetes duration (< 5 vs. ≥ 5 years), and insulin regimen (injections vs. pump). As meter download provided the most objective data, it was used to confirm the relationship of BGM with A1c. For each additional daily BG check, there was a 0.2% decrease in A1c ($p < .0001$). BGM remains a potent predictor of glycemic control. As BGM is a modifiable component of diabetes self-management, it warrants continued targeting in efforts to improve glycemic control in youth with T1D.

Poster # 12

Understanding Revisits to a Pediatric Emergency Department: A Pilot Study in the Patient Experience

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Tiffani Barham

Background: Revisits to the emergency department (ED) may represent a gap in quality healthcare. Current literature suggests adult patients who rate an ED visit with high satisfaction are less likely to present for a revisit. Dissatisfied patients have cited wait times and interpersonal interactions with providers as domains for improvement. However, there is little data in regards to the experience of pediatric patients and their caregivers in an ED revisit.

Objective: In this study we evaluate caregiver satisfaction with the index visit. We then identify themes among those less satisfied with the initial ED visit.

Methods: We conducted a mixed-methods study in a convenience sample of patients presenting to Rady Children's Hospital ED. A revisit was defined as any patient returning to the ED within 9 days from the index visit. Patient caregivers were interviewed with semi-structured questions regarding initial discharge process, medication administration, outpatient follow up, transportation, and social support. A written survey was then completed asking about primary care services used, quality of life, and satisfaction level of initial visit. We used a modified grounded approach to identify themes from the qualitative interviews.

Results: 24 patients were enrolled and caregivers interviewed. 83% (n=20) were somewhat or very satisfied with their initial ED visit. 17% (n=4) reported they were somewhat dissatisfied or neither satisfied nor dissatisfied. No participant was entirely dissatisfied. There was no difference in public insurance status (55% vs 50%, $p = 0.9$). From the interviews with less satisfied caregivers, we identified patient-provider communication and ED treatment process as top domains of dissatisfaction.

Conclusions: The majority of caregivers presenting for a revisit were satisfied with their initial ED visit. Similar to adult literature, our study identifies communication as an area for improvement. Future iterations of this investigation may focus on patient-provider communication and the treatment experience.

Poster # 13

Mindfulness-Based Stress Reduction (MBSR): A new elective course for medical and pharmacy students at California Northstate University



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Attending medical school is considered to be a highly stressful life event and a large number of research studies suggest that medical students may be at increased risk of psychological issues, anxiety and burnout. Importantly, stress and anxiety experienced during medical school has been shown to predict mental health issues experienced in the postgraduate years. Although there is little research on pharmacy students, several papers suggest that it is comparable to students in other healthcare fields. The Association of American Medical Colleges (AAMC) recently held a leadership forum focused on creating a culture of wellbeing and resilience in academic medicine. The suggested interventions from this forum were meditation and mindfulness-based stress reduction (MBSR), communication skills training and self-care workshops. At CNUCOM, we are in the process of adding several new elective courses for medical and pharmacy students, including MBSR. The MBSR program was created at the University of Massachusetts by Dr. Jon Kabat-Zinn in the 1970s. MBSR uses mindfulness meditation to help participants pay attention to present moment experiences. Although the MBSR program began as a program for patients with chronic pain, its utility has been recognized for physicians and students during periods of high stress. The MBSR course will be offered to both medical and pharmacy students in the fall and spring semesters and future studies will examine the effects of an MBSR curriculum on student wellness. There is a critical need to support student wellbeing during the preclinical years and determine if there are interventions that can increase student wellness. Our research may lead to the finding that certain programs, such as MBSR, would be beneficial to the psychological wellbeing of medical and pharmacy students and this could be implemented during the preclinical years in numerous professional schools around the globe.

Poster # 14

Creation and validation of a EMR clone to prepare medical students for EMR use on rotations

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Kenneth Hui

Abstract

Since 2010 Electronic Medical Records (EMR) have been increasingly adopted by health systems and individual practitioners due to benefits to quality of patient care, improve care coordination, improve patient participation, and federal subsidies and penalties. While EMR proficiency is widely expected from physicians our literature search returned little documentation of formal training by medical schools and no utilization of EMR as an educational tool beyond familiarization. We hypothesize that by creating and providing students with a EMR clone we can improve preparedness for using EMR on rotations/future practice.

Poster # 15

Synergistic Anti-Tumor Activity Of Sesquiterpene Lactones And Flavonoids: An In Vitro Study Using Human Cancer Cell Lines

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Shawna Evans

To find bioactive natural plant products as an efficacious means of treatment of cancer, we generated and evaluated a diversified group of compounds for possible *in vitro* cytotoxic activity against Human HT-29 colon carcinoma cells. Sesquiterpene lactones which were extracted from *Taraxacum officinale* (Dandelion) leaf and flavonoids from *Glycyrrhiza uralensis* (Licorice) root were found to demonstrate substantial antitumor effects. Various fractionations of the methanol extractions exhibited a significant reduction in cell viability based on our observation. Examination by utilizing a fluorescent microscope alluded that the cells were dying by an apoptotic mechanism, however the precise mechanism of cell death is currently being explored on a biochemical level. The unique blending of fractions containing the sesquiterpene lactones and flavonoids showed superior IC_{50} values and the results of the synergistic anti-tumor activity as well as the individual compounds were analyzed and documented. These discoveries emphasize the significance of the use of combining various compounds to enhance direct synergistic therapeutic effects when active components are combined between numerous medicinal herbs.

Poster # 16

Searching for a Standard: Variation in Hospice Operating Practices in Michigan

Kayla Sheehan MS BA; Maria J Silveira MD MA MPH



Kayla Sheehan

I. Original Research Background: More Americans than ever are receiving hospice care, but access to that care may not be equal. Stringent admission criteria, limitations in services offered, and rigid payment schema may limit access to hospice or compromise the care patients receive.

II. Research Objectives: To describe variation in the hospice operating practices in Michigan and identify those practices that may restrict access to hospice services.

III. Methods: We conducted an online survey of hospices in Michigan using questions developed through an iterative process involving multiple stakeholders. The survey was conducted in two parts, one for the medical director and one for the hospice administrator. Respondents answered benchmarking to FY2016. Responses were tabulated.

IV. Results: We received data from 54 medical directors (56%) and 42 hospice administrators (50%). We observed variation in access to some therapies, such as palliative chemotherapy (72% did not cover), blood products such as blood transfusions (53%), hormonal cancer treatment such as Lupron for prostate cancer (60%), TPN (63%), and vaccines (38%). The reasons for not offering these treatments included: cost, perceived futility, hospice philosophy, and lack of trained staff. Importantly, 18% could not support patients on methadone. Most hospices (60%) reported recommending temporary disenrollment for patients to access services hospice could not provide. One third of hospices lacked the ability to provide charity care (33%) or offer sliding scale payment (52%) to indigent patients. Many hospices lacked services tailored toward racial or ethnic minorities (33%).

V. Conclusion: There is variation in the kinds of services hospices in Michigan can offer. We discovered a significant proportion of hospices limit access to some palliative treatments and medications, and cannot offer supports for impoverished patients or ethnic minorities.

VI. Implications for research, policy or practice: Further work is needed to understand what will improve access to palliative treatments through hospice. Developing and enforcing standards may not be successful if hospices lack the financial ability to pay for the services in question.

Poster # 17

Improving Electronic Medical Record (EMR) System Training for Medical Students

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Kyumin Shim

Background: Electronic medical record (EMR) systems, essential and invaluable in patient management, have functions and capabilities to allow providers to easily access previous records, observe trends in laboratory data and even provide appropriate educational materials for patients. Albeit useful, these systems require adequate training and regular use for comfortable navigation. Therefore, it is important for medical students to get sufficient exposure to EMR before beginning clinical rotations.

Methods: Surveys were sent out to current third year students and preceptors at California Northstate University College of Medicine (CNUCOM) in order to gauge current EMR use.

Results: The students reported being exposed to common EMR systems EPIC and Cerner during their rotations. For future students, they suggested improving preparation methods such as an increased amount of training and focusing on learning shortcuts specific to various systems. The preceptors emphasized the importance of having familiarity and practice with EMR prior to rotations as students would be given significant access and responsibilities.

Conclusion: Introducing EMR as a part of first and second year curriculum at CNUCOM may greatly improve students' comfort levels with these systems before beginning clinical rotation years. Currently, there is a simplified EMR system being created specifically for CNUCOM students which will eventually become integrated as a part of the first year students' curriculum. Once students are able to master this system, they will then be exposed to a more complex EMR system that more resembles EPIC or Cerner used in rotation sites. Only when training for both systems are completed, the students will be taught shortcut phrases, or "dot-phrases," essential in gaining full proficiency in EMR. Such early and systematic incorporation of EMR at CNUCOM will improve long term proficiency and confidence in students' abilities in EMR as well as their capabilities as future physicians.

Poster # 18

Integrating Electronic Medical Record (EMR) Skills into Medical School Education: A Look at OpenEMR

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Jessica Doctor

Background: Most students are expected to utilize the hospital or clinic Electronic Medical Record (EMR) system when entering clinical rotational years but receive little to no comprehensive education or exposure in medical school for best EMR practices and skills.

Methods: We researched various free and open source EMRs online looking at the most popular. Three EMRs were evaluated: VistA, Practice Fusion, and OpenEMR. They were evaluated for cost effectiveness, functionality, and realistic implementation.

Results: OpenEMR is an open source software program with a large user and professional community. With over 7000 downloads per month, it is regarded as the most popular free EMR in use today. Preliminary evaluation of OpenEMR has shown its potential to adequately teach students necessary EMR skills. Functionalities are similar to widely used EMRs such as Epic and Cerner. It has the potential to be onboarded into existing IT infrastructure.

Conclusion: By integrating usage of an EMR into the California Northstate University College of Medicine curriculum, students will demonstrate many of the university's Program Learning Outcomes/Objectives while also preparing them for clinical rotations. These include but are not limited to the role of an effective EMR in a healthcare delivery system, communication, documentation of history and physical, writing a well-organized SOAP note, and ethical practice. Incorporating OpenEMR will require additional IT resources, computer hardware, and faculty training.

Poster # 19

miR-155: a negative modulator of Acute Oscillatory Shear Stress (OSS)-induced Inflammation & Vascular Dysfunction

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Introduction: Shear-sensitive micro-RNAs (miR) play an integral role in dictating vascular wall pro-inflammatory response and development of atherosclerosis. Previously, our group and others have identified an inverse relationship between micro-RNA-155 (miR-155) and inflammation in atheroprone areas of chronic low magnitude oscillatory shear stress (OSS) in vasculature and in-vitro.

Hypothesis: we hypothesized that miR-155 negatively regulates acute OSS-induced vascular inflammation and dysfunction, via modulation of the MAPK-ETS-1 pathway.

Methods: 12-week old C57B/6J wild type (WT) and miR-155 knockout mice (KO) were subjected to abdominal aortic coarctation (AAC), a unique model of acute induction of OSS, for 3-7 days. Downstream acute OSS segments were compared to upstream unidirectional shear stress (USS) segments of thoracic aorta using RT-PCR, western blot and two-way ANOVA followed by Tukey's multiple comparison analyses.

Results: In WT mice, acute OSS induced vascular inflammation evidenced by upregulation of MCP-1 and VCAM-1 expression in OSS segments compared with USS. This was associated with loss of vascular barrier function as evaluated by extravasation of Evans-blue dye assay along with increased MMP-9 and MMP-3 expression. However, vascular miR-155 levels were also higher in OSS segments compared with USS (n=6-12, P<0.05). Nevertheless, miR-155 KO mice showed enhanced expression and activation of ERK and p-38 MAPKs and downstream ETS-1, VCAM-1 and MMP-9 expression in OSS segments compared with USS versus WT controls (n=3-4, P<0.05). Whereas, tail vein injections of miR-155 overexpressing lentivirus particles in WT mice after AAC resulted in further upregulation of miR-155 and abolished OSS-induced upregulation of p-38 and downstream ETS-1, VCAM-1 and MMP-9 expression in OSS segments compared with USS versus scramble controls (n=5-6, P<0.05).

Conclusions: Despite the early upregulation of shear-sensitive miR-155, our data suggest that miR-155 serves as a negative feedback regulator to acute OSS-induced vascular inflammation via inhibition of p-38 and ETS-1, which are known targets of miR-155. Further studies are in progress to evaluate the effect of exogenous miR-155 on OSS-induced oxidative stress and vascular function, which can serve as basis for developing novel miRNA-based therapeutic modalities.

Poster # 20

Effectiveness of Using Specifically Designed Infographics for Pharmacy Students as a Teaching Strategy for Advanced Pharmacotherapeutic Topics

Subtopic: New Understanding of Multiple Myeloma and It's Novel Treatment

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California Northstate University College of pharmacy



Objective: To investigate the effectiveness of using infographics as a new teaching approach to facilitate learning, and increase level of attention span and engagement of audiences during advanced pharmacotherapeutic presentations or lectures.

Method: Developed a game strategy to present novel immunoengineering approaches in treatment of multiple myeloma in a poster format. Participants' level of knowledge about this advanced topic will be measured using questionnaires that are provided to them before and after the presentation.

Discussion: Multiple myeloma (MM) is a hematologic disorder formed by malignant plasma cells that produce monoclonal antibodies or M-proteins. Cytogenetic analysis of multiple myeloma cells has revealed over seventy subgroups of multiple myeloma cells with different cytogenetic abnormalities (CA). The type of cytogenetic abnormality has impact on protein expression and phenotype of microenvironment of the surface of multiple myeloma cells. Abnormal molecular structures on MM cells can trigger activation of lymphocytes and act as antigens. A breakthrough therapeutic technique that is called Adaptive Cell Transfer Therapy (ACTT) has been utilized for treatment of patients with refractory or relapsed multiple. This technique involves immunoengineering of patients' T lymphocytes to enable them to express receptors against tumor antigens (TA) of MM cells. Depending on the initial source of T Lymphocytes that is used in the AACT technique, there are two therapeutic approaches to targeting MM tumor antigens. One approach is the CAR T cell therapy which empowers patients' CD4 T cells through immunoengineering to express artificial T cell receptors AKA chimeric antigen receptors (CAR) to target specific antigens of patient's MM cells. The other approach is the TA-specific CTL therapy which transforms patients' CD8 t cells to CD8 cytotoxic T lymphocytes to fight against cancer. The CAR T cell therapy and the TA-specific CTL therapy are novel immunoengineering approaches in treatment of patients with multiple myeloma.

Implication: The level of cognitive development and understanding of challenging subjects greatly depends of the method of delivery of the information to the audiences. It is anticipated that result of the surveys support the utilization of infographic as an effective teaching strategy to deliver advanced therapeutic topics to pharmacy students.