# 12th Annual Research Forum

## Wednesday, November 4, 2015

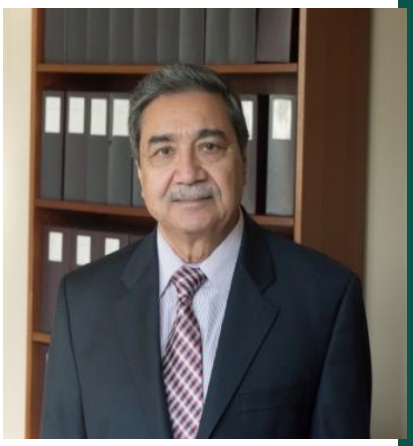
Eugene Applebaum College of Pharmacy and Health Sciences

Eugene Applebaum College of Pharmacy and Health Sciences

# Table of Contents

## Table of Contents

# Welcome



Welcome to the 12th Annual Research Forum of the Eugene Applebaum College of Pharmacy and Health Sciences. After a humble beginning in 2004, this Forum has steadily gained momentum to become a premier event and a platform for exchange of ideas and presentation of research discoveries made by our students and faculty. It displays research excellence at multiple fronts, reflecting diversity in a vibrant atmosphere.

Research in this college is highly diversified and our researchers are leaders in their field. They are involved in cutting edge projects that range from discovery of basic biological mechanisms to clinical concepts and application of healthcare. State of the art molecular, cellular, biochemical and physiological approaches tackle chronic diseases, such as Parkinson's, Cancer, Diabetes, Pulmonary, Neurological and Cardiovascular Disorders, to name a few. The current extramural research funding exceeds four million dollars.

Besides research presentations, this event offers an opportunity to host a nationally renowned scientist. This year, we are fortunate to have Dr. Rick Woychik, the Deputy Director of the National Institute of Environmental Health Sciences as our keynote speaker. His talk on *Promoting Game Changing Science in Environmental Health* is likely to generate much enthusiasm in our research community.

We also avail this opportunity to recognize our outstanding faculty who have established themselves as leaders, with exemplary records, and we honor our rising star students and Postdoctoral researchers by showing our appreciation and presentation of awards for best posters.

In conclusion, I thank all participants and guests for making this event a huge success and I welcome everyone to enjoy the day as you reflect on past accomplishments, engage in exciting dialogues and envision a bright future.

*Deepak Bhalla, Ph.D.*
*Associate Dean for Research*

Eugene Applebaum College of Pharmacy and Health Sciences

# Organizing Committees

## Research and Grants Committee

Fei Chen, Chair

Diane Adamo, Vice Chair

Deepak Bhalla (Ex officio), Associate Dean for Research

Kyle Burghardt

Steven Firestine

Sujay Galen

Lindsay Gietzen

Kashif Haque

Paul Kilgore

Qian Lin, Student member

Moh Malek

Anna Moszcynska

Michael J. Rybak

Preethy Samuel

Timothy Stemmler

## Research Forum Administrative Committee

David Asman

Sonya Bell

Sue Christie

Aaron Swift

Tracy Walker

Eugene Applebaum College of Pharmacy and Health Sciences

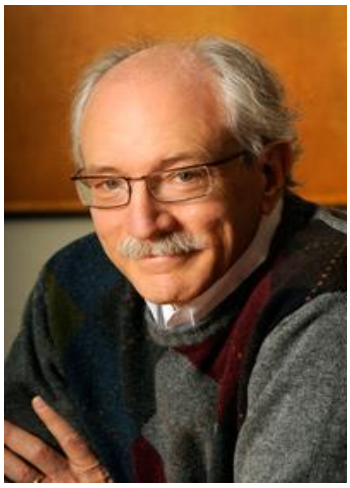
## Agenda

| | |
|---|---|
| 8:00 a.m. | Poster Setup |
| 9:00 a.m. | Student Poster Judging |
| 11:00 a.m. | Welcome<br>Deepak K. Bhalla, Ph.D.<br>Associate Dean for Research |
| 11:15 a.m. | Keynote Speaker<br>Richard Woychik, Ph.D.<br>Deputy Director, National Institute of Environmental Health Sciences<br><br>*"NIEHS: Promoting Game Changing Science in Environmental Health"* |
| 12:00 p.m. | Presentation of Awards<br>Howard J. Normile, Ph.D.<br>Dean |
| 12:30 p.m. | Lunch |
| 12:30-3:00 p.m. | Poster Display and Presentation |

Agenda

Eugene Applebaum College of Pharmacy and Health Sciences

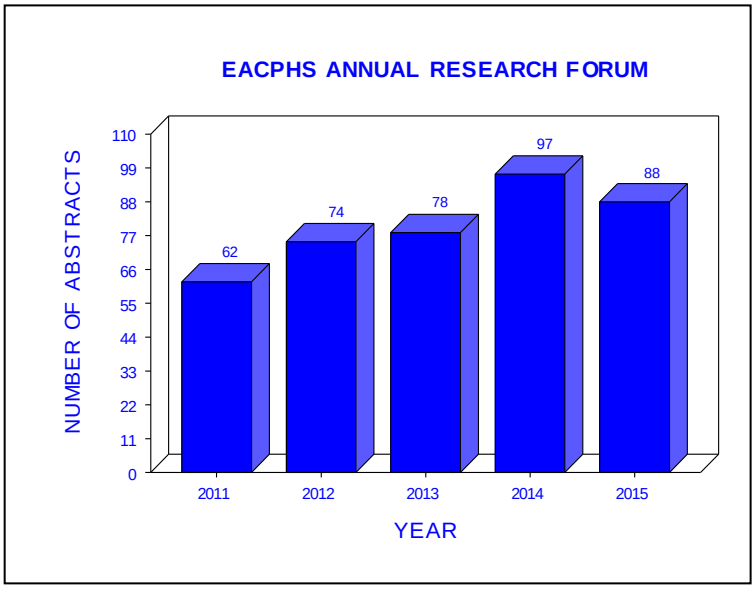
# Speaker



Dr. Richard Woychik is deputy director of the National Institute of Environmental Health Sciences (NIEHS). He is a molecular geneticist with a Ph.D. in molecular biology from Case Western Reserve University and Postdoctoral training with Dr. Philip Leder at Harvard Medical School. He spent almost 10 years at Oak Ridge National Laboratory, rising through the ranks to become head of the Mammalian Genetics Section, then director of the Office of Functional Genomics. In August 1997, he assumed the role of vice chairman for research and professor in the Department of Pediatrics at Case Western Reserve University. In 1998, he moved to the San Francisco Bay area, where he served first as the head of the Parke-Davis Laboratory for Molecular Genetics and then as chief scientific officer at Lynx Therapeutics. He returned to academics as the president and chief executive officer of The Jackson Laboratory in August 2002 and served in that role until January 2011. He has been in his current position since February 2011.

Eugene Applebaum College of Pharmacy and Health Sciences

# Abstracts



# ABSTRACTS

## BASIC SCIENCES

### Abstract No. 1 (Student_Graduate) (Basic_Sciences)

**Title**

A Structural Analysis of C-Terminal Truncated Isu Protein in Saccharomyces cerevisiae

**Affilliations**

Department of Pharmaceutical Sciences, Wayne State University
Department of Hematology, University of Pennsylvania, Philadelphia

**Authors**

Brianne Lewis (B.S), Luke Antonczak, Dr. Andrew Dancis (University of Pennsylvania), Dr. Timothy L Stemmler (Wayne State University)

**Abstract**

Friedriech's ataxia (FA), a neurodegenerative disease affecting children, is caused by decreased frataxin expression. In yeast, frataxin has a role as an iron donor to Isu in mitochondrial iron sulfur cluster biogenesis. Here, we focus on the C-terminal region on the iron recipient, Isu. We hypothesize the C-terminus is the binding region to frataxin. In addition to the wild type, three YIsu protein constructs with truncated C-termini were analyzed: YIsu Δ ... 10, YIsu Δ ... 17 and YIsu Δ ... 22. Using circular dichroism spectroscopy, we measured the secondary structure and we are able to show that the truncated YIsu proteins contain less a-helical structure and greater b-strand content.

### Abstract No. 2 (Post_Doctoral_Fellow) (Basic_Sciences)

**Title**

Hyaluronic Acid Engineered Nanomicelles Loaded with 3,4-Difluorobenzylidene Curcumin for Targeted Killing of CD44+ Stem-Like Pancreatic Cancer Cells

**Affilliations**

Use-inspired Biomaterials & Integrated Nano Delivery (U-BiND) Systems Laboratory, Department of Pharmaceutical Sciences, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, 259 Mack Avenue, Detroit, Michigan 48201, United States

**Authors**

Prashant Kesharwani, PhD and Arun K. Iyer, PhD

**Abstract**

Cancer stem-like cells (CSLCs) play a pivotal role in acquiring multidrug resistant (MDR) phenotypes. It has been established that pancreatic cancers overexpressing CD44 receptors (a target of hyaluronic acid ... HA) is one of the major contributors for causing MDR. Therefore, targeted killing of CD44 expressing tumor cells using HA based active targeting strategies may be beneficial for eradicating MDR-pancreatic cancers. Here, we report the synthesis of a new HA conjugate of copoly(styrene maleic acid) (HA-SMA) that could be engineered to form nanomicelles with a potent anticancer agent, 3,4-difluorobenzylidene curcumin (CDF). The anticancer activity of CDF loaded nanomicelles against MiaPaCa-2 and AsPC-1 human pancreatic cancer cells revealed dose-dependent cell killing. Results of cellular internalization further confirmed better uptake of HA engineered nanomicelles in triple-marker

positive (CD44+/CD133+/EpCAM+) pancreatic CSLCs compared with triple-marker negative (CD44-/CD133-/EpCAM-) counterparts. More importantly, HA-SMA-CDF exhibited superior anticancer response toward CD44+ pancreatic CSLCs. Results further confirmed that triple-marker positive cells treated with HA-SMA-CDF caused significant reduction in CD44 expression and marked inhibition of NF-κ ... B that in-turn can mitigate their proliferative and invasive behavior. Conclusively, these results suggest that the newly developed CD44 targeted nanomicelles may have great implications in treating pancreatic cancers including the more aggressive pancreatic CSLCs.

---

## Abstract No. 3 (Student_Graduate) (Basic_Sciences)

### Title

In vitro characterization of a novel primary scaffold homologue for de novo Fe-S cluster formation from Drosophila melanogaster.

### Affilliations

1: Wayne State University, Department of Biochemistry and Molecular Biology
2: University of Pennsylvania, Cell and Molecular Biology, Medicine

### Authors

1: Stephen Dzul, BSE
1: Swati Rawat, PhD
2: Andrew Dancis, MD
1: Tim Stemmler, PhD

### Abstract

Fe/S clusters are essential cofactors utilized by a variety of essential proteins in all forms of life. One of the most important pathways for general Fe/S cluster production is the iron-sulfur cluster pathway (ISC). Among eukaryotic systems, ISC has been best described in Saccharomyces cerevesiae where it localizes to the mitochondria and is essential for the formation of all cellular Fe/S clusters. In yeast ISC, de novo Fe/S cluster formation occurs on the primary scaffold protein "YIsu1". The cysteine desulfurase "Nfs1" with its essential protein cofactor "Isd11" provide reduced sulfur for assembly and frataxin (Yfh1) helps direct cluster assembly by serving as a modulator of Nfs1 activity, by assisting in Fe(II) delivery to Isu1, or through a combination of roles. In vitro studies of the yeast ISC system are limited, however, because recombinant YIsu is notoriously prone to aggregation and degredation. Recent work in the Lill laboratory on the yeast ISC system replaced YIsu with the thermophillic (Chaetomium Thermophilum) Isu facilitating novel experimentation of this pathway. In this work, we characterize the activity within the Yeast ISC system of the Drosophila melanogaster Isu (DIsu). DIsu demonstrates increased stability and yield compared to the YIsu ortholog in vitro. Recombinant DIsu has similar properties to YIsu, being a dimeric species with similar affinity for Fe(II) and forming two 2Fe-2S clusters per dimer. DIsu and yeast ISC are compatible, as DIsu has a binding interaction with yeast Nfs-Isd11 and addition of Yfh increases the rate of Fe/S cluster formation to a similar extent as observed with YIsu. These results demonstrate that DIsu is a viable replacement for YIsu for the in vitro characterization of yeast ISC.

---

## Abstract No. 4 (Faculty) (Basic_Sciences)

### Title

The Chemical Chaperone 4PBA Reduces Myofiber Damage
in Dystrophin-null mdx Mice

### Affilliations


- Department of Health Care Sciences, Wayne State University, Detroit, MI, USA.

# Department of Physiology, University of Maryland School of Medicine, Baltimore, MD, USA.


### Authors


- Morium Begam, BS., # Amber L. Mueller, BS., and * Joseph A. Roche, PT, PhD.


### Abstract


Duchenne Muscular Dystrophy (DMD) is associated with the absence of the sarcolemmal protein dystrophin, and results in severe muscle weakness, disability and early death. We hypothesized that chronically elevated endoplasmic reticulum (ER) stress is a key player in the pathogenesis of DMD. We therefore predicted that in mdx mice, which model DMD, pharmacotherapy with the chemical chaperone 4-phenylbutyric acid (4PBA), which is known to reduce ER stress, will also reduce eccentric-exercise-induced muscle damage that is characteristic of dystrophin-deficiency. In the unexercised tibialis anterior muscle (TA), we found that the ER stress marker CHOP was increased 329 % in mdx mice over control mice. Mice treated with 4PBA showed greater functional recovery and lesser myofiber damage and macrophage infiltration at 72 hr post-exercise. Our data suggest that pharmacotherapy with the chemical chaperone 4PBA reduces injury from mechanical stress in dystrophin-deficient murine muscle. Our novel findings warrant further investigation as chemical chaperones might be able to reduce disease severity in patients with DMD.


---

## Abstract No. 5 (Student_Graduate) (Basic_Sciences)

### Title

Mdig orchestrates oncogenic crosstalk between c-myc and IL-6 pathways in multiple myeloma

### Affilliations


School of Pharmacy


### Authors


Kai Wu,MD. Yongju Lu. Xiangmin Zhang, PhD. Zhengping Yi, PhD. Fei Chen, PhD


### Abstract


Emerging evidence indicates oncogenic crosstalk between dysregulated c-myc and hyperactivated interleukin-6 (IL-6) signaling in multiple myeloma (MM). The underlying mechanisms, however, remain to be fully elucidated. In the present study, we applied integrative genomics and proteomics approaches to demonstrate that mineral dust-induced gene (mdig), a key interaction partner in c-myc regulatory machinery, was actively involved in the crosstalk between c-myc and IL-6 pathway. Additional molecular biology tests suggested that genetic silencing of mdig reduced GP130 (IL6ST) expression and thus inhibited activity of the major downstream effectors in IL-6 pathway, including STAT3 and Akt. Furthermore, we unraveled cytosolic localization of mdig that was able to bind to and demethylate JAK1, a key signal transducer in the IL-6 pathway in MM cells. Such an interaction of mdig with JAK1 might maintain

the strength of the IL-6 signaling in promoting tumorigenesis of MM. Thus, these data may provide new insights into the mechanism of MM and molecular targeting for future anti-MM therapy.

---

## Abstract No. 6 (Student_Graduate) (Basic_Sciences)

### Title

Global Kinome Interactome in Human Skeletal Muscle Revealed by ATP Affinity Probes and Proteomics

### Affilliations

Department of Pharmaceutical Sciences, Wayne State University, Detroit, MI, 48202

### Authors

Yue Qi, Abdullah Mallisho, Danjun Ma, Xiangmin Zhang, Michael Caruso, Divyasri Damacharla, Rodney O Berry, Nishit Shah, Majed Abdullah Alharbi, Berhane Seyoum, Zhengping Yi

### Abstract

Protein kinases are core modulators in cell signaling (such as insulin signaling) and their functions are regulated by their protein interaction partners. However, currently, no large scale analysis have been reported for kinase interaction partners in human skeletal muscle, a key tissue in the pathogenesis of insulin resistance and type 2 diabetes (T2D). In the present study, lysate proteins from muscle biopsies from 4 lean healthy subjects were labeled with an ATP probe, while equal amount of lysate proteins without probe labeling were served as nonspecific controls. Co-Immunoprecipitations were performed to pull down the labeled proteins as well as their interaction partners, followed by in-solution tryptic digestion. The resulting tryptic peptides were analyzed by HPLC-ESI-MS/MS using an Orbitrap Elite, followed by bioinformatics. We identified 542 distinct human proteins with at least 2 unique peptides and with an enrichment ratio greater than 10 fold compared to the nonspecific control. Of the 542 identified proteins, 58 are kinases, the rest proteins were considered interaction partners of those kinases. This is the largest kinome interactome in human tissue to date. Among the 58 kinases, 14 kinases are involved in the insulin signaling pathway, 7 participate in glucose metabolic process, and 7 contribute to pathway related to diabetes, such as MAPK, PKA, ILK, PFKM, PGK1 and HK1. In order to fully understand the signaling pathways of these kinases, we also mapped interaction partners of kinases into pathways. Eighty of these kinase interaction partners are involved in pathways related to diabetes, 22 in glucose disposal, 11 in lipid oxidation, 5 in protein degradation, 5 in protein synthesis and 4 in inflammation. These results indicated the establishment of an ATP probe based proteomics platform to profile the kinome interactome in human skeletal muscle, which may be useful to provide novel insights into the molecular mechanism of skeletal muscle insulin resistance and T2D.

---

## Abstract No. 7 (Student_Graduate) (Basic_Sciences)

### Title

Protein Interaction Partners of Protein Phosphatase 2A Catalytic Subunit in Rat β ... -Islet cells Using Quantitative Mass Spectrometry


### Affilliations

wayne state university, detroit, MI

### Authors

Divyasri Damacharla ... xiangmin Zhang ... Danjun Ma ... Yue Qi ... Anjaneyulu Kowluru ... Zhengping Yi



### Abstract

Functional roles of protein phosphatases in islet function remain understudied. Protein phosphatase 2A (PP2A) is one of the major serine/threonine phosphatases. Its activity is upregulated under glucolipotoxic conditions in liver, retina and pancreatic-islet cells. However, it remains unknown about the various interactions of PP2Ac in rat pancreatic islet cells that may contribute to increased PP2A activity and regulation of cellular function. Here, using HPLCE-ESI-MS/MS, we aimed to identify the PP2Ac interaction partners involved in insulin secretion or other pathways which may lead to dysfunction or demise of the β ... -islet cells. Rat insulin-secreting β ... cells were cultured in low and high glucose (48h) conditions. The cells were lysed and Co-Immunoprecipitation is carried out with normaI IgG antibody (negative control) followed by PP2Ac antibody. The proteins were resolved using 1D-SDS-PAGE, further digested using trypsin followed by extraction and then desalting using C18-ziptip. The samples were analyzed using HPLC/nano-ESI-LTQ-Orbitrap Elite. The Xcalibur 'RAW' files were searched against the Uniprot database using the MaxQuant. The LFQ intensity of each protein was normalized against the total intensity of proteins identified in each sample. The normalized LFQ intensity was used to determine enrichment ratio of PP2Ac-specific binding (PP2Ac/NIgG) for each protein identified. Proteins which showed a 1.5 fold change between different glucose conditions were also determined.
Using HPLC-ESI-MS/MS, we identified 1131 proteins with atleast 2 unique peptides with FDR at 0.01 in at least one PP2Ac co-immunoprecipitation. For the proteins to be considered as interaction partner they need to have following criteria.1) An enrichment ratio greater than 10, 606 proteins satisfied this criterion, 2) LFQ peak area (PA) in more than half (e.g., > 4 out of 8) PP2Ac co-immunoprecipitations. In total, 514 proteins satisfied these two criteria and are classified as PP2Ac interaction partners. Among these, 38 were previously identified (BioGRID3.2 database) while 476 are novel interaction partners. This is the biggest interaction network of PP2Ac found till date. The 38 reported PP2Ac protein partners included regulatory subunits of PP2Ac (positive control for our study). Among these 514 PP2Ac partners, 265 proteins had a fold change of 1.5 (increase or decrease) when compared between low and high glucose conditions and 89 out of these 265 proteins showed significant difference ($p<0.05$). Among these 89 are regulatory subunits of PP2Ac which play key role in the localization and activity of PP2A. Ingenuity pathway analysis and extensive literature search identified multiple significantly enriched pathways of the 514 partners such as insulin secretion, protection of beta cells from apoptosis, and vesicle trafficking. In summary, we were able to identify specific proteins that are involved in significant β ... -islet cell functions as partners of PP2Ac, some of which might be potentially responsible for its increased PP2Ac activity in glucotoxic conditions. Data accrued in these studies might form basis for future studies to decipher regulatory roles of protein phosphatase 2A in β ... islet cell dysfunction under the duress of glucotoxic conditions.

## Abstract No. 8 (Student_Graduate) (Basic_Sciences)

### Title

Arsenic-induced reactive oxygen species in Akt activation and cell migration


### Affilliations

Department of Pharmaceutical Sciences, Wayne State University,, 259 Mack Avenue, Detroit, MI 48201, USA

### Authors

Lingzhi Li ... Yongju Lu ... Fei Chen


### Abstract


We have previously reported that arsenic, a well-known environmental carcinogen, induces phosphorylation of several putative Akt substrates. In the present report, we characterized one of these substrates by immunoprecipitation and mass spectrometry. The results indicate that a cytoskeleton remodeling protein, filamin A, with a molecular weight of 280kD, is phosphorylated by Akt in HEK-293 cells treated with arsenic, which was also confirmed in human bronchial epithelial cell line, BEAS-2B cells. Additional biochemical and biological studies revealed that serine 2152 (S2152) of filamin A is phosphorylated by Akt in cellular response to arsenic. Inhibition of the reactive oxygene species by NAC attenuated arsenic-induced Akt activation and filamin A phosphorylation. Thus, these data suggest that Akt dependent filamin A phosphorylation may be one of the key events in mediating arsenic-induced carcinogenesis. Antioxidant that antagonizes reactive oxygen species can ameliorate arsenic-induced Akt activation and filamin A phosphorylation, which may serve as a molecular targeting strategy for malignancies associated with environmental arsenic exposure.


## Abstract No. 9 (Student_Graduate) (Basic_Sciences)

### Title

Mdig counters Filamin A in arsenic-induced cell migration


### Affilliations

Department of Pharmaceutical Sciences, Wayne State University, 259 Mack Avenue, Detroit, MI 48201, USA

### Authors

Lingzhi Li ... Yongju Lu ... Xiangmin Zhang ... Zhengping Yi ... Fei Chen


### Abstract


Arsenic has been recognized as a common environmental threat for decades, and there are myriads of studies conducted to unveil its carcinogenic effects, including the mechanisms underlying arsenic-induced cell growth, the intracellular interactions of key proteins and the epigenetic regulations. However, it remains elusive how these effects contributed to malignant transformation of the cells. Previously, we had reported that Filamin A, a cytoskeleton remodeler, sustains arsenic-induced cell migration. In addition, we also demonstrate that arsenic is able to induce expression of the mineral dust-induced gene, mdig that represses cell migration and invasion. In the present study, we provided evidence suggesting direct interaction between mdig and Filamin A, which accounted for the down-regulation of cell migration by mdig. Meanwhile, we found that Akt-dependent phosphorylation of Filamin A weakens its interaction with mdig. On the other hand, overexpression of mdig appears to be able to reduce the level of Filamin A phosphorylation but enhance Akt activation, suggesting that mdig interaction with Filamin A prevents Akt

phosphorylation on this protein. Furthermore, silencing Akt reduced expression of c-myc, an up-stream regulator of mdig. These observations, thus, suggested an intricate interaction among Akt, Filamin A, mdig, and c-myc during arsenic-induced cell motility.

---

## Abstract No. 10 (Student_Graduate) (Basic_Sciences)

### Title

Three Layered Biodegradable Micelles as Efficient Gene Delivery System

### Affilliations

Pharmaceutical Sciences, EACPHS

### Authors

Ying Li, Master Student

### Abstract

Therapeutic nucleic acids such as siRNA, plasmid DNA or oligonucleotides are difficult to transfect into cells by themselves due to their negative charge and susceptibility to fast degradation in vivo. Non-viral gene delivery is a useful tool to deliver synthetic genes into cells. PEI-PEG is one of most explored polymers that have been used as non-viral vectors for DNA. To address the shortcomings of PEI-PEG, we synthesized triblock copolymers of low molecular weight PLLA-PEI-PLLA. These polymers form nanoparticles which load therapeutic genes in the core and are shielded with PLLA on the outside. Cationic PEI can bind with anionic DNA, and the hydrophobic PLLA remains on the surface of the PEI and DNA polyplex. Then PLLA-PEG-PLLA is added to cover this micelle and to form three-layered micelles (3LM) which release their load under acidic conditions and form hydrogels at body temperature based on stereo-complexation. Also, we can add folic acid (FA) as targeting ligand on the surface of 3LM. According to the literature, activated macrophages play a central role in Rheumatoid Arthritis (RA) and overexpress folate receptor β ... (FR-β ... ). Therefore, FR on macrophage can bind FA-3LM and subsequently endocytose them. Due to the pH and temperature being different in inflamed joints from normal physiological conditions, therapeutic genes can be released from 3LM hydrogels in inflamed joints and thus treatment can be achieved with our novel RA nanomedicine.

---

## Abstract No. 11 (Student_Graduate) (Basic_Sciences)

### Title

Investigating the Mechanism of Isatin Inhibition of the Microbial Enzyme N5-CAIR Synthetase

### Affilliations

(1) Pharmaceutical Sciences, Eugene Applebaum College of Pharmacy and Health Sciences, Detroit, Michigan

(2) MD/PhD Program, Wayne State School of Medicine, Detroit, Michigan

### Authors

Cale C. Streeter (1,2), Shiv K. Sharma PhD (1), Maria Fawaz (1), Matthew Simon (1), Prateek Sharma (1) and Steven M. Firestine PhD (1)

### Abstract

Microbes have developed resistant mechanisms to every clinically relevant anti-microbial therapeutic agent. Drug resistant microbial infections result in higher mortality rates, increased duration of hospital stays and increased health care costs.
The development of a novel anti-microbial agent, leveraging the divergence in de novo purine biosynthesis between bacteria, fungi and

lower eukaryotes and higher eukaryotes, is a promising route of investigation.
Microorganisms utilize two enzymes to convert AIR (Amino Imidazole Ribotide) into CAIR (Carboxy Amino Imidazole Ribotide). The first is N5-CAIR synthetase and the second N5-CAIR mutase. In contrast, vertebrates directly convert AIR to CAIR via the action of the enzyme AIR carboxylase. High through put screening identified the compound isatin as an inhibitor of the first enzyme in the divergent pathway of microorganisms, N5-CAIR synthetase.
Analysis of isatin analogues has revealed key findings that will help to elucidate the mechanism of inhibition. First, the position of substituents on the aromatic ring of isatin plays an important role in determining the kinetic and steady state inhibition. Second, the carbonyl at position 3 of the dione in isatin is required for inhibition. Finally, evidence suggests that a rapid reaction between isatin and the substrate AIR may occur.

---

## Abstract No. 12 (Student_Graduate) (Basic_Sciences)

### Title

Dendrimer-coated iron oxide theranostic nanoparticles for cancer imaging and therapy

### Affilliations

Department of Pharmaceutical Sciences,
Eugene Applebaum College of Pharmacy and Health Sciences,
Wayne State University, Detroit, Michigan, 48201, USA

### Authors

Duy Luong ... Prashant Kesharwani, PhD ... Rahul Deshmukh, PhD ... Arun K. Iyer, PhD

### Abstract

Background: Cancer is a major health problem next only to heart diseases and is expected to be the first leading cause of death in the next few years. Non-invasive diagnosis to detect early-stage tumors is one of the current challenges. Magnetic resonance (MR) imaging is an effective and non-invasive technique. However, the sensitivity of MR imaging strongly depends on the contrast agent and the ability of nano-carrier to selectively target cancer cells. On the other hand, anticancer therapies that use conventional chemotherapeutic agents have several limitations such as non-specific distribution in the body leading to acute toxicity in normal tissues and organs with diminished efficacy in cancer cells/tumors.

Intent: The aim of the present work is to develop a multifunctional theranostic nano-carrier, which can be used as a MR imaging contrast agent as well as a tumor homing carrier to deliver anticancer drugs specifically to cancer cells. The nano-carrier is composed of iron oxide (Fe3O4) nanoparticles decorated with folate-conjugated polyamidoamine (PAMAM) dendrimer. Iron oxide is biodegradable, non-toxic and known to be excellent material for MR imaging. PAMAM dendrimer is hyper-branched, nano-sized carrier with hydrophobic inner core with hydrophilic amine groups on the surface. PAMAM dendrimer can be used to encapsulate poorly water-soluble anticancer drugs in their hydrophobic cavities, protect anticancer drugs from premature degradation. Also, with many reactive amine groups with cationic charge, PAMAM surface can be complexed with genes or conjugated with targeting ligands such as folic acid to co-deliver anticancer drugs/genes to specific sites of interest for effective cancer therapy.

Methods: The fabrication of PAMAM-functionalized Fe3O4 nanoparticles was performed by utilizing electrostatic layer-by-layer self-assembly technique. For this purpose, Fe3O4 nanoparticles were modified with a multilayer coating composed of poly(L-glutamic

acid) (PGA), poly(L-lysine) (PLL) . Subsequently, PAMAM dendrimer conjugated with folic was bound to the nano-carrier by electrostatic interacation. Finally, acetylation reaction was used to neutralize the amine groups of PAMAM. The conjugation of PAMAM and folic acid was confirmed by H1NMR and FTIR spectroscopy. Zeta potential measurement were performed to confirm the assembly of the coating. Transmission electron microscopy was used to study the size and the morphology of the particles.

Results: H1NMR, and FTIR spectroscopy confirmed the characteristic peaks for PAMAM conjugated folic acid. Zeta potential measurements confirmed the self-assembly of PGA, PLL and PAMAM in each step. The zeta potential of the carrier was measured after the acetylation reaction and was found to be negative suggesting that all of the remaining amine groups were converted to acetamide groups.
Conclusion: Iron oxide nanoparticles were successfully coated with folate conjugate-PAMAM dendrimers for targeting and therapy of folate overexpressing cancers.

Future Direction: The future work involves loading the carriers with anticancer agents and/or siRNAs. The resulting multifunctional carriers will be analyzed by vibrating sample magnetometer analysis, and tested in vitro in cell cultures followed by in vivo studies. This approach could be extended to various nanoparticles and targeting ligands to develop promising theranostic carriers that could be used for imaging as well as treatment of different types of cancer.

---

## Abstract No. 13 (Post_Doctoral_Fellow) (Basic_Sciences)

### Title

Mdig gene-environment interaction in human cancers

### Affilliations

Department of Pharmaceutical Sciences, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI, USA

### Authors

Chitra Thakur, PhD
Fei Chen, PhD

### Abstract

ABSTRACT:
Mineral dust-induced gene, mdig has recently been identified and is known to be overexpressed in a majority of human cancers and holds predictive power in the poor prognosis of the disease. Mdig is an environmentally expressed gene that is involved in cell proliferation, neoplastic transformation and immune regulation. With the advancement in deciphering the prognostic role of mdig in human cancers, our understanding on how mdig renders a normal cell to undergo malignant transformation is still very limited. This work reviews the current knowledge of the mdig gene in context to human neoplasias and its relation to the clinico-pathologic factors predicting the outcome of the disease in patients. It also emphasizes on the promising role of mdig that can serve as a potential candidate for biomarker discovery and as a therapeutic target in inflammation and cancers. Considering the recent advances in understanding the underlying mechanisms of tumor formation, more preclinical and clinical research is required to validate the potential of using mdig as a novel biological target of therapeutic and diagnostic value.

SUMMARY:
Expression level of mdig influences the prognosis of several human cancers especially cancers of the breast and lung. Evaluation of mdig in cancers can offer novel biomarker with potential therapeutic interventions for the early assessment of cancer development in patients.

---

## Abstract No. 14 (Student_Graduate) (Basic_Sciences)

### Title

Multifunctional polymeric nanodelivery system as a modular platform for targeted cancer therapy

### Affilliations

1 Use-inspired Biomaterials & Integrated Nano Delivery (U-BiND) Systems Laboratory, Department of Pharmaceutical Sciences, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, 259 Mack Ave, , Detroit, MI 48201, USA ... 2Molecular Therapeutics Program, Barbara Ann Karmanos Cancer Institute, Wayne State University, School of Medicine, Detroit, Michigan, 48201, USA

### Authors

Shaimaa Yousef1,B.S. ... Arun K. Iyer1,2,PhD

### Abstract

Background:
Cancer is characterized by uncontrolled cell proliferation and resistance to cell death. According to the center of disease control, it is the second leading cause of death in USA after cardiovascular diseases. Chemotherapy is one of the most commonly used therapeutic strategies to fight cancer. However two major limitations for the cancer chemotherapy are toxicity towards rapidly growing normal cells, as well as the emergence of multi drug resistance (MDR) mechanisms leading to poor therapeutic outcomes in addition to serious side effects.

Objective:
The objective of the present work is to develop multifunctional polymeric nano-delivery system as a modular platform for delivering drugs and siRNA in a targeted fashion for effective cancer therapy. This carrier is composed of styrene co-maleic anhydride copolymer grafted to the branched polymer polyethylenimine (PEI). The amphiphilic nature of this copolymer allows it to self-assemble to form micelles in water which can encapsulate hydrophobic chemotherapeutic drugs in its core. Also, cationic charge of PEI can be used to condense siRNAs so that genes involved in drug resistance and/or tumor cells proliferation could be downregulated. Some of the primary amine groups on PEI are converted to azide groups, so by click chemistry, we can attach one or more targeting ligands such as galactosamine for specific cancer therapy.

Methods:
The synthesis of our modular micellar platform was determined by H1NMR, and FT-IR. Characterization of the nanocarrier for Size and zeta potential was performed by the dynamic light scattering as well as transmission electron microscopy. Critical micelle concentration (CMC) was determined by fluorescent spectroscopy using pyrene as a fluorescent probe.

Results:
The characteristic peaks in H1NMR, and FT-IR confirmed the synthesis of water soluble azide decorated nano-micelles. The hydrodynamic size of the nano-micelles was found to be around 160 nm with a narrow poly dispersity index (PDI) of 0.25. The micelles had low CMC of 0.0112 mg/ml.

Conclusion:
The results so-far reveal that we were successful in fabricating nano system that could serve as multi-functional delivery system for delivering drugs and siRNA for site specific cancer

therapy. The modular nature of the delivery system can also be extended for the delivery of various chemotherapeutic agents and genes in the management of several MDR cancers.

---

## Abstract No. 15 (Student_Graduate) (Basic_Sciences)

### Title

Molecular insight into the Frataxin-bypass activity of Isu1 suppressor mutant

### Affilliations

Wayne State University

- University of Pennsylvania

### Authors

April L. Kusowski, Ashoka Kandegedara, Andrew Dancis*, and Timothy L Stemmler

### Abstract

Iron-sulfur (Fe-S) clusters are utilized ubiquitously in nature to provide diverse functionality as cofactors bound to proteins that drive in some regard nearly every biochemical pathway. In eukaryotes, the mitochondrial Fe-S cluster bioassembly pathway provides the majority of the Fe-S clusters required by cells. This pathway is driven within the mitochondrial matrix by the cofactor assembly scaffold protein, Isu1 (in yeast). Isu1 receives iron and sulfur from protein partners and will assemble the 2Fe-2S cluster, which it can then provide for downstream insertion into proteins that require the cofactor for activity. The protein Frataxin, which when deficient is the direct cause of the neurodegenerative disease Friedreich's Ataxia, acts in some capacity with other proteins to regulate Isu1 activity. Recently, the Dancis laboratory has discovered a suppressor mutant of Isu1 that functions in the absence of Frataxin. This Isu1 bypass mutant, M107I, rescues iron homeostasis and Fe-S cluster assembly activity that is impaired in Frataxin-deleted cells. The M>I mutation occurs at a conserved amino acid in eukaryotes and resembles the E. Coli ortholog, IscU. The goal of this work is to characterize the biophysical properties and reactivity of the suppressor mutant in order to provide an enhanced understanding of the role of Frataxin in driving eukaryotic Fe-S cluster assembly.

---

## Abstract No. 16 (Student_Graduate) (Basic_Sciences)

### Title

Discovery of Piperlongumine-Histone Deacetylase Inhibitor Hybrids as Potent Antileukemic Agents against Acute Myeloid Leukemia Cells

### Affilliations

1.Department of Pharmaceutical Sciences, Eugene Applebaum College of Pharmacy and Health Sciences, 259 Mack Ave., Detroit, MI 48201, USA ...
2.Department of Oncology, Barbara Ann Karmanos Cancer Institute, 4100 John R., Detroit, MI 48201, USA ...

### Authors

Yi Liao,PhD 1 ... Xiaojia Niu,PhD 2 ... Bailing Chen,PhD 1 ... Yubin Ge* PhD 2 ... Zhihui Qin* PhD 1

### Abstract

Acute myeloid leukemia (AML) remains a disease with poor outcomes.1 Long term disease-free survival among elderly patients is only 10-15%.The discovery of innovative therapeutic agents for AML treatment represents an urgent and essential medical need.

Piperlongumine (PL) is a natural product selectively kills cancer cells in vitro and in vivo. PL induces primary myeloid leukemia cell death, and causes severe cytotoxicity to CD34+ AML cells from patient specimen, which may be attributed to its capability of disrupting cellular antioxidant defense. In addition, PL was found to induce DNA double strand breaks (DSBs) and to suppress homologous recombination DNA repair mechanism. PL-induced DNA damage has been reported in pancreatic cancer cell lines. Histone deacetylase inhibitors (HDACis) display diverse mechanisms of action in preclinical AML models and DNA damage was proposed as a major mechanism contributing to HDACi-induced growth arrest and apoptosis in both AML cell lines and in patient blasts. Because of complementary and overlapped antileukemic properties, we envisioned that when combined together, PL could reinforce anti-AML activities of HDACi and partially overcome HDACi resistance mechanisms conveyed by upregulation of oxidative stress defense systems in AML cells. In current study, a novel class of PL-HDACi hybrid compounds was designed, synthesized and tested in AML cells. Compared to co-administration, single-molecule hybrid drug approach could more efficiently co-localize synergistic pharmacophores in the same cell and greatly simplify the optimization of drug-like properties, PK and dose-toxicity profiles. We found that PL and HDACi pharmacophores cooperatively enhanced DNA damage, modulated DNA damage repair response and apoptotic pathways. The prototype compounds displayed potent anti-proliferative activities against AML cells.

---

## Abstract No. 17 (Student_Graduate) (Basic_Sciences)

### Title

Design, synthesis and initial structure-activity relationship (SAR) study of novel multifunctional dopamine D2/D3 agonists with modulatory property against α ... -synuclein aggregation and toxicity

### Affilliations

1. Wayne State University, Department of Pharmaceutical Sciences, Detroit, MI 48202
2. New York University, Department of Psychiatry, New York, N.Y. 10016

### Authors

1Dan Luo, 1Horrick Sharma, 2Tamara Antonio 2 Maarten Reith, 1 Aloke Dutta

### Abstract

Parkinson's disease (PD) is a neurodegenerative disorder with a progressive loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc) and the presence of "Lewy bodies (LBs)" as its pathogenic hallmarks. Symptoms of PD are broad in spectrum, and usually are classified into motor and non-motor features. Bradykinesia, resting tremor, rigidity, and postural instability are its key clinical features. Studies have revealed that the pathogenesis of PD, although not well defined, is multifactorial with a great degree of complexity. Oxidative stress, protein aggregation, mitochondrial dysfunction, and genetic/environmental factors are strongly implicated in the PD progression. Based on the multifactorial nature of PD pathogenesis, treatments targeting multiple pathogenic factors could be promising in terms of symptomatic and neuroprotective treatment of PD and overcoming the shortcomings presented by the current therapies. α ... -synuclein (ASN) protein, as the main component of Lewy bodies, has been one of the major targets for the development of PD therapeutics. Toxicity of aggregated ASN has been implicated in the pathogenesis of PD. Our goal is to develop multifunctional agents by modulating ASN aggregation derived toxicity while maintaining the potent D2/D3 agonistic activity. Based on our recently developed modified hybrid molecular template, an initial SAR study was carried out by covalently

attaching the D2/D3 agonist head group to suitable moieties which have been shown to modulate ASN aggregation. Compounds were characterized both in the in vitro binding assay and GTPγ ... S functional assay. Among them, D-606 exerted highest affinity for D2/D3 receptors (Ki ... D2 (58.5 ± 7.3 nM) and D3 (0.675 ± 0.17 nM). In vitro biological characterization as well as in vivo efficacy will be presented. This work is supported by NS047198 (AD).

---

## Abstract No. 18 (Student_Graduate) (Basic_Sciences)

### Title

Targeted Delivery of siRNA to Activated T Cells via Transferrin-Polyethylenimine (Tf-PEI) as a Potential Therapy of Asthma

### Affilliations

1 Wayne State University, DETROIT, MI, United States of America
2 Karmanos Cancer Institute, DETROIT, MI, United States of America
3 Ludwig-Maximilians Universität München, Munich, Germany

### Authors

Yuran Xie1, Na Hyung Kim1, Venkatareddy Nadithe1, Dana Schalk1,2, Archana Thakur1,2, Lawrence G. Lum1,2, David JP Bassett1, Olivia M Merkel1,2,3

### Abstract

Asthma is a worldwide health problem. Activated T cells (ATCs) in the lung, particularly T helper 2 cells (Th2), are strongly associated with inducement of airway inflammatory responses and chemoattraction of inflammatory cells in asthma. Small interfering RNA (siRNA) as a promising anti-sense molecule can specifically silence inflammation related genes in ATCs, however, lack of safe and efficient siRNA delivery systems limits the application of siRNA as a therapeutic molecule in asthma. Here, we designed a novel pulmonary delivery system of siRNA, transferrin- polyethylenimine (Tf-PEI), to selectively deliver siRNA to ATCs in the lung. Tf-PEI polyplexes demonstrated satisfactory physicochemical properties (size, size distribution, zeta-potential and siRNA condensation efficiency). Moreover, in vitro studies showed significantly enhanced cellular uptake and gene knockdown mediated by Tf-PEI polyplexes in human primary ATCs. Biodistribution of polyplexes in a murine asthmatic model confirmed that Tf-PEI polyplexes can efficiently and selectively deliver siRNA to ATCs. In conclusion, the present work proves the feasibility to target ATCs in asthma via Tf receptor. This strategy could potentially be used to design an efficient siRNA delivery system for asthma therapy.

---

## Abstract No. 19 (Student_Graduate) (Basic_Sciences)

### Title

GASC1 oncogene targeting with siRNA-nanoparticle for Basal-like Breast Cancer

### Affilliations

Department of Pharmaceutical Sciences, EACPHS, Wayne State University.

### Authors

Barani Govindarajan, MS

### Abstract

Triple-negative or Basal-like breast cancer (BLBC) is the most aggressive type of breast cancer and cannot be treated with any hormone or antibody therapies due to low or lack of estrogen, progesterone and Her2/neu receptors.

There are no well-established targeted therapies, other than a combination of surgery, radiation and chemotherapy. The aim of this study was to use a receptor that made targeting effective in BLBC and perform siRNA mediated oncogene knock down that are of therapeutic relevance. In this project the epigenetically relevant histone-demethylaseGASC1 was chosen for knock-down using siRNA, as it is over expressed in many cancers including the chosen BLBC model contributing to tumorigenesis. The targeting delivery was made possible by directing the nanoparticles to Transferrin (Tf) receptors, as they are of significantly higher levels in BLBC. The conjugates were prepared by coupling ligand-Tf to LMW-PEI, and encapsulating siRNA within these nanoparticles by electrostatic forces. In this way specific siRNA mediated GASC1 gene knock down was achieved in receptor-overexpressing cancer cell lines, as it showed higher transfection efficiency and gene knockdown on a post-transcriptional and translational level than the control of just LMW-PEI and siRNA.

---

## Abstract No. 20 (Student_Graduate) (Basic_Sciences)

### Title

Characterization of the cysteine desulfurase complex for mitochondrial iron-sulfur cluster biogenesis

### Affilliations

Department of Biochemistry and Molecular Biology and Department of Pharmaceutical Sciences, Wayne State University, Detroit, MI.
Department of Medicine, University of Pennsylvania, Philadelphia, PA.
Department of Pharmacology and Physiology, New Jersey Medical School, Rutgers University, Newark, NJ.

### Authors

Dulmini Barupala, Andrew Dancis MD., Debkumar Pain PhD., Timothy Stemmler PhD.

### Abstract

Iron-Sulfur (Fe-S) clusters are a versatile class of inorganic cofactors that are essential in vital biochemical tasks in every living cell. Due to the ubiquitous usage of Fe-S clusters in a number of biochemical activities, Fe-S cluster biogenesis in mitochondria is an indispensable function for the viability of cells. Defects in this pathway are now recognized as the cause for several human diseases and among them is Friedreich's ataxia (FRDA) a debilitating disease in which the patients accumulate extensive amounts of iron in mitochondria in the heart and CNS causing oxidative damage to nerve cells. Developing treatments for FRDA suffer from lack of molecular level understanding of the proteins involved in Fe-S cluster biogenesis pathway and our goal is to provide insights into biophysical and functional characters of core proteins involved in it.
ISC pathway not only assembles mitochondrial Fe-S proteins but also is crucial in the formation of cytosolic and nuclear Fe-S proteins in yeast and mammalian cells. Among other key players in this pathway, Nfs1-Isd11 (Cysteine desulfurase and desulfurase interacting protein) pair generates a persulfide from free Cysteine to provide the sulfur component for Fe-S clusters and Frataxin provides iron for the process. Here we characterize the molecular details of the cysteine desulfurase reaction mechanism by exploring the role of interactions between Nfs1, Isd11 and Frataxin in yeast. Our hypothesis is that Frataxin binds to Nfs1 in order to facilitate substrate binding by exposing the buried substrate binding sites. Isd11, which is already bound to Nfs1, facilitates persulfide formation on Nfs1 in another step.

---

## Abstract No. 21 (Faculty) (Basic_Sciences)

### Title

Enhanced Apoptotic Cancer Cell Killing after Foscan Photodynamic Therapy Combined with Fenretinide via De Novo Sphingolipid Biosynthesis

### Affilliations

(all 3 authors have the same affiliation) Department of Pharmaceutical Sciences, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, 259 Mack Ave., Detroit, MI 48201

### Authors

Duska Separovic, PhD
Jeremy Steven DeLor, BS
Nithin Boppana, MS

### Abstract

Photodynamic therapy (PDT), a cancer treatment modality, can effectively eradicate local malignancies. Because tumors recur, however, PDT needs to be optimized to improve its therapeutic benefit. To accomplish that, the objective of our research is to determine how bioactive sphingolipids contribute to more effective cancer cell killing after PDT. Sphingolipids include membrane-bound bioactive lipids that can act as anticancer agents. We and others have shown that stresses, including PDT, can disrupt the de novo sphingolipid biosynthesis pathway, leading to changes in the levels of its intermediates, which are potent regulators of cell death. The de novo sphingolipid biosynthesis pathway includes a ceramide synthase-dependent reaction, giving rise to dihydroceramide, which is then converted in a desaturase-dependent reaction to ceramide. It is not known whether targeting this pathway in combined treatment with PDT could enhance cancer cell killing. In this study we tested the hypothesis that combining PDT with fenretinide (HPR), an inhibitor of desaturase 1, the ubiquitous isoform of desaturase, enhances cancer cell killing. We found that by subjecting head and neck squamous cell carcinoma cells to the combination FoscanPDT + HPR resulted in enhanced clonogenic cell death, which was sensitive to fumonisin B1 (FB), a ceramide synthase inhibitor, as well as an antiapoptotic Bcl2 and caspase inhibitors. Using mass spectrometry we discovered that enhanced accumulation of C16-dihydroceramide, but not ceramide was induced after combination treatment at 2 and 24 h. PDT- or HPR-induced mitochondrial depolarization was enhanced after PDT+HPR at 2 h. Concomitantly, PDT±HPR-induced downregulation of Bcl2 was reversed by FB. Enhanced caspase-3 activation induced by PDT+HPR was inhibited by FB at 2 and 24 h. Overall, our data show that enhanced clonogenic cell killing after PDT+HPR is CERS-, Bcl2 inhibition-, and caspase-dependent and that enhanced accumulation of C16-dihydroceramide correlates with enhanced FB-sensitive mitochondrial apoptosis. The data suggest the involvement of the de novo sphingolipid biosynthesis pathway in enhanced apoptotic cell killing after PDT+HPR, identify PDT+HPR as a more effective combination than either treatment alone, and that the combination has potential for cancer treatment.

---

## Abstract No. 22 (Faculty) (Basic_Sciences)

### Title

The Chemical Chaperone 4PBA Reduces Myofiber Damage in Dystrophin-null mdx Mice

### Affilliations

- Wayne State University, Eugene Applebaum College of Pharmacy and Health Sciences, Department of Health Care Sciences, Physical Therapy Program, Detroit, MI 48201, USA.

# University of Maryland School of Medicine, Department of Physiology, Baltimore, MD 21201, USA.

**Authors**

Morium Begam, BS *
Amber L. Mueller, BS #
Joseph A. Roche, PT, PhD *

**Abstract**

BACKGROUND AND HYPOTHESIS. Duchenne Muscular Dystrophy (DMD) is associated with the absence of the sarcolemmal protein dystrophin, and results in severe muscle weakness, disability and early death. We hypothesized that chronically elevated endoplasmic reticulum (ER) stress is a key player in the pathogenesis of DMD. We therefore predicted that in mdx mice, which model DMD, pharmacotherapy with the chemical chaperone 4-phenylbutyric acid (4PBA), which is known to reduce ER stress, will also reduce eccentric-exercise-induced muscle damage that is characteristic of dystrophin-deficiency. METHODS. We administered 4PBA (200 mg/kg/day in 0.15M NaHCO3, Experimental Group) or vehicle (0.15M NaHCO3, Control Group) by IP injection (N = 4 mdx mice per group), once daily for 7 days pre-exercise, and until tissue collection. Eccentrically-biased exercise was performed on a custom built dynamometry rig. Exercise involved stretching the tetanized tibialis anterior muscle (TA, primary ankle dorsiflexor) muscle by plantarflexing the ankle from 90- ... 180 ° (20 repetitions at 1 repetition/min). We recorded maximum tetanic torque of the TA before exercise, soon after, and at 72 hr post-exercise to assess the magnitude of injury and recovery. After torque measurement at 72 hr, animals were euthanized, and TA muscles were harvested, snap frozen in liquid N2 and stored at - ... 80 °C. We made frozen cross sections (5 µ ... m) of TA muscles and stained them with hematoxylin and eosin to count damaged fibers. RESULTS. At 72 hr post-exercise, mice treated with 4PBA showed greater functional recovery (75 ± 3 % Vs. 36 ± 3 % pre-exercise contractile torque in Experimental and Control group, respectively) and lesser myofiber damage (12.6 ± 9 % Vs. 29 ± 8 % damaged fibers in Experimental and Control Group, respectively). Data are reported as Mean ± S.E.M.). CONCLUSION. Our data suggest that pharmacotherapy with the chemical chaperone 4PBA reduces mechanical injury in dystrophin-deficient murine muscle. Our findings warrant further investigation, as chemical chaperones might be able to reduce disease severity in patients with DMD.

This work was supported by a Grant from the Jain Foundation Inc. and a Faculty Startup Package to JAR

---

## Abstract No. 23 (Faculty) (Basic_Sciences)

**Title**

Physiological and Histological Changes in Muscles of 1-Year-Old BLAJ Mice

**Affilliations**

- Wayne State University, College of Pharmacy and Health Sciences, Department of Health Care Sciences, Physical Therapy Program. Detroit, Michigan, USA.

**Authors**

- Morium Begam, BS
- Joseph A. Roche, PT, PhD

**Abstract**

BACKGROUND AND HYPOTHESIS. The BLAJ (B6.A-Dysfprmd/GeneJ) mouse is a murine model of dysferlin-linked muscular dystrophy. We hypothesized that lipid accumulation and wasting in BLAJ muscle are

associated with muscle fiber damage. METHODS. We studied the tibialis anterior (TA) muscle in dysferlin-deficient BLAJ and wild-type (WT) C57BL/6J mice for its response to a single bout of eccentrically-biased exercise, and also assessed spontaneous morphological changes in several other muscles (quadriceps femoris, psoas major, gluteus superficialis, thoracic diaphragm and soleus) by hematoxylin and eosin staining. RESULTS. Compared to WT, the TA muscle in BLAJ mice was not more susceptible to initial injury from eccentric exercise, and not more limited in functional recovery at 1 and 3 days post-exercise. BLAJ TA muscle did however show more damaged fibers at 1 day (26 ± 1 vs. 1.4 ± 0.2 %) and 3 days (22 ± 2 vs. 4.4 ± 0.5 %) post-exercise compared to WT. Spontaneous muscle fiber damage was highest in the psoas major muscle (38 ± 2 % in BLAJ versus 0.6 ± 0.2 % in WT). In both, the TA and the psoas major muscles, lipid accumulation was mainly observed in regions of muscle fiber damage. The psoas muscle in BLAJ mice was ~65 % smaller in cross-sectional area compared to WT mice. CONCLUSION. Lipid accumulation and wasting in BLAJ muscle are associated with muscle fiber damage.

This work was supported by a Grant from the Jain Foundation Inc. and a Faculty Startup Package to JAR

---

## Abstract No. 24 (Faculty) (Basic_Sciences)

### Title

Response of Dysferlin-deficient Murine Muscle to Targeted Long-term Exercise

### Affilliations

Wayne State University. College of Pharmacy and Health Sciences, Department of Health Care Sciences, Physical Therapy Program. Detroit, Michigan, USA.

### Authors

Morium Begam, BS
Sujay S. Galen, PT, PhD
Joseph A. Roche, PT, PhD

### Abstract

BACKGROUND AND HYPOTHESIS. Dysferlin-deficiency in humans leads to limb-girdle muscular dystrophy type 2B, Miyoshi myopathy and distal anterior compartment myopathy. It is unclear as to whether physical exercise is beneficial or harmful to dysferlin-deficient muscle, although many patients mention worsening of their symptoms after periods of intense exercise. We hypothesized that concentrically-biased exercise is protective to dysferlin-deficient muscle and predicted that it would improve muscle strength without inducing muscle damage. METHODS. We studied the tibialis anterior (TA) muscle in dysferlin-deficient A/J mice and dysferlin-sufficient CRAJ mice (males, 3-4 months at inclusion) for its response to 23 sessions of concentrically-biased exercise over 12 weeks. RESULTS. In A/J mice, after 12 wk of exercise, the strength, weight and area of the exercised TA muscle increased by ~25 %, ~ 12 % and ~6 %, respectively ... whereas in CRAJ mice, these parameters decreased by ~8 %, ~2 % and ~6 %, respectively. Muscle fiber damage and inflammation in exercised muscles were very minimal in both A/J and CRAJ mice, but there were ~30 % centrally nucleated fibers (CNFs, measure of myogenesis) in A/J muscle compared to ~3 % CNFs in CRAJ muscle, and there was moderate lipid deposition in A/J muscle but not CRAJ muscle. CONCLUSION. Our data suggest that the threshold for turning on myogenesis might be low in dysferlin-deficient muscle, and that although concentrically-biased exercise is not damaging, further investigation is needed to establish the dosage that would minimize the increase in CNFs and lipid deposition seen with long-term exercise.

This work was supported by a Grant from the Jain Foundation Inc. and a Faculty Startup Package to JAR

## Abstract No. 25 (Student_Graduate) (Basic_Sciences)

### Title

Glucotoxic conditions promote activation of ATM kinase and p53 in pancreatic β ... -cells: Evidence for a role of protein prenylation

### Affilliations

Department of Pharmaceutical Sciences, Eugene Applebaum College of Pharmacy And Health Sciences, Wayne State University.
John D. Dingell VA Medical Center, Detroit, MI 48201

### Authors

Vaibhav Sidarala,
Anil Poudel, Ph.D
Anjaneyulu Kowluru, Ph.D

### Abstract

Ataxia Telangiectasia Mutated kinase [ATM kinase] and p53 tumor suppressor have been implicated in DNA repair and cellular apoptosis under the duress of specific stimuli in multiple cell types. Recent investigations have also been focused on the involvement of these proteins in regulating glucose homeostasis and insulin secretion. However, potential roles of ATM kinase and p53 in pancreatic islet dysfunction under hyperglycemic conditions remain elusive. It is well established that chronic exposure of pancreatic β ... -cells to elevated glucose concentrations [HG], as seen in T2DM, leads to significant dysregulation of the islet function. Herein, we investigated the effects of HG [20 mM ... 24 hrs] on ATM kinase and p53 in INS-1 832/13 cells and normal rodent islets. Our findings suggested significant activation of these proteins under HG conditions. Furthermore, KU-55933, a known inhibitor of ATM kinase inhibited HG-induced ATM kinase, but not p53 phosphorylation, suggesting that phosphorylation events of ATM kinase and p53 could be independent. To identify the signaling molecules regulating these proteins, we determined regulation of HG-induced ATM kinase and p53 activation by simvastatin, a global inhibitor of post-translational prenylation [farnesylation and geranylgeranylation] of G proteins. We noticed significant attenuation of HG-induced ATM kinase and p53 activation by simvastatin in INS-1 832/13 cells suggesting involvement of a prenylation step in these signaling events. Similar effects on HG-induced phosphorylation were observed with EHT1864, a known inhibitor of Rac1, which also undergoes prenylation. In conclusion, these observations indicate that HG-induced effects on islet β ... -cell may, in part, be due to activation of pro-apoptotic ATM kinase and p53, which is regulated by a prenylated protein(s) including Rac1. In light of our recent findings demonstrating the involvement of Rac1-Nox2 mediated oxidative stress in p38MAPK activation leading to β ... -cell death [Biochem Pharmacol 2015 ... 95(4) ... 301-10], studies are in progress to determine the regulatory roles of Rac1-Nox2-p38MAPK module in the activation of ATM kinase and p53, culminating in HG-induced β ... -cell dysfunction and demise.

## Abstract No. 26 (Post_Doctoral_Fellow) (Basic_Sciences)

### Title

Development of a Metal Binding Competition Assay for the Accurate Determination of Metal Binding Affinities of Iron Binding Metalloproteins under In Vivo Like Conditions

### Affilliations

Wayne State University

**Authors**

Ashoka Kandegedara, Ph.D. ... Timothy L. Stemmler, Ph.D.

**Abstract**

Cells harness the reactive properties of metals to drive complex biological pathways that require chemistry that cannot be easily accomplished by only organic molecules. Attenuation and control of metal reactivity is regulated at the molecular level by ligands on biological molecules that bind the metal. The transfer of metal cofactor to the biological partner apomolecule is accomplished through a highly regulated metal homeostasis pathway, a pathway that controls both the availability of the metal and the direct handoff of the element to the partner biomolecule. Delivery is controlled in part by the energetics related to the metal binding affinity of the partner molecule, therefore the accurate determination of metal binding affinity in the form of dissociation constants (Kd) is important if one wants to understand the reaction pathways which involve metalloprotein/enzyme systems. Within a cell, the delivery of the metal to an apoprotein is performed in the presence of multiple metal binding molecules that are competing with the protein to bind the metal. To mimic the in vivo metal loading environment within our in vitro protein systems, we have developed a competition binding assay to allow us to better determine the affinity of the partner proteins for their corresponding metals. In this study, we present a series of small ferrous iron binding molecule that have been investigated by our laboratory to determine their binding affinity and if they can compete with apoproteins for binding their native metals as a way to tune our understanding of the protein metal-binding affinities.
Ferrous complexations of a series of commercially available small molecules were measured using UV-Visible absorption and/or fluorescence spectroscopy. Samples were prepared in 20 mM HEPES (pH – 7.4), 0.15 M NaCl at $25^0$ ... C. All samples were prepared in an anaerobic wet chamber to stabilize the reduced (ferrous) form of iron and data were collected under anaerobic conditions. Under the experimental conditions, these molecules form a 1:1 complex with ferrous ion. Data calculations used to determine the small molecule binding affinity were performed using the Dynafit Software (BioKin). The calculated Kd values for the complexes are given here: Gallic acid (25.0 µM), Magfura-2 (2 .0 µM), Fura-4F( 0.36 µM), Fura-FF(0.24 µM), and Fura-2 (0.025 µM). Under competition conditions, these molecules were used in association with one of two proteins that have known Fe(II) dissociation constants to determine the impact of the competition on the molecules metal binding affinity. The calculated dissociation constants we measure under the competition conditions are in agreement with our reported values, indicating under competition conditions, the affinity of these molecules and of the apoprotein metal binding control molecules, are only partially attenuated.

---

## Abstract No. 27 (Student_Graduate) (Basic_Sciences)

**Title**

Inhibition of acetylcholinesterase by diazinon and physostigmine decreases the respiratory function of an aquatic keystone species: Daphnia pulex

**Affilliations**

EACPHS PharmD Program, Department of Pharmaceutical Science

**Authors**

Jacalyn Gualtieri, B.S., Jessica Hadchiti, B.S., Laila Khraizat, B.A., Samantha La Rocque, B.S., B.ED, Vibhuti V Matta, M.S., David K. Pitts, Ph.D.

**Abstract**

Currently there are many chemical contaminants that enter the environment that are unregulated. These are referred to as emerging contaminants and a major source is wastewater treatment plants. The impact of emerging contaminants on ecosystem health and human health is an area of increasing concern. Emerging contaminants consist of a diverse group of chemicals including: pharmaceuticals, personal care products, plasticizers, detergents, herbicides, insecticides, and many other organic waste products. Insecticides that have both agricultural and residential use are frequently found as contaminants in our surface water. There are many standardized water quality tests that utilize aquatic animals. Daphnia pulex is a zooplankton found in freshwater ecosystems, including the Great Lakes watershed, and is used in standardized Environmental Protection Agency (EPA) bioassays. D. pulex is a keystone species and is considered a non-target species of insecticides. As a keystone species, D. pulex is vital to the ecosystem function and impacts on this organism can result in alteration in the ecosystem. Ecosystems provide services such as freshwater for drinking, food, and recreation. Any alteration in the ecosystem can impact human life. Diazinon is an organophosphate insecticide and emerging contaminant that is found in surface water. This study compares the toxicity of diazinon to that of physostigmine, an acetylcholinesterase inhibitor whose effects have been previously studied by this laboratory in the D. pulex species.

An optical tracking assay was utilized to analyze cardio-respiratory function after exposure to diazinon. Cardiac function in D. pulex was assessed through recordings and calculations of heart rate (HR) and respiratory function was measured via appendage beat rate (ABR). Physostigmine was used as a model acetylcholinesterase inhibitor because it has been used extensively as a pharmacologic tool. Following exposure to 1 uM and 2 uM concentrations of physostigmine, the ABR decreased at approximately 30 minutes, with complete suppression at about 60 minutes. After exposure to 0.5 uM concentration of diazinon, ABR was significantly inhibited at 140 minutes and complete inhibition occurred at 3 hours. ABR was significantly inhibited after 140 minutes at a concentration of 1 uM diazinon. Furthermore, 4 uM of diazinon resulted in inhibition of ABR after 90 minutes. Diazinon and physostigmine were similar in that neither had an effect on HR. The ABR inhibitory response for physostigmine occurred much earlier than that of diazinon ... relatively 30 to 40 minutes compared to 2 hours for similar concentrations.

D. pulex respiratory function is inhibited by both physostigmine and diazinon. However, physostigmine exhibited a more immediate effect than diazinon on ABR in this species. This suggests that there may be a toxicokinetic difference in the effect of these agents on ABR, which may be related to lipophilicity. This non-target species is sensitive to effects of acetylcholinesterase inhibitors like diazinon and this may affect their survival in aquatic ecosystems.

---

## Abstract No. 28 (Student_Graduate) (Basic_Sciences)

**Title**

Characterization of chronic methamphetamine neurotoxicity in Parkin knockout rats

**Affilliations**

Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University

**Authors**

Akhil Sharma, MS ... Anna Moszczynska, PhD

**Abstract**

Methamphetamine (METH) is one of the most widely used addictive substances. METH is a potent sympathomimetic amine, which affects both central and peripheral nervous system. Both binge and chronic METH is highly toxic to dopaminergic (DAergic) and serotonergic (5HTergic) nerve terminals in the striatum. Neurotoxicity of METH occurs by multiple mechanisms, primarily via DA-mediated oxidative stress and is manifested by persistent decreases in DAergic and 5HTergic markers, including DA, 5-HT, and their metabolites as well as by astrogliosis. We have previously shown that binge METH oxidatively damages Parkin and decreases its levels in rat striatal synaptosomes shortly after the last dose of the drug. We have also shown that overexpression of Parkin protects against neurotoxicity of binge METH. The objective of the present study was to characterize neurotoxicity of chronic METH in wild type (wt) and Parkin knockout (KO) Long Evans rats. We hypothesized that Parkin-deficient rats would be more sensitive to METH toxic effects. To test this hypothesis, adult male Long Evans rats were treated with chronic doses of METH (wt: 20 mg/kg ... KO: 10 mg/kg, for 10 days, once a day, i.p) or saline and sacrificed 5 or 10 days after the last injection. High performance liquid chromatography (HPLC) analysis of striata revealed no statistically significant decreases in 5HTergic or DAergic markers after drug administration. When striatal sections from saline- and METH-treated rats were immunolabeled for tyrosine hydroxylase (TH), a DAergic marker, and glial fibrillary acidic protein (GFAP), an astrocyte marker, TH immunofluorescence was decreased (-25%) while GFAP immunofluorescence was increased (5d: 4 fold ... 10d: 3 fold) in METH-treated wt rats as compared to wt saline controls. Parkin KO rats showed no statistically significant decreases in striatal DAergic and 5HTergic markers and similar changes in TH and GFAP as wt rats, a 25% decrease and 3 fold increase, respectively, at 10 days after chronic METH as wt rats. As Parkin KO rats were treated with two times lower doses of METH (due to high mortality rate), our findings suggest that Parkin KO rats are more sensitive to METH toxic effects than wtLong Evans rats. Moreover, our data also suggest that wt Long Evans rats are more resistant to METH neurotoxicity than Sprague Dawley rats. In summary, our study demonstrates reactive increased astrogliosis in chronic METH-treated Long Evans rats and suggests that loss of parkin protein results in higher response of astrocytes to METH neurotoxicity. Further studies are warranted to establish the factors responsible for species differences in response to chronic METH and role of parkin in METH-induced astrogliosis.
Supported by NIH NIDA DA034783
Keywords: Methamphetamine, tyrosine hydroxylase, glial fibrillary acidic protein.

---

## Abstract No. 29 (Student_Graduate) (Basic_Sciences)

**Title**

Particle ingestion by Daphnia magna: Are microplastics a problem?

**Affilliations**

1Department of Pharmaceutical Sciences, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University

**Authors**

Kaustubh Gawde,B.Pharmacy, Neha Reddy,B.Pharmacy, Shukurat Sulaiman,B.S, Manahil Monshi, PharmD, David K. Pitts, Ph.D

**Abstract**

Microplastics have been found as environmental pollutants in both marine and freshwater aquatic systems. The impact of these microplastics on ecosystems and the food web has become a topic of increasing research interest. Microplasticshave been reported to be ingested by various aquatic organisms and these

contaminants can be transferred up the food chain.
Daphnia, also known as water fleas,are small freshwater planktonic crustaceans. Daphnia magna is one of the larger species and it has been commonly used to evaluate the toxicity of contaminants found in aquatic systems. This keystone species is also employed in a number of standard EPA bioassays. Daphnia are filter feeders that eat algae, bacteria, and detritus. They trap food particles with their specialized appendages, which then moves as a bolus down the digestive track.The types of particles that Daphnia can ingest are of particular interest, since these animals are at the bottom of the food web, just above the phytoplankton (e.g., algae). When combined with algae, polystyrene particleshave been reported tobe ingested by Daphnia. When the Daphnia were eaten by fish, this produced significant effects on fish behavior (Mattsson et al., 2015).This project focuses on a novel optical method to quantify the ingestion of polystyrene microplastic particles as a potential ecotoxicological tool. Optical image analysis techniques were used to monitor heart rate (HR), appendage beat rate (ABR), and particle ingestion. Daphnia were fed 1 um polystyrene particles and the effects of particle exposure on these three parameters was monitored. Preliminary results suggest that all three parameters can be quantified using these optical techniques. The optical technique can be used to examine the influence of temperature,particle concentration, and particle size on the rate of ingestion. Of particular importance is the potential of this technique to assess the impact of individual microplasticcontaminants and combinations of contaminants on toxicity. Can microplastics also serve as a delivery vehicle for other aquatic contaminants? If so, how will this affect ecosystem health and human health?

---

## Abstract No. 30 (Student_Graduate) (Basic_Sciences)

### Title

Microfluidic Mixing of Nanoparticle-Based Therapeutics

### Affilliations

Graduate Program in Cancer Biology,Department of Oncology, Wayne State University School of Medicine
Department of Pharmaceutical Sciences, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University
Department of Physics and Astronomy, Wayne State University

### Authors

Daniel Feldmann, B.S. ... Joshua Jacob Kovoor ... Olivia M. Merkel,PhD

### Abstract

RNA interference (RNAi) is a post-transcriptional gene silencing mechanism that occurs naturally in the cell in a sequence-specific manner to break down double stranded RNA (dsRNA) and regulate RNA expression. Small interfering RNA (siRNA) is an intermediate in the RNAi process and is double stranded RNA measuring 21-25 nucleotides in length. Synthetic siRNA can be used to achieve RNAi and to downregulate overexpressed genes. In 2001, siRNA was reported to induce RNAi in mammalian cells. The primary challenge of siRNA therapeutics, however, is the hurdle of intracellular delivery. siRNA cannot cross a biological membrane due to being a hydrophilic, negatively charged macromolecule and highly prone to nuclease degradation. Viral vectors achieve high transduction but are associated with many safety problems at the clinical level such as immune responses and carcinogensis. Therefore, safe and effective non-viral siRNA carriers are required for in-vivo delivery of siRNA. Cationic

polymers interact with negatively charged oligonucleoutides via charge complexation to form poly-electrolyte complexes. Polyethylenimine (PEI) is a polymer with a repeating unit composed of amine followed by a two carbon aliphatic spacer. PEI is able to be produced on the industrial scale and is widely used as a carrier system for siRNA. To increase bioavailability and biocompatibility, PEI can be grafted with other polymers known to reduce toxicity or slow clearance in the blood. One such mixture is the triblock copolymer polyethyleniminepolycaprolactone - polyethylene glycol (PEI-PCL-PEG). These amphiphilic cationic block copolymers spontaneously assemble to nano-sized particulate carriers, which can be utilized for complexation of nucleic acids for drug and gene delivery. Microfluidic mixing techniques, bringing cationic polymer and nucleic acid together at a constant ratio during the entire mixing process, have the potential for a gentler complexation. A more homogeneous complexation could lead to a more uniform charge distribution, increase colloidal stability, RNA protection, and consequently improve transfection efficiency. In this project, nanoparticles formed through microfluidic mixing were compared to those made in a batch reactor for their size distribution and ability to be delivered into cells.

---

## Abstract No. 31 (Student) (Basic Sciences)

### Title

Park2 Knockout Rats are Hypersensitive to the Neurotoxic Effects of Methamphetamine

### Affilliations

Wayne State University, Eugene Applebaum College of Pharmacy and Health Sciences, Detroit, MI, USA

### Authors

Bryan Killinger, MA
Anna Moszczynska, PhD

### Abstract

Parkinson's disease (PD) is a neurodegenerative disease characterized by the progressive loss of nigrostriatal dopamine neurons, which produces symptomatic motor disturbances. Loss-of-function mutations of Park2, a gene encoding the E3 ligase parkin, have been found in patients with familial PD. Despite intense investigation, the exact role of parkin in the development of PD is still unclear. It is not known whether loss of parkin influences dopamine signaling and/or increases the susceptibility of dopamine neurons to environmental neurotoxic insult. Here we tested the hypothesis that parkin knockout (PKO) rats display abnormal dopaminergic neurotransmission, without gross dopamine loss, in the nigrostriatal pathway. To test this hypothesis we administered both toxic (6 mg/kg, 4 injections, 2 h apart, i.p.) and non-toxic (2 mg/kg, 1 injection, i.p.) doses of the potent dopamine agonist methamphetamine (METH) to PKO rats and measured open-field locomotor behavior. We have found that PKO rats develop acute motor behavior abnormalities both during and following binge METH. These motor behavior abnormalities are consistent with those seen in animal PD models and manifest themselves following the third administration of toxic METH. Strikingly, several animals (40%) displayed a complete loss of motor control following the fourth dose of METH. Although these PKO rats recovered, they continued to display long-term motor deficits, including rigidity, tremors, difficulty initiating movement, and uncoordinated movements. Such abnormalities in motor behavior are consistent with large deficits (>70%) in striatal dopamine. In agreement, we observed significant reductions (-75%) in striatal dopamine content in PKO rats treated with binge METH. We also found that PKO rats display an abnormal locomotor response to a single injection of low-dose METH. In general,

low doses of METH transiently increase locomotor activity while high dose METH suppresses locomotor activity. Here, PKO rats displayed the inverse reaction to single injection of METH. Drug naïve PKO rats had a blunted locomotor response to a single low dose of METH while displaying an exacerbated response to a single-high dose METH. Despite the apparent insensitivity of PKO rats to METH-induced hyperlocomotion these animals did not have reductions in striatal dopamine or its metabolites. In summary, we demonstrate that PKO rats are hypersensitive to the neurotoxic effects of METH while conversely being hyposensitive to METH-induced hyperlocomotion. This suggests that dopamine signaling in the nigrostriatal pathway is likely impaired in PKO rats, which may predispose them to neurodegeneration.

---

## Abstract No. 32 (Student) (Basic Sciences)

### Title

Folate Receptor Targeted Delivery of siRNA and Paclitaxel to Ovarian Cancer Cells via Folate Conjugated Triblock Co-polymer to Overcome TLR4 Driven Chemotherapy Resistance

### Affilliations

Wayne State University Cancer Biology Program

### Authors

Steven, Jones, Ph.D. Candidate

### Abstract

Purpose: Our project had two purposes. First, we wanted to use our Folate-receptor-α ... (FRα ... ) targeted tri-block copolymers to increase the delivery of siRNA to cancer cells that over-express FRα ... . Secondly, by doing so, we aim to sidestep challenges in standard treatment of ovarian cancers ... such as drug and chemo-resistance, relapse and toxicity.
Methods: Our tri-block copolymer consists of polyethyleneimine-graft-polycaprolactone-block-poly(ethylene glycol), or folate coupled PEI-g-PCL-b-PEG-Fol. In our work, we looked at these polymers with different molecular weights of PEG, as well as different grafting degrees of the (g-PCL-b-PEG-Fol) chains to PEI to find the optimal delivery mechanism for siRNA uptake into the cancerous cells. For characterization of the polymers we used Dynamic Light Scattering, Transmission Electron Microscopy, Confocal Microscopy, NMR, and other biological assays for determining optimal polymer-to-siRNA (N/P) ratios for best siRNA uptake.
Results: The different PEI-g-PCL-b-PEG-Fol conjugates that were tested showed suitable sizes below 260nm, especially at N/P 5 which also allowed for full siRNA condensation. Furthermore, at N/P 5, each polymer was able to deliver the siRNA effectively in comparison to our positive control PEI. Confocal and Transmission microscopy showed the particle sizes, siRNA condensation and delivery. Previous work for our project has shown that our polymers are effectively able to knock down GAPDH in the cell by delivering the respective siRNA.
Conclusion: We have demonstrated that our polymers are effectively able to condense and deliver siRNA and achieve knockdown within the cell. This suggests that our polymers could be a good mechanism to deliver siRNA for oncogene knockdown.

## Abstract No. 33 (Faculty) (Clinical_Sciences)

### Title

The Impact of Pharmacist's Intervention on Hypertensive Patients' Compliance to their Medication Regimen

### Affilliations

School of Pharmacy, Centro Escolar University, Makati City, Philippines

### Authors

Syringa Floria Q. Balano, Pharm.D, RPh ... Hedy Mae V. Bautista, Pharm.D, RPh ... Ana Francesca D. Jacinto, Pharm.D, RPh and Leeland Anthony L. dela Luna, Pharm.D, RPh

### Abstract

Introduction: Hypertension is considered as the biggest single risk factor for deaths worldwide. Furthermore, it has been estimated that within the first year of treatment, 16 to 50% of patients with hypertension discontinue their antihypertensive medication mostly because of lack of knowledge about the disease. With this in mind, the researchers wished to determine if the interventions provided by the pharmacists were an effective means to improve compliance and adherence of patients to their medication.

Methodology: The researchers developed counseling tools to give knowledge to the patients about their condition, to monitor their blood pressure daily and answer any queries they have regarding their medication. Impact of the said tool was then measured using patients' adherence to medication therapy before and after the intervention, change in their salt intake, change in their appointment keeping with their doctors, and as well as the changes in their blood pressure.

Results: There was a significant difference in the medication adherence of the patients, their salt intake and blood pressure, before and after the pharmacist's intervention was done. The patients started with a mean systolic blood pressure (SBP) of 143 mmHg & a mean diastolic blood pressure (DBP) of 93 mmHg. After 14 days of providing patient care, the mean SBP was reduced to 129 mmHg and the mean DBP was reduced to 84 mmHg. However, there was no significant change in the appointment keeping of the patients with their physicians.

Discussion: The pharmacist intervention provided to the patients significantly increased the compliance of the patients towards their medication and low salt diet, thus improving their daily blood pressure. It is evident that pharmacist play a major role in the health care team and in providing better health outcomes for the patients. K

---

## Abstract No. 34 (Faculty) (Clinical_Sciences)

### Title

A Survey on Patient Knowledge, Attitude and Awareness on Appropriate Antibiotic Use on Selected Branch of Community Pharmacy in Metro Manila

### Affilliations

School of Pharmacy, Centro Escolar University, Makati City, Philippines

### Authors

Anna Catherine Frugalidad, Pharm.D, RPh ... Katherine Lao, Pharm.D, RPh ... Fatima Rose Mateo,Pharm.D,RPh and Leeland Anthony Dela Luna, Pharm.D, RPh

**Abstract**

Introduction: The inappropriate use of antibiotics for the treatment of patients with common infections is a worldwide problem, with implications for increasing treatment costs, adverse events, and selection of antibiotic-resistant germs. The aim of this study was to assess the knowledge and attitude regarding antibiotics use.

Methodology: The study represents a cross sectional survey using a self-administered questionnaire. A total of 75 respondents completed the questionnaire.

Results: The result shows that majority of the respondents (76.0%) is aware that antibiotics can't be purchased without a doctor's prescription and that antibiotics might develop allergy leading to patient death (82.7%). On the other hand, most of the respondents (72.0%) have incorrect knowledge regarding that all antibiotics are used for treating infection and more than half of the respondents agreed incorrectly that antibiotics will always be effective in the treatment of the same infection in the future (54.7%) and that the effectiveness of antibiotic is dependent on the brand (56.0%). Overall 49.3% of respondents have poor level of knowledge, 20.0% have moderate level of knowledge, and 30.7% have adequate knowledge ... where the median is 3 ... ranged from 0 to 5 (a potential maximum of 5).With regards to attitude and behavior, majority of the respondents have inappropriate attitude and behavior such as keeping antibiotics at home for emergency purposes (58.7%) and sharing antibiotics with their family/ friends with similar symptoms to them (52.0%). Percentage of respondents with appropriate attitude and behavior is 33.3% ... moderately appropriate is 21.3% ... inappropriate attitude and behavior is 45.3%.

Discussion: The relationship between the knowledge, attitude and behavior suggest that the lesser knowledge they have the more it contributes to inappropriate use of antibiotics.

## Abstract No. 35 () (Clinical_Sciences)

**Title**

Evaluation of aztreonam (ATM) and piperacillin/tazobactam (PIP-TAZ) pharmacodynamics with Pseudomonas aeruginosa, Escherichia coli and methicillin-resistant Staphylococcus aureus (MRSA) in combination with telavancin (TLV) in an in-vitro pharmacokinetic/pharmacodynamic (PK/PD) model

**Affilliations**

Anti-Infective Research Laboratory
Wayne State University
Detroit MI, USA

**Authors**

Juwon Yim, PharmD., Jordan R Smith, PharmD., Katie E Barber, PharmD., Jessica A Hallesy and Michael J Rybak, PharmD.,MPH

**Abstract**

Backgrounds
In clinical trials comparing TLV with vancomycin for treatment of hospital-acquired pneumonia, TLV demonstrated lower clinical cure rates than vancomycin in patients with mixed infections with Gram-negative pathogens. Here, we investigated interactions between TLV and ATM and TLV and PIP-TAZ for evidence of therapeutic antagonism in an in-vitro PK/PD model under simulated reduced renal function conditions.

Methods
In vitro models were run over 96 hrs simulating renally reduced dosing of TLV 10 mg/kg every 48 hrs, ATM 500 mg every 8 hrs, and PIP-TAZ continuous infusion 13.5 g over 24 hrs both alone and in combination against P. aeruginosa, E. coli, and methicillin-resistant S. aureus (MRSA). Samples were collected from each

model at predefined time points, plated on Tryptic soy agar plates and incubated at 37°C for 24 hrs to perform a colony count. The efficacy of antimicrobial agents was evaluated by plotting time-kill curves based on the number of remaining organisms and calculating the total reduction in log10 CFU/ml over the 96-hour time period.

Results
Against both MRSA strains, TLV was rapidly bactericidal, reducing the inoculum to 2.2 CFU/ml (-4.92 CFU/ml ± 0.3 changed from baseline) and 2 CFU/ml (-5.12 CFU/ml ± 0.04 changed from baseline) at 96 hrs, respectively, with no observed antagonism by either ATM or PIP-TAZ. PIP-TAZ maintained bacteriostatic and bactericidal activities against E. coli ATCC 25922 (-2.56 CFU/ml ± 0.36 changed from baseline) and clinical E. coli strain R1022 (-5.03 CFU/ml ± 0.37 changed from baseline) at 96 hrs, respectively whereas both strains regrew as soon as 24 hrs in ATM models. Against P. aeruginosa ATCC 27853, regrowth was noted at 24hrs in both models simulating ATM and PIP-TAZ. The addition of TLV to ATM or PIP-TAZ had no appreciable impact on activity against the two E. coli strains and P. aeruginosa strain.

Conclusions
The combinations of TLV and either ATM or PIP-TAZ did not demonstrate any antagonistic activities in the study. Clinical variables and patient characteristics should be further explored to determine possible reasons for discrepancies in outcomes.

---

## Abstract No. 36 (Student_Graduate) (Clinical_Sciences)

### Title

TRENDS IN EMERGENCY DEPARTMENT VISITS ASSOCIATED WITH Clostridium difficile INFECTION IN THE UNITED STATES, 2010-2012

### Affilliations

Department of Family Medicine and Public Health Sciences of Wayne State University School of Medicine ... Department of Pharmacy Practice of Eugene Applebaum College of Pharmacy and Health Sciences.

### Authors

Resha Shrestha MBBS, MPH, Abdulbaset Salim MBChB, MPH, Paul E. Kilgore MPH, MD.

### Abstract

Objectives: In the United States, Clostridium difficile is associated with an estimated 29,000 death each year. The objective of this study was to describe trends of C. difficile infection (CDI) associated Emergency Department (ED) visits in the United States from 2010 through 2012.
Methods: We used Healthcare Cost and Utilization Project (HCUP) datasets for the years from 2010 through 2012 to extract demographic characteristics of patients seen in United States Emergency Departments. We compiled data on patient age, gender, payer and region of the United States for International Classification Diseases-Clinical Modification, 9th Revision (ICD-9-CM) code 008.45 (C. difficile infection). We performed trend analysis and sub-group comparison across the years 2010 to 2012.
Results: From the year 2010-2012, we identified a total of 887,188 CDI-associated ED visits of which 821,790 (92.6%) resulted in admission. There was significant increase in CDIs from 30.7% to 35.2% from the year 2010 to 2012 (P <0.01). CDI-associated ED visits occurred more

in females (59.8%) as compared to males (40.2%). Majority of C. difficile infection associated visits were 65 years and above for age (64.1%). From 2010 to 2012, the greatest number of the patients with CDI-associated ED visits occurred in the Southern region of the U.S. (34.8%) and in persons with Medicare (69.3%).
Conclusion: Our study results showed an increasing trend of CDI-associated ED visits from the year 2010 through 2012. Our analysis also demonstrated that CDI-associated ED visits were more frequent in older age groups, females and the Southern region of the United States. Interventions to reduce the impact of CDI among older adults in the U.S. are urgently needed and are likely to yield large savings in healthcare costs.

---

## Abstract No. 37 (Student_Graduate) (Clinical_Sciences)

### Title

Vancomycin-Related Renal Insufficiency: Does Race Play a Role?

### Affilliations

1. Eugene Applebaum College of Pharmacy and Health Sciences
2. St. John Hospital and Medical Center

### Authors

Malak Abbas, Pharm.D. Candidate (1) ... Kaylin Braekevelt, Pharm.D. Candidate (1) ... Pramodini B. Kale-Pradhan, PharmD (1, 2) ... Mamta Sharma, MD (2) ... Susan Szpunar (2), PhD ... Riad Khatib (2), MD

### Abstract

Background: African Americans (AA) have a two to four times higher lifetime risk of chronic kidney disease and end stage renal disease than Whites. Vancomycin is often used in serious infections and has a potential for nephrotoxicity. The objective of this study is to determine if the incidence of renal insufficiency differs by race among patients being treated with vancomycin.
Methods: We conducted a retrospective study of adult (³ 18 y) inpatients who were on vancomycin for at least 48 hours during the period January 2014 until December 2014. Data on demographics (age, gender, and race), co-morbid conditions, clinical characteristics, vancomycin dose, duration, and nephrotoxic drugs were collected. Patients with a CrCl <30ml/min or undergoing dialysis were excluded. Acute kidney injury (AKI) was defined as an increase in serum creatinine by 0.3 mg/dL or ≥ ... 1.5 times the baseline value within 48 hours or an increase ≥ ... 1.5 times the baseline value within seven days.
Results: Ninety patients were identified during the study period, 46.7% (42) were AA. No differences were noted between groups in age, gender, BMI, Charlson Weighted Index of Comorbidity, nephrotoxic drugs, or duration of therapy. The most common indication of using vancomycin was for skin and soft tissue infection 55.6% (50) with no significant difference between the groups. Vancomycin levels were therapeutic in 33.3%, sub-therapeutic in 38% and supra-therapeutic in 22% with a comparable incidence in both groups. The mean initial trough level was 12.1 ± 6.5 in Whites and 12.3 ± 7.9 in AA (p=0.93) ... the mean maximum trough level was 15.4 ± 7.8 in Whites and 16.4 ± 8.9 in AA (p=0.59). AKI was seen in 7.8% (7) of patients ... 4/7 AA and 3/7 Whites (p=0.56). Older age (p <0.0001), high BMI (p <0.0001), and higher baseline serum creatinine correlated with a decrease in creatinine clearance (p <0.0001). A rise in serum creatinine at the end of vancomycin therapy correlated with higher BMI and higher baseline serum creatinine (p <0.0001).
Conclusion: A non-significant decrease in creatinine clearance was noted in 4/42 (9.5%) AA and 3/48 (6.3%) Whites receiving vancomycin. AKI was correlated with older age, higher BMI and higher baseline serum creatinine. A larger study is needed to verify these observations.

## Abstract No. 38 (Student_Graduate) (Clinical_Sciences)

### Title

Correlation of Pre-Hypertensive and Hypertensive Blood Pressure Readings to Self-Reported Health Behaviors in a Pro Bono Physical Therapy Clinic

### Affilliations

### Authors

Al-Qattan Hussain DPT student, Mhaid Dalia DPT student, Neda Robert DPT student, Pysh Jill DPT student, Schwartz Matthew DPT student
Advisors : Sara Arena , Martha Schiller

### Abstract

Introduction: A physical therapist (PT) is positioned to examine blood pressure (BP) and the associated health behaviors that optimize a BP reading ... however, there is paucity of evidence describing or analyzing a correlative relationship for uninsured individuals under the care of a PT. Therefore, the purposes of this study are to describe prevalence rates and correlations between pre-hypertensive (P-HTN) and hypertensive (HTN) BP readings and self-reported health behaviors among uninsured individuals evaluated by PT in a pro bono outpatient clinic.
Number of Subjects: Thirty-six (36) females
Materials/Methods: Referrals for PT evaluation were received from one family health clinic serving uninsured women in a large urban community. Age, ethnicity, referring diagnosis and a prior HTN diagnosis were recorded. Two BP readings were measured, averaged and then categorized as normal, P-HTN or HTN utilizing guidelines set forth by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Additionally, a health behaviors questionnaire (HBQ) (Black et al., 2012) recorded self-report adherence of the study participant to recommend levels of: 1) physical activity, 2) consumption of fruits and vegetables, 3) smoking and 4) weight management. Individuals were excluded if at least one BP measurement or the HBQ were not available. Descriptive statistics reported nominal data ... whereas a chi-square test ($p \leq ...$ .05) was utilized to compare P-HTN and HTN readings to each health behavior. Results: Mean age was 52 years (28-75). Thirty-four individuals were African-American, one Caucasian and one of unknown ethnicity. Low back, knee and shoulder pain comprised 83% of the referred diagnosis. Blood pressure readings were P-HTN (55.6%) and HTN (19.4%) ... whereas 10 individuals with no HTN diagnosis had P-HTN and HTN at rates of 40% and 10% and individuals with a prior HTN diagnosis had P-HTN and HTN rates of 61.5% and 23.1% respectively. Results of the HBQ were as follows ... 50% engaged in regular physical activity, 50% consumed at least five fruits and vegetables, 33% did not smoke and 28% had a healthy weight. No statistically significant correlations were identified between a P-HTN and HTN BP category and any of the four health behaviors. Conclusions: Uninsured females in an outpatient physical therapy clinic were identified with P-HTN and HTN BP readings at rates of 75%. Additionally, more than 50% reported not engaging in health behaviors associated with optimization of BP readings. Statistically significant correlations between BP category and the four health behavior were not observed ... however, small frequencies of some variables may have contributed to an inability to detect differences. Clinical Relevance: Identification of a suboptimal BP reading and/or reduced adherence to recommended healthy behaviors may guide a PT to choose health promoting interventions to optimize the BP or other health related outcomes of an individual.
KEYWORDS: Blood Pressure, Health Behaviors, Physical Therapy

## Abstract No. 39 (Faculty) (Clinical_Sciences)

### Title

Adherence to Inpatient COPD Guidelines


### Affilliations

1. Wayne State University
2. St. John Hospital and Medical Center
3. Henry Ford Hospital
4. Harper University Hospital

### Authors

Melissa Lipari, PharmD, BCACP,1,2, Amber Lanae Smith, PharmD, BCPS,1,3, Pramodini Kale-Pradhan, PharmD, FCCP,1,2, Sheila Wilhelm, PharmD, FCCP, BCPS,1,4


### Abstract


Background

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines provide evidence-based recommendations for the inpatient management of severe COPD exacerbations. It is unknown how consistently clinicians adhere to these guidelines in an urban teaching hospital. The purpose of this study was to assess the management of inpatient COPD exacerbations at a large teaching institution. The objectives were to: (1) assess adherence to GOLD guidelines, and (2) evaluate readmission rates following inpatient COPD management.

Methods

A retrospective chart review within a large academic institution was performed. Patients 18-89 years admitted between December 2010 and August 2012 with ICD9 code indicating COPD were included if they had documented shortness of breath due to COPD exacerbation in an initial inpatient note. Patient demographics, length of stay (LOS), Charlson Comorbidity score, pulmonary medications, and 30-day readmission were collected. Descriptive statistics were used to characterize guideline adherence and readmission.

Results

615 patients were screened ... 94 met the inclusion criteria for analysis. The majority of patients were female (70.2%) and African American (85.1%), with a median age of 68 years (IQR 58-75 years). Median LOS was 3 days (IQR 1-5 days), and median Charlson comorbidity score was 6 (IQR 5-8). All patients received an inhaled short-acting beta agonist, 52/94 (55.3%) also received an inhaled short-acting anticholinergic agent. Seventy-eight (83%) received systemic corticosteroids, of which three patients (3.9%) received guideline-recommended doses (30-40mg prednisolone/day). Sixty-four patients (68.1%) received antibiotics for a pulmonary indication, of which 71.9% received appropriate antibiotics for the indication. Two of 94 patients were managed in complete adherence with GOLD recommendations. A total of 24 patients (25.5%) were readmitted within 30 days of discharge, nine of these patients were readmitted for a COPD reason.

Conclusion

While all patients received some guideline-recommended therapy, the majority had aspects of their therapy that deviated from GOLD recommendations. This provides opportunities for further optimization of treatment of COPD exacerbations.


---

## Abstract No. 40 (Student_Graduate) (Clinical_Sciences)

### Title

Prescribing Patterns of Antimicrobials for Suspected Nosocomial Urinary Tract Infections: Pre- and Post-Educational Intervention

**Affilliations**

1. Eugene Applebaum College of Pharmacy and Health Sciences
2. St. John Hospital and Medical Center

**Authors**

Nathan French, Pharm.D. Candidate(1,2)
Raymond Phung, Pharm.D. Candidate (1,2)
Pramodini Kale-Pradhan, Pharm.D.(1,2)
Susan Szpunar, Ph.D. (2)
Leonard Johnson, M.D.(2)

**Abstract**

Background: In 2008, the Centers for Medicare and Medicaid Services decided that treatment of catheter-associated urinary tract infections (UTIs) acquired in the hospital would no longer be reimbursed. In May 2014 an educational initiative (EI) was provided to the prescribing staff focusing on unnecessary catheterization and urine cultures. The purpose of this project is to determine if the EI led to a change in the prescribing pattern of antimicrobials in patients with a urinalysis at a community teaching institution.

Methods: This was a pre-post quasi experimental study. We conducted an EI with the prescribing staff in May 2014. We retrospectively reviewed antimicrobial prescribing patterns in adult patients with an urinalysis greater than 48 hours post admission in March 2014 (pre-EI) and in March 2015 (post-EI), and compared the findings. Patients who received antibiotics for other infections or for surgical prophylaxis were excluded. Data collection included: patient demographics, laboratory information including UA and urine cultures, antimicrobials used, duration of therapy and the medical services that ordered the antimicrobials. Data were analyzed using the chi-squared test and Student's t-test. All data were analyzed using SPSS v. 23.0.

Results: A total of 1454 patients were evaluated. For each time period, 202 met the inclusion criteria for analysis. The mean age of patients in the pre-EI group and post-EI group was 61.0 ± 19.4 and 61.5 ± 20.3 years, respectively. The number of urine cultures increased in the post-EI group by 14.7%. Antimicrobials were administered to 40.6% (82/202) of patients in the pre-EI and 31.7% (64/202) of patients in the post-EI group (p = 0.06). In patients that received antimicrobials the median duration of therapy was 3 and 4 days in pre and post EI groups, respectively. Antimicrobials were predominantly utilized by the Internal medicine service in patients with a positive UA in both time periods.

Conclusion: This educational initiative did not significantly reduce antimicrobials being prescribed for the treatment of a UTI.

---

## Abstract No. 41 () (Clinical_Sciences)

**Title**

Physician Feedback of a Pharmacy-Implemented Formulary on Medical Relief Trips within the World Health Student Organization

**Affilliations**

Wayne State University, EACPHS
Wayne State Univeristy, SOM

**Authors**

Mollie Pertuso, Alison Britt, Chih Chuang, Helen Berlie

**Abstract**

Purpose: The WHSO pharmacy chapter created and introduced formularies into WHSO medical relief trips. The purpose is to report physician satisfaction, evaluation and feedback of formularies utilized on WHSO medical relief trips

Methods: Surveys were sent to physicians that participated in medical relief trips with WHSO. Participation in the survey was optional and responses were anonymous. The surveys were distributed via an online survey platform, SurveyMonkey®. There was a total of 20 questions: 7 Likert Scale, 6 open-ended, 6 yes/no responses, and 1 multiple choice question. The topics assessed included the physicians' past experiences with medical relief trips and formularies as well as their evaluation of their most recent experience with the formulary and the pharmacy team (if applicable).

Results: Surveys were sent out to physicians from 4 medical relief trips with WHSO between 2014-2015. A total of 9 physicians (including 1 resident and 1 fellow) responded to the survey. Areas of clinical expertise varied among respondents. Their history of previous participation in medical relief trips also varied widely. One hundred percent of the physicians used the formulary on their most recent trip with WHSO and 88% of the physicians agreed that the formulary was either moderately (55%) or extremely (33%) useful in guiding clinical decision making throughout the trip. While only 63% of physicians reported that the formulary met the basic needs of the communities they cared for, 88% of them felt that it was either moderately (22%) or extremely (66%) important to have a formulary on future WHSO trips. Overall, a majority of the physicians agreed that the formulary was beneficial on the medical relief trips but feel that adjustments can help improve future medical relief experiences with WHSO. Sixty-six (66) percent of physicians agreed that the formulary was either moderately (22%) or extremely (44%) useful in terms of saving time. Sixty-two (62) percent of physicians indicated that the formulary was either moderately (50%) or extremely (12%) useful as an educational tool for the medical students. In the future, efforts will be made to provide formularies to physicians and medical students prior to the trips for review. Additionally, we hope to provide more education to the medical students in regards to formulary use in clinical practice.

Conclusion: The implementation of a formulary for WHSO medical relief trips was associated with overall positive feedback from physicians. Results indicated that all physicians utilized the formulary. The majority of physicians believed the formulary was useful, was beneficial in guiding clinical decision-making, and was important to have on future medical relief trips. WHSO-EACPHS will strive to enhance and adjust the formulary not only to meet the needs of the communities we take care of but also to enhance the educational experiences of the students who attend the relief trips.

---

## Abstract No. 42 (Student_Graduate) (Clinical_Sciences)

### Title

Evaluation of Appropriate Apixaban Use, Safety, and Patient Knowledge across the Continuum of Care

### Affilliations

Eugene Applebaum College of Pharmacy and Health Sciences - Wayne State University, Department of Pharmaceutical Services - Beaumont Health System Royal Oak

### Authors

Grande D, Roberson NM, Mehta SP, Koerber JM, Hoffman JL, Smythe MA

### Abstract

**Introduction:** Apixaban is a novel oral anticoagulant that is approved for use in patients with atrial fibrillation and in patients to treat or prevent venous thromboembolism. Patient adherence and sound knowledge of apixaban therapy is necessary given its short half-life, potential drug interactions, lack of reversibility,

and adverse effect profile. The objectives of this study were to evaluate the appropriateness of apixaban use across the continuum of care and to assess patient knowledge of apixaban. **Methods:** This IRB reviewed study was divided into 2 phases. Phase 1 was a retrospective evaluation of 40 hospitalized patients receiving apixaban therapy. Apixaban use was assessed against approved hospital guidelines, prescribing information and clinical trial inclusion/exclusion criteria. Transition of care was assessed by evaluating the documentation of patient education and discharge instructions. A systematic data abstraction form was used to obtain the relevant data. Areas of concern were evaluated. Phase 2 was a prospective study of apixaban knowledge in 25 hospitalized patients. Patient knowledge was determined through the use of an internally developed patient questionnaire. Acceptable responses were determined apriori. The patient interview was timed after the provision of initial apixaban education for new starts. **Results:** The mean age for patients in Phase 1 and 2 were 75.9 ± 12.4 and 72.9 ± 11.6 years respectively. Most patients were receiving apixaban for atrial fibrillation (82.5% Phase 1, 88% Phase 2). Major findings appear below:

| Phase 1: Area of concern identified | Apixaban (n, %) |
|---|---|
| Use in patients with acute kidney injury | 10 (25) |
| Use in patients on dialysis | 2 (5) |
| Dose lower than labelled recommendation for indication | 9 (22.5) |
| Use in patients with bioprosthetic valve replacement | 3 (7.5) |
| Use in patients with concurrent antiplatelet therapy | 25 (62.5) |
| Patient discharged without documented education of apixaban | 32 (80) |
| Discharge instructions for apixaban not consistent with record documentation | 5 (12.5) |
| Lack of a designated physician to manage apixaban therapy upon discharge in a treatment naïve patient | 12 (30) |

| Phase 2: Patient Question | Incorrect Response (n,%) |
|---|---|
| Why are you taking apixaban? | 7 (28) |
| Why would it be important to not miss a dose of the medication? | 11 (44) |
| What would you do if you missed a dose? | 10 (40) |
| What is the most significant side effect? | 11 (44) |
| Has anyone given you advice about a doctor starting a new medication? | 13 (52) |
| Has anyone given you advice about over-the-counter or herbal products as it relates to this medication? | 23 (92) |
| Correctly identified situations in which to immediately contact their physician | 11 (44) |
| Do you carry an ID card or any item that says you take a blood thinner? | 10 (40) |

**Conclusion:** Opportunities to improve the safe use of apixaban were identified. Eighty percent of patients were discharged without education. In patients who were newly started, documentation of a designated physician to manage apixaban therapy post discharge was

not identified. These concerns were further amplified by the apparent gaps in patient knowledge. Opportunities exist for the community pharmacist to bridge the transition of care through clarification of apixaban discharge instructions and reinforcement of patient education.

---

## Abstract No. 43 (Student_Graduate) (Clinical_Sciences)

### Title

Does Music Therapy Effect Perioperative Anxiety?

### Affilliations

Detroit Medical Center

### Authors

Allison Atchoo, BSN, SRNA ...
Iryna Chykivska, BSN,SRNA ...
Melissa Essian, BSN,SRNA,
Kelly Ducharme,BSN,SRNA
Prudentia A. Worth,CRNA, PhD ...
Mary Walczyk, CRNA, MS ...
George McKelvey, PhD

### Abstract

Background: Patients undergoing surgical procedures experience a high degree of anxiety prior to surgical interventions. Responses to anxiety are exhibited in many physiological and psychological symptoms.1 These physiological changes present significant challenges to anesthesia providers as they consider the most optimal and safe anesthetic for their patients. The purpose of this study is to explore the effects of music therapy in reducing anxiety in the surgical patient who is undergoing epidural steroid injection. Medications such as Midazolam, a benzodiazepine, is usually used to reduce anxiety associated with this procedure. An additional goal is to investigate if patients who receive music therapy will also receive less Midazolam.
A considerable amount of information exists in the literature on the effectiveness of music therapy in minimizing anxiety behaviors. It has been identified as one of the interventions that could be used to reduce patient anxiety in the hospital setting. Music helps to reduce pain by activating sensory pathways that compete with pain pathways, stimulating emotional responses, and engaging cognitive attention (taking the focus away from pain). It reduces the psychophysiological effects of anxiety and stress through the relaxation response.2
Methods: This is a pilot study with a convenience sample of 32 participants per group (64 total), consisting of both male and female patients undergoing epidural steroid injections under intravenous sedation. Age, gender, race, and American Society of Anesthesiologist Physical Classification status (ASA Status) will be considered. A prospective randomized controlled trial will be used. Participants will be assigned to one of two groups ... a music intervention or a control group. The music intervention group will have the following music genres to choose from: new age, classical, soft rock/alternative, R&B and hip-hop. The control group will have no music therapy. Participants in the study will be randomly assigned to either group regardless of their age, gender, race, and ASA status. A Visual Analogue Scale (VAS) for anxiety will be utilized. The VAS is a useful tool that allows patients to rate their anxiety on a horizontal line anchored with word descriptors on each end. Repeated measures ANOVA will be used to analyze the VAS data between the intervention and control groups.
Results: The preliminary data based on 20 participants demonstrates that music therapy has significantly decreased anxiety scores in the music treatment group. In addition, the music treatment group used 15% less Midazolam when compared to control group.
Conclusions: Based on the preliminary study results, music therapy aids in decreasing anxiety and promoting positive change in patient's

emotional state. It also reduces the amount of Midazolam needed to alleviate anxiety associated with surgery.

References:
1.Johnson, B, Raymond S, Goss, J. Perioperative Music or Headsets to Decrease Anxiety. Journal of PeriAnesthesia Nursing. 2012 ... 27(3): 146-154.
2. Engwall M, MSc, Duppils G. Music as a Nursing Intervention for Postoperative Pain: A Systematic Review. Journal of PeriAnesthesia Nursing. 2009 ... 24(6): 370-383.

## Abstract No. 44 (Student_Graduate) (Clinical_Sciences)

### Title

Use of educational videos to improve patient understanding of Apixaban

### Affilliations

Eugene Applebaum College of Pharmacy & Health Sciences, St. John Hospital & Medical Center

### Authors

Thomas Nofar, Christopher Giuliano, PharmD, Stephanie Edwin, PharmD, Alison Gravelin

### Abstract

Purpose
The purpose of this study was to assess the efficacy of an apixaban video by evaluating patient knowledge gain.

Methods
This study was a quasi-experimental study of adult patients between the ages of 18-90 who received apixaban for atrial fibrillation, deep vein thrombosis, or pulmonary emboli. Patients were excluded if they had a history of dementia or were unable to complete study procedures. Prior to conduction of the study, two separate apixaban educational videos were developed by the investigators, along with a questionnaire to assess knowledge. Once consent was obtained, a pre-test was administered to the patient. The same test was administered immediately after viewing the video and thirty days later to determine long term recall of the information. A satisfaction survey was also administered after video completion.

Results
Preliminary results from eighteen patients were obtained. Patients' average age was 69.2 +-12.5 years and the majority of patients (72.2%) were prescribed apixaban to prevent clot formation in atrial fibrillation. Patients scored an average of 62.5% +-22.3% on the pre-test. Patients significantly improved their knowledge on the immediate post-test to 83.5%, resulting in a 21 % improvement in knowledge (95% CI 13.3-28.7%). We did not have a sufficient sample to analyze 30-day post-test data at this time. A subgroup analysis showed that both patients that had previously been prescribed an anticoagulant or had not been previously prescribed anticoagulants had significant ($p<0.05$) improvements in knowledge of 21% and 21.5%, respectively. On the satisfaction survey, 44% of patients indicated they learned a large amount, 44% learned quite a bit, 5.6% learned some, and 5.6% learned a little bit. 66.7% of patients thought the video was very helpful, 27.8% thought the video was helpful, and 5.6% thought the video somewhat helpful. 94% of patients would recommend that another family member on apixaban watch the video.

Conclusions
A preliminary analysis indicated an apixaban educational video improved patients' knowledge from baseline. 30-day knowledge retention will be collected to ensure long-term effectiveness.

## Abstract No. 45 (Student_Graduate) (Clinical_Sciences)

### Title

Barriers of Pharmacist-Provided Immunizations Among Urban Community Pharmacies.


### Affilliations

1) Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Science and
2) Department of Clinical Pharmacy, University of Michigan College of Pharmacy

### Authors

Alexis Tarcha, PharmD Candidate, 2016 (1), Leyla Zorkot, PharmD Candidate 2016 (1), Jared McPhail, PharmD Candidate 2017 (2), Sarah Kim, PharmD Candidate 2017 (2), Abdulbaset Salim, M.B.Ch.B., M.P.H.(1), Paul E. Kilgore, M.P.H, M.D. (1), Sarah Kelling, PharmD, M.P.H, BCACP (2), Steve Erickson, PharmD (2)



### Abstract

Introduction:
Immunizations are highly effective in the prevention of diseases such as influenza, pneumococcal disease, tetanus, diphtheria, and pertussis. However, only 46.9% of Medicare beneficiaries in Wayne County received their influenza vaccine versus 50.5% in Michigan for the 2013—2014 season. This gap is further widened (29.56-63.23%) when comparing coverage across zip codes in Wayne County. We hypothesized that urban community pharmacists may play an important role in reducing disparities in coverage for adult vaccines in Wayne County.

Methods:
Independent and small chain pharmacies in twenty-six zip codes within Detroit and the Detroit-Metro area were included in the study. Zip codes were chosen if <40% of community pharmacies provide immunization services. One pharmacist from each location was surveyed to identify the barriers pharmacies have in deciding to provide or not provide immunization services. The survey included 27 questions evaluating a variety of factors that contribute to possible barriers in choosing to provide immunizations. The factors evaluated were: prescription volume, hours of operation, patient preferences, pharmacist/owner beliefs, availability of staff, services provided, and the pharmacy environment. Questionnaire items included a field available for pharmacists to provide tailored responses and comments. The results of the survey were analyzed to identify barriers and implementation strategies that increase the prevalence of pharmacist-provided immunizations.

Results:
A total of 187 independent and small-chain (2-5 locations) pharmacies were contacted, and 109 participated in the study. Large chain pharmacies (i.e., CVS, Krogers, Walgreens) were excluded from the study. Pharmacies that were contacted but were not surveyed either chose not to participate or were closed. The surveys were conducted in person or over the phone. A total of seven pharmacies provided immunizations, 102 pharmacies did not. The results of the survey identified the most common reasons pharmacies chose not to provide immunizations. The most common answer selected was other (n=47) followed by lack of interest by the owner (n=15), insufficient work space in the pharmacy (n=7), lack of patient demand (n=7), insufficient time available (n=6), lack of perceived need among patients (n=5), insufficient staff (n=4), belief that vaccines are not profitable (n=3), belief that vaccines were unaffordable for patients (n=1). The prerequisites noted by pharmacists that would support provision of immunizations included: presence of patient demand (n=38), appropriate work space (n=20), adequate staff time (n=19), appropriately trained staff (n=15), increased awareness (n=12), ability to earn a profit giving vaccines (n=11) and other reasons (n=24).

Conclusion:
The most common barrier for pharmacists choosing not to provide immunizations was related to prescriber-pharmacy relations. For pharmacies to begin providing immunizations, increased patient demand, and/or a collaborative practice agreements are needed. A systematic in-pharmacy consultation to tailor a plan for individual pharmacies to take up immunization activities may accelerate introduction of vaccines in Wayne County.

---

## Abstract No. 46 (Student_Graduate) (Clinical_Sciences)

### Title

Linezolid (LZD) versus High-Dose (HD) Daptomycin (DAP) in Vancomycin-Resistant Enterococcus (VRE) Bloodstream Infections (BSI)

### Affilliations

Anti-Infective Research Laboratory, College of Pharmacy and Health Sciences Wayne State University
School of Medicine, Wayne State University
Detroit Medical Center, Detroit, MI

### Authors

Jacob Witt, B.S. ... Evan Zasowski, PharmD ... Kimberly Claeys, PharmD ... Abdalhamid Lagnf ... Michael Rybak, PharmD, M.P.H

### Abstract

Background: Several retrospective studies and meta-analysis have been done comparing daptomycin to linezolid in vancomycin-resistant enterococcus (VRE) bloodstream infections. However, these studies used an average daptomycin dose of 6 mg/kg, which may be suboptimal based on in vitro endocardial vegetation models. Furthermore, there is clinical data to support the safety of high-dose daptomycin. Finally, there are currently no studies comparing higher doses of daptomycin to linezolid. This study compared outcomes of high-dose daptomycin (> 6mg/kg) to linezolid.

Methods: This is a retrospective cohort study comparing high-dose daptomycin and linezolid at the Detroit Medical Center between 1/2010-6/2015. The inclusion criteria were age ≥ ... 18, and ≥ ... 1 positive VRE blood culture. The exclusion criteria were neutropenia (absolute neutrophil count<500), received daptomycin or linezolid ≥ ... 72 hours after index culture, received ≤ ... 48 hours of study drug, and received ≤ ... 6 mg/kg of daptomycin. The primary outcome was clinical success defined as cessation of signs and symptoms at the end of therapy and microbiological clearance. Secondary outcomes included in–hospital mortality, 30-day mortality, and 30 and 60 day recurrence of VRE-BSI. Nominal variables were compared between groups using the Chi-square test and Fisher's exact test. Ordinal and continuous variables were compared using the Mann-Whitney-U test and student's t-test where appropriate. Multivariable logistic regression was conducted in order to determine if there was an independent association between antimicrobial therapy and clinical outcomes.

Results: There were 134 patients included (LZD n=80 and DAP n=54). There average dose of daptomycin was 8.9 mg/kg. There were significant differences in the following baseline characteristics (LZD vs DAP): prior hospitalization 83.8% vs 98.1%, p=.008 ... CVA 33.8% vs 16.7%, p=.026 ... ICU at index 22.5% vs 38.9%, p=0.041. The outcomes of the study are shown below:
Linezolid Daptomycin P-value
30-day mortality
n, (%) 16 (20) 10 (18.5) 0.832
Mortality attributed to
EB n, (%) 8 (10) 7 (13.0) 0.849
In-hospital mortality
n, (%) 9 (11.3) 12 (22.2) 0.087
Clinical success
n, (%) 58 (72.5) 39 (72.2) 0.972

30-day recurrence
n, (%) 3 (3.8) 0 (0) -
60-day recurrence
n, (%) 3 (3.8) 1 (1.9) 0.648
Microbiological failure
n, (%) 4 (5) 0 (0) -
Inpatient duration of
study drug, median days
(IQR) 8 (5,11) 8 (6, 12.5) 0.845

In multiple variable analysis, APACHE II score (aOR 1.133, 95% CI 1.053-1.218) and two positive VRE blood cultures (aOR 3.470, 95% CI 1.153-10.448) were significantly associated with in-hospital mortality, but not daptomycin therapy (aOR 2.913, 95% CI 0.996-8.522).

Conclusions: No difference in clinical success, 30-day mortality, in-hospital mortality, 30-day and 60-day recurrence, and microbiologic failure was observed between daptomycin and linezolid. Results must be interpreted with caution due to the retrospective design of the study and limited sample size.

---

## Abstract No. 47 (Student_Graduate) (Clinical_Sciences)

### Title

Skin infections in the emergency department: opportunities for antimicrobial stewardship

### Affilliations

Wayne State University, Detroit, MI ... Henry Ford Hospital, Detroit, MI

### Authors

Jessica Mourani, BS
Misa Jajjoka, BS
Michael Veve, PharmD
Susan Davis, PharmD

### Abstract

Background: Acute bacterial skin and skin structure infections (ABSSSI) are frequently managed in emergency departments (EDs). Vancomycin is a mainstay of ABSSSI therapy for methicillin-resistant Staphylococcus aureus (MRSA), but is not necessary in cases with low risk or when other medications including clindamycin and sulfamethoxazole-trimethoprim can be considered. Therefore, overuse of vancomycin for ABSSSI is a potential target for antimicrobial stewardship in the ED. The objective of this study was to characterize use of vancomycin and identify opportunities for improvement.

Methods: This was a retrospective cross sectional, IRB approved study conducted at a healthcare system in Detroit, MI. The study population included patients seen at ED from January 2015 to June 2015 who presented with clinical signs and symptoms of ABSSSI. The primary endpoint of interest was appropriate use of vancomycin based on the Infectious Diseases Society of America (IDSA) national guideline criteria. Other variables collected included demographics, comorbidities, microbiology, antimicrobial therapy and 30-day readmissions.

Results: A total of 80 patients were enrolled ... 37 (46%) with abscess, 30 (38%) with cellulitis, and 13 (16%) with both ... 39 male patients (49%) and 41 females (51%). The most common comorbid conditions were diabetes (25%), renal disease (13%), and injection drug use 9 (11%). Twenty-four (30%) were hospitalized in the past 90 days and 7 (9%) received systemic antibiotics in the past 90 days. 6 patients were categorized as having severe ABSSSI (CREST class 3 or 4) ... among the remaining 74 mild-to-moderate infections, 46 (62%) were purulent, 28 (38%) were nonpurulent. Thirty-six (45%) patients had cultures obtained from skin or blood ... organisms isolated were methicillin-susceptible Staphyloccocus aureus (MSSA) 5 (6%), MRSA 5 (6%), Streptococcus spp. 9 (11%), Candida spp. 2 (3%), anaerobes 3 (9%) and other 6 (9%).

Thirty-five (44%) received vancomycin and 57 received other or no antimicrobial therapy. Among patients who received vancomycin, only 4 (11%) had infections with severity to warrant intravenous MRSA coverage according to IDSA guidelines.

Conclusions: The majority of ABSSSI encountered in the DEM are mild to moderate in severity. We identified opportunities for improvement in antimicrobial management, including both overuse and underuse of vancomycin. Future antimicrobial stewardship interventions targeting MRSA risk assessment and appropriate selection of antimicrobials.

---

## Abstract No. 48 (Student_Graduate) (Clinical_Sciences)

### Title

Characteristics associated with non-susceptibility to fosfomycin (FOS) in urinary isolates

### Affilliations

1Wayne State University and 2Henry Ford Hospital, Detroit, MI

### Authors

Jasmin Badwal1 ... Mariam Saco1 ... Michael Veve1,2, Pharm.D. ... Susan Davis1,2, Pharm.D.

### Abstract

Background: Urinary tract infections (UTIs) are a common cause of infection. Uncomplicated cases can be effectively treated with fosfomycin (FOS), a broad-spectrum antibiotic usually given as a single oral dose. However, fosfomycin non-susceptibility (FOS-NS) is a major limitation in use and certain characteristics may be associated with these cases.

Methods: Retrospective case-control study of urinary isolates tested for susceptibility to fosfomycin (FOS) from 2011-2015. FOS susceptible and non-susceptible isolates were defined according to CLSI breakpoints. Risk factors for resistance were collected from electronic medical records using a standardized case report form. Data collected included: all antimicrobial susceptibilities, patient demographics, location, comorbid conditions and history of antimicrobial exposures. Risk factors were compared between cases and controls using bivariate statistical techniques.

Results: 121 urinary isolates were included in the study population: 103 FOS susceptible, 18 FOS-NS. The most common organisms were: 65 ESBL Escherichia coli, 22 Escherichia coli, 10 Klebsiella pneumoniae, and 4 ESBL Klebsiella pneumoniae. History of FOS exposure in the last 60 days was associated with FOS NS (16.7%, p=0.042). History of trimethoprim/sulfamethoxazole and fluoroquinolone use were more common in FOS-NS isolates, however the relationships were not significant. FOS-NS was not associated with recent hospitalization in the last 90 days (27.8% p= 0.371) or history of carbapenem exposure in the last 60 days (11.1% p= 1).

Conclusion: FOS exposure within the last 60 days was associated with FOS non-susceptibility (p =0.042). Other analyzed characteristics were not significant, however this may be due to the small sample size. Future studies with a larger population should be conducted to look for association between these characteristics and FOS susceptibility. Identification of risk factors will lead to more effective prescribing practices and optimal antimicrobial therapy.

---

## Abstract No. 49 (Student_Graduate) (Clinical_Sciences)

### Title

Skin Conductance Responses: Effects of Variability Within & Between Individuals and as a Marker of Psychopathology

### Affilliations

Wayne State University Eugene Applebaum College of Pharmacy and Health Sciences

### Authors

DeLor Jeremy, BS, PharmD Candidate Class of 2018 ... 1st author
Bauer Miranda, BS, PharmD Candidate Class of 2018 ... 1st author
Rabinak Christine, PhD ... Primary Investigator

### Abstract

Skin Conductance Response (SCR) is a sympathetic response in which the skin momentarily becomes a better conductor of electricity when either external or internal stimuli occur that are physiologically arousing. SCRs are often used as a measure of fear learning in Pavlovian fear conditioning paradigms and is being considered as a diagnostic tool to predict posttraumatic stress disorder (PTSD) risk. For instance, SCR levels measured shortly after a trauma may predict whether an individual will develop PTSD. However, SCR magnitude is highly variable within and between individuals, which can hinder its efficacy as a measure of fear or as a predictor of PTSD. In fact, most SCR recordings are taken from the nondominant hand (left hand), and during fear conditioning participants that show no evidence of SCR are often excluded as "non-learners." However, this may be an erroneous assumption and optimal recording site may not be uniform across participants. In the present studies we examined intra- and inter-individual variability in SCR in healthy volunteers and compared SCR magnitude as a measure of conditioned fear between healthy controls and PTSD patients using a Pavlovian fear conditioning paradigm. In Experiment 1, SCRs from the left and right hands were measured during an auditory task in 21 healthy adult volunteers. Participants heard 9 sounds (1 – 2 sec each, with 5 – 10 sec between sounds) per hand. Some participants demonstrated greater right-hand laterality, while others presented with left-hand laterality ... yet others did not present with significant laterality. These results indicate the need for a standardization process of patient data before it can be used as a predictive, analytical tool about emotional responses to external stressors. In Experiment 2, SCR of patients meeting criteria for PTSD (n=5) was compared to that of controls (n=18) using a Pavlovian fear conditioning paradigm. Two conditioned stimuli (CSs) were paired with an aversive unconditioned stimulus (US, 0.5 msec 100dB white noise burst) with a 66% reinforcement rate for a total of 20 CS presentations (12 CS+US trials ... 8 CS-alone trials). There were no between group differences in fear acquisition to the CS, as evidenced by similar levels of SCR and rate of acquisition. However, PTSD patients displayed significantly higher SCR levels in response to the US compared to controls ($p < 0.05$), suggesting increased arousal to inherently aversive stimuli. It is possible that how strongly an individual responds during a traumatic event could be a risk marker for later PTSD development, however given the retrospective nature of the current study we cannot discern whether increased SCR to the US is a result of PTSD development or may be a risk factor for PTSD. Therefore, this hypothesis requires further investigation. Together, these aims may yield complementary results and aid in the advance of SCR data collection that is both reliable and clinically useful.

## Abstract No. 50 (Student_Undergrad) (Clinical_Sciences)

### Title

Medical student feedback of pharmacy services within the World Health Student Organization


### Affilliations

Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI
Health Centers Detroit Medical Group, Detroit, MI

### Authors

Bethany L. Hill, Alex C. Chaben, Mandy K. Pattah, Helen Berlie



### Abstract

Purpose: The World Health Student Organization (WHSO) pharmacy chapter created and implemented a medication formulary and country-specific pharmacy labels into their medical relief trips. The purpose is to report medical student feedback on the utilization of the formulary and the labels during the medical relief trips.

Methods: Medical students that attended medical relief trips with WHSO between 2014 and 2015 were given voluntary and anonymous surveys. The surveys were distributed via e-mail with a link to SurveyMonkey®. The survey included a total of 31 questions: 16 Likert scale, 9 open-ended, 5 yes/no, and 1 multiple-choice. Medical students provided feedback on the utilization of the formulary and the country-specific labels with auxiliary stickers. The feedback included: overall satisfaction, enhancement of knowledge of medication-related information, and confidence with patient education. Overall satisfaction with pharmacy services were also assessed.

Results: Surveys were completed by 35 medical students [21 first year (M1), 10 second year (M2), 3 fourth year (M4), and 1 student of unknown year]. Of the 35 students, 19 attended trips that included a pharmacy team and 16 attended medical relief trips without a pharmacy team. Medical student's use of the formulary was reported to be 63% for trips with a pharmacy team and 100% for trips without pharmacy. The formulary was reported to be useful by 79% of those with pharmacy and 87% of those without pharmacy. Furthermore, the formulary enhanced the medical students understanding of medication related information for 73% of those with pharmacy and 63% of those without pharmacy. Overall, 91% of medical students found the formulary to be an important component of future WHSO medical relief trips. Application of the country-specific pharmacy labels was reported to be used by 63% with pharmacy and 94% of students without pharmacy. The labels were found to enhance the knowledge of medication-related information for 68% of students with pharmacy and 56% without pharmacy. Feedback also indicated that the labels increased confidence with patient education for 63% of students with pharmacy and 75% without pharmacy.

Conclusion: Medical students reported that the formulary was an important tool for WHSO relief trips. Feedback on its usefulness demonstrated that it is well received as an educational tool in understanding medication-related information. The formulary was perceived to be more useful when a pharmacy student team was present. The involvement of pharmacy students may enhance the interpretation and understanding of the formulary. Country-specific labels were an integral addition to WHSO medical relief trips and will continue to be utilized on all future trips. WHSO's pharmacy chapter will continuously evaluate the pre-trip formulary and medication training we provide to medical students to maximize their educational experiences and medical knowledge during the medical relief trips.

## Abstract No. 51 (Student_Graduate) (Clinical_Sciences)

### Title

Complementary Alternative Medicine

### Affilliations

Harper Hospital

### Authors

Riam Yacoub, Riham Kiston, Mri Kolicaj, Mashal Khan, Sheila Wilhelm, Pharm.D., Jesse Shuster, Pharm.D.

### Abstract

Title: Use of Complementary and Alternative Medicine (CAM) in an Urban Teaching Hospital.

Background: Complementary and alternative medicine (CAM) covers a broad range of practices and products. The National Center for Complementary and Alternative Medicine (NCCAM) categorizes CAM into two subgroups – natural products or mind and body practices. The natural product group includes a wide variety of options, such as herbals, vitamins, minerals and probiotics. Mind and body practices include various groups of procedures or techniques, such as acupuncture and massage therapy. Data from the 2007 National Health Interview Survey (NHIS) found that almost 4 out of 10 American adults use CM therapy. However, the patterns of CAM use in urban populations have not been extensively studied.

Purpose: To prospectively categorize and assess an urban patient population's current and past use of CAM therapies.

Methods: For this study we conducted live, verbal, face-to-face interviews with patients admitted to Harper University Hospital who have had a pharmacy driven medication history completed within 72 hours of admittance. The interviews were done by pharmacy students using a standardized CAM questionnaire to categorize and assess the patients' current and past use of CAM therapies.

Results: Of the 40 patients approached, 39 patients consented and completed the survey (100% response). The mean age of included patients was 62 with a range of 38 to 85 years. The included patients were primarily African American (94.8%) and female (64%). The majority of our patient population found out about CAM use through the Internet (54%) and the second most common source was family members (22%). Of those who used CAM, 77% disclosed that information to their primary care physician. The top 5 reported CAM products used included vitamin D, potassium, fish oil, multi-vitamin, calcium and iron(tied). Other mind/body practices reported include massage, deep breathing, guided imagery and chiropractic therapy. Some reported alternatives to medical practices such as family remedies, traditional Chinese and healer, naturopathy and homeopathy.

Conclusion: Although majority of our patient population did not start the use of CAM due to the recommendation of a health care provider, most patients still notified their primary care physician of the use of these products. The use of CAM varied extensively between herbals and mind/body practices, but the use of vitamins and minerals was most concentrated.

## Abstract No. 52 (Student_Graduate) (Clinical_Sciences)

### Title

Increasing knowledge about the nonmedical use of prescription drugs and underage drinking among Detroit adolescents through student pharmacist-led peer-to-peer education

### Affilliations

Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University ... The Love Detroit Prevention Coalition, Detroit, Mi ... The Youth Connection, Detroit, Mi

### Authors

Brittany Stewart, PharmD, RD ... Nancy Lewis, PharmD, MPH ... Grenae Dudley, PhD ... Michael Fisher ... Amber Lanae Smith, PharmD, MS, BCPS

### Abstract

Background
Nonmedical use of prescription drugs is a growing public health concern across the nation. The nonmedical use of controlled medications is most prevalent among adolescents and young adults in the United States, and has significantly increased over the past two decades. Recently, Michigan was noted to have one of the highest rates of prescription drug abuse among teens in the country (12%). Given that a majority of young adults believe that prescription drugs are safer to use than illicit drugs (55.5%), there is a need to educate youth in Michigan about the dangers of prescription drug abuse. Previous literature has demonstrated the benefit of peer-to-peer prevention programs on reducing drinking and smoking rates and conclude that peer leadership can be an effective tool for drug abuse prevention among adolescents. We sought to increase knowledge and awareness about the realities of underage drinking and prescription drug abuse among Detroit adolescents through a collaborative, interactive educational event hosted by student pharmacists in partnership with The Love Detroit Prevention Coalition (LDPC), a Detroit community-based substance abuse prevention organization.

Methods
Pre-post surveys were conducted at a peer-to-peer educational event that was held at the Eugene Applebaum College of Pharmacy and Health Sciences. The event focused on providing key educational messages about the dangers of the nonmedical use of prescription drugs and underage drinking through three sessions of 30-minute interactive activities that were led by student pharmacists. The event participants were urban Detroit adolescents identified through the Youth Connection organization. The pre-post surveys evaluated each participant's knowledge and their perceptions about prescription drug abuse and underage drinking, as well as the quality of the event. The questions were developed using evaluation tools from the American Pharmacists Association-Academy of Student Pharmacists Generation Rx patient care initiative. Descriptive statistics were used to analyze the survey results.

Results
Twenty-eight African American adolescents participated in the peer-to-peer educational event. In the pre-survey group, there were equal numbers of males and females with an average age of 14-16 years (71%). Twenty-six students participated in the post-survey. Participants showed a 17.5% increase ($p < 0.02$) in knowledge for the ten knowledge-based questions. Participant surveys also suggested that the event increased awareness of the dangers of prescription drug abuse. Additionally, 62-73% of participants indicated that the event influenced their willingness to share the information learned with family and friends. The post-survey showed that 77-85% of participants found the event fun, interesting, and useful.

Conclusion
This event demonstrated that peer-to-peer

education provided by pharmacy students in collaboration with a community-based organization could increase knowledge and awareness about the realities of prescription drug abuse and underage drinking. Furthermore, our analysis found that this type of community event could be a fun and interesting way for adolescents to learn. This project in collaboration with the LDPC has since expanded into other opportunities for student pharmacists to provide peer-to-peer community education events in Detroit related to this topic.

---

## Abstract No. 53 (Student_Graduate) (Clinical_Sciences)

### Title

Evaluation of Prescribing Patterns for Acetylsalicylic Acid (ASA) in Patients Taking Ticagrelor.

### Affilliations

Wayne State University
Beaumont Hospital Dearborn

### Authors

Samantha Scalia,PharmD Candidate 2016
Larry Diamond, PharmD
Ray Cha, PharmD

### Abstract

Background:
Dual anti-platelet therapy is the mainstay in patients who have experienced an acute coronary syndrome (ACS). Ticagrelor, a P2Y12 ADP –receptor inhibitor, is a new anti-platelet medication used in combination with Acetylsalicylic acid (ASA) for ACS. The PLATO trial demonstrated that higher rates of thrombotic events occur with ASA doses over 100 mg. The purpose of this study is to evaluate if the patients were switched to low dose ASA upon admission to the hospital and assess the appropriateness of their ACS medications.

Methods:
This retrospective analysis was conducted on 133 adult patients admitted to Beaumont Hospital Dearborn, a community teaching hospital, from January 2014 to March 2014, and August 2015 to September 2015. Patients >18 years of age on Ticagrelor and ASA were included in the study. Patients were sub-stratified based on ASA dosing. Data collection includes medication administration records, physician's reports and population demographic information. Other ACS medications were also analyzed to determine if the patient was in accordance with the ACC/AHA guidelines both upon admission and at discharge. In addition, general outcome metrics, such as adverse events during admission, bleeding rates, and aPTT times, will be described.

Results:
Preliminary results indicate that 86 % of the patients treated with Ticagrelor were on low dose ASA upon admission to the hospital. Furthermore, 7 % of the patients were admitted on 162 mg of ASA were switched to 81 mg after initiation of Ticagrelor. The remaining 7 % were continued at 162 mg of ASA in hospital, despite being on Ticagrelor.

Conclusion:
Despite clear evidence for low dose ASA in patients also receiving Ticagrelor, we report a small but significant discrepancy in prescribing practices. Impending evaluations will reveal the potential impact on impatient care of these patients. Future evaluation of clinical pathways on appropriate ACS treatment across a spectrum of cardiovascular risk is warranted.

---

## Abstract No. 54 (Student_Graduate) (Clinical_Sciences)

### Title

Ceftaroline fosfomil, a potential alternative to vancomycin for treatment of Methicillin-Resistant Staphylococcus aureus bloodstream infections


### Affilliations

Anti-Infective Research Laboratory, College of Pharmacy & Health Sciences Wayne State University

### Authors

Noor Sabagha ,
BS Pharmacy, MPH


### Abstract


Ceftaroline fosfomil, a potential alternative to vancomycin for treatment of Methicillin-Resistant Staphylococcus aureus bloodstream infections

N. Sabagha1, E.J Zasowski1, K.C. Claeys1, S.L. Davis1, 4, M.J. Rybak1, 2

1Anti-Infective Research Laboratory, Eugene Applebaum College of Pharmacy & Health Sciences Wayne State University,
2School of Medicine, Wayne State University
3Detroit Medical Center, Detroit, MI
4 Henry Ford Hospital, Detroit, MI

Background: The clinical and economic burden of Staphylococcus aureus bloodstream infections (BSI), particularly methicillin-resistant Staphylococcus aureus (MRSA) BSI is high. Vancomycin (VAN) is considered a standard treatment of systemic infections caused by MRSA, including BSI. However, as a result of widespread use, isolates with reduced susceptibility to VAN have emerged prompting the need for alternative therapies that target MRSA. In this investigation we examined whether ceftaroline fosamil (CPT), a novel advanced generation cephalosporin, can be used successfully as a monotherapy for MRSA BSI.

Method: A retrospective, observational cohort study of patients treated for MRSA BSI with CPT monotherapy was preformed across three medical centers from 2011 through 2015. Inclusion criteria included adult patients (age > 18 years), with MRSA BSI treated with CPT for more than 72 hrs. Those receiving concomitant combination therapy for more 24 hours and with polymicrobial BSI were excluded. Primary outcomes measures included clinical in-hospital treatment success by end of therapy. Secondary outcomes included 30-day mortality, hospital length of stay, and duration of BSI post-CPT in patients with positive blood cultures (active BSI) at start of CPT.

Result: 138 patients received CPT after prior antibiotic therapy either for BSI bacteremia (68.1%) or for both positive MRSA BSI and PNA (31.9%). Overall, 65% of patients were male ... 73.9% age 18 to 65, 25.4% age ≥ ... 66, 67.4% of the patients evaluated were African American and 17.4% were Caucasian. The sources of BSI were ... 25.3% infective endocarditis ... 20.3% bone/joint ... 38.4% pneumonia ... 6.5% skin infection ... 19.6% other with 92.3% meeting the definition for complicated BSI. The median (IQR) APACHE II & Carlson Comorbidity scores were 16 (11,19) and 4 (2,6) respectively. Reason for CPT: 43.5% prior therapy failure ... 8% pulmonary coverage ... 10.9% prior therapy toxicity. Microbiology: active BSI at CPT initiation 50.7% ... 3 VAN-intermediate S. aureus ... 6 DAP non-susceptible ... 2 CPT-intermediate (40 isolates tested)., median (IQR) duration prior therapy 4 (3,6) days. CPT was given Q8H in 50% of cases. Outcomes: Clinical success, defined as an outcome of cured or improved at the end of CPT therapy, 79% ... 30-day mortality 13.8% ... microbiological eradication 70.3% ... median (IQR) duration BSI post-CPT initiation 3 (1,4) days ... median (IQR) hospital-LOS 16(10,27) days. Only neutropenia was associated with 30-day

mortality (76 vs 11.8% mortality, P=0.009)

Conclusion: Patients with MRSA BSI treated with CPT had favorable outcomes even after prior VAN failed therapy. Further comparative studies are needed to define the role of ceftaroline in MRSA BSI.

---

## Abstract No. 55 (Student_Undergrad) (Clinical_Sciences)

### Title

Use of Twitter for Communication at International Infectious Diseases Conferences: ECCMID versus ICAAC

### Affilliations

Henry Ford Hospital, Detroit, MI, USA1 ... Wayne State University, Detroit, MI, USA2

### Authors

Mariam Ghazi, 1,2, Michael P. Veve, PharmD 1,2 ... Susan L. Davis, PharmD 1,2

### Abstract

Background: Social media websites are popular tools used by some clinicians as a social interaction mechanism to increase awareness and dissemination of scientific data. The drastic rise in social media popularity provides additional opportunities to share information amongst healthcare practitioners at professional conferences. The objective of this study was to characterize Twitter use during the 54th Interscience Conference of Antimicrobial Agents and Chemotherapy (ICAAC) and the 25th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID.

Methods: A cross-sectional study assessed Twitter use during the infectious diseases conferences ICAAC 2014 and ECCMID 2015. All “tweets” two weeks prior to, during and after each conference and contained the following keywords were included for analysis: ICAAC, ICAAC 2014, ICAAC2014, #ICAAC, #ICAAC 2014, #ICAAC2014, ECCMID, ECCMID 2015, ECCMID2015, #ECCMID, #ECCMID 2015 and #ECCMID2015. Data were collected using the search functions through the free software Topsy (www.topsy.com) and Twitter (www.twitter.com). Descriptive measures were used to characterize Twitter content.

Results: 559 total tweets were evaluated: 276 for ICAAC 2014, 283 for ECCMID 2015. 150 (54%) individual and 126 (46%) institutions/corporations for ICAAC and for ECCMID 168 (60%) and 113 (40%) respectively. The most common professions identified in user profiles were: ICAAC multiple health-related professions 21% (59), ECCMID government agencies 16% (46). Peak tweet activity was observed during day 1-3 of each, with sporadic use before and after. The most common tweet content amongst all meetings was scientific news (27%, 149) and social discussion (30%, 166). Scientific topics varied between meetings. ICAAC tweets were more commonly about viral disease (21%) and new drugs (19%), while ECCMID tweets were more frequently about antimicrobial resistance (18%) and new drugs (12%).
Both meetings had a large proportion of tweets with no specific scientific content (promotion or social networking), 28% of ICAAC and 41% of ECCMID.

Conclusion: The majority of tweet content was scientific for both meetings. We observed that the nature of tweet content (scientific, social) differs across time relative to the conference (before/during/after) and between meetings (ECCMID more non-scientific content than ICAAC). Clinical and basic scientists should consider Twitter as a potential means of promoting their research and networking with others.

Keywords: Social media, Twitter, ID conference

## Abstract No. 56 (Student_Undergrad) (Clinical_Sciences)

### Title

Assessment of adjusted body weight dosing of daptomycin in the obese population

### Affilliations

1. Wayne State University Eugene Applebaum College of Pharmacy and Health Sciences

2. Beaumont Hospital – Dearborn

### Authors

Sarah Eisho, PharmD Candidate
Lama Hsaiky, PharmD
Raymond Cha, PharmD

### Abstract

Background/Purpose: The Food and Drug Administration has approved daptomycin to be dosed based on total body weight (TBW) for all patient populations. Previous studies have demonstrated that TBW dosing leads to increased serum levels as well as increased creatinine phosphokinase levels in obese patients. Recent modeling data suggests using adjusted body weight (ABW) dosing in the obese population. Therefore, the objective of this study is to measure clinical efficacy and safety outcomes of dosing daptomycin using ABW in obese patients.

Methods: This study will be submitted to the Institutional Review Board for approval. A retrospective analysis will be performed on obese patients (body mass index greater than or equal to 35 kilograms per meter squared) that received ABW dosing of daptomycin for treatment of an infection. Patients will be identified for inclusion via a computerized report generated for all patients who had received ABW daptomycin dosing between March 2014 and September 2015. Patients must have received daptomycin treatment for a minimum of 72 hours without other similar spectrum antibiotic treatment. The following data will be collected: baseline demographic data, comorbidities, severity of illness at admission, type of infection and related parameters, prior and/or concomitant antimicrobial therapy, surgical interventions, and daptomycin dosing regimen. Efficacy outcomes will include clinical success rates, microbiological success rates, length of hospital stay, readmission rates, and mortality. Safety outcomes will include incidence and type of adverse events. Excel and SPSS will be used for statistical analysis to assess clinical efficacy and safety outcomes of dosing daptomycin using ABW in the obese population.

Anticipated Outcomes: Data collection is currently in process. We expect to evaluate approximately 40 subjects. We anticipate a spectrum of different doses and success rates because various weights will be observed. The data collected from this study will be compared to active treatment control groups in the future. Study results will contribute towards defining a new dosing algorithm for daptomycin in the obese population.

## Abstract No. 57 (Student_Graduate) (Clinical_Sciences)

### Title

Pharmacokinetics and safety of ertapenem given as 1 gram post hemodialysis

### Affilliations

a.Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI ... b.Department of Pharmaceutical

Services, Beaumont Health System, Dearborn, MI

**Authors**

Alison Lobkovich, Pharm.D. Candidate,a,b Lama Hsaiky, Pharm.D.,b Francine Salinitri, Pharm.D. a,b, Raymond Cha, Pharm.D.a,b

**Abstract**

Purpose: Ertapenem is a carbapenem antibiotic used to treat a variety of infections. Ertapenem is highly protein bound and exhibits near linear pharmacokinetics due to concentration-dependent plasma protein binding. Since renal excretion accounts for approximately 45% of its total clearance, it requires dosage adjustment in patients with compromised kidney function. It is currently dosed at 500mg once daily in patients requiring intermittent hemodialysis (HD). This current dosing frequency and waste of manufactur-formulated 1gm vials is inconvenient and costly for patients and institutions. The objective of this study is to evaluate the pharmacokinetics and safety of ertapenem 1gm given post hemodialysis.

Methods: This is a prospective, cohort, single-dose open-label study in ten volunteer subjects between the ages of 18 to 88 and diagnosed with ESRD that requires HD three times a week. Patients were excluded if they have a history of seizures, suspected infection, allergy to beta-lactams, a history of Clostridium difficile infection, prescribed probenecid, or pregnant. Nine blood draws accompanied a single 1gm dose of ertapenem for pre-specified time points: 0h (baseline prior to ertapenem administration), 0.5h, 1h, 2h, 6h, 12h, and prior to the next HD session. Additionally, two samples were collected after the subsequent hemodialysis session, one immediately after dialysis and another sample one hour later. Vital signs such as systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and respiratory rate (RR) was recorded prior to and 24-hours post drug administration, and prior to the next HD session. Naranjo's Scale will be used for adverse effect assessment. Blood samples will be assayed with fluorescent HPLC to determine concentrations. A non-compartmental model will be applied to concentration-time data in order to calculate area-under-the-curve (AUC) and estimate pharmacokinetic parameters including t1/2, Cmin, and AUC24. Descriptive statistics will be applied to demographic, safety, and pharmacokinetic data.

Results: Data collection and analysis are ongoing. Thus far, six subjects have been enrolled and completed sampling and safety assessments. Of these, two were female, four male and their ages ranged from 41 to 68 years. Weight and height ranged from 50.3 to 102.1 kg and 64 to 71 inches, respectively. Two subjects experienced cardiovascular adverse events, one experienced multiple respiratory events, one experienced multiple gastrointestinal events, and three experienced endocrine related adverse events. In addition, the patients' vital signs did not significantly differ pre and post HD.

Conclusion: Ertapenem is relatively safe and does not produce any attributable adverse events when given as a 1gm dose post HD. Additional studies with extended durations would augment long-term safety data. Bioequivalency of the 1gm dose will be extrapolated pharmacodynamically to the recommended 500mg post HD dosing upon completion of pharmacokinetic analyses.

---

## Abstract No. 58 (Faculty) (Clinical_Sciences)

**Title**

Psychoactive Medication Use in Urban Youth

**Affilliations**

Pharmacy Practice, EACPHS, Wayne State University Department Public Health Sciences, Henry Ford Health System
Pharmaceutical Science, EACPHS, Wayne State

University
Department of Engineering, Wayne State University

**Authors**

Victoria Tutag Lehr, BS Pharm, Pharm D Associate Professor
George W. Divine, Ph.D. Senior Research Biostatistician
David K. Pitts, Ph.D. Associate Professor
Shawn McElMurray, Ph.D. Associate Professor
Kyle Burghardt Pharm D, Assistant Professor

**Abstract**

Background: The prescribing of psychoactive medications for the pediatric population continues to escalate. Children and adolescents residing in neighborhoods with high environmental lead (Pb) are at greater risk for mental health conditions (depression, anxiety, ADHD) for which psychoactive medications including atypical antipsychotics (AAPs) may be prescribed. The frequencies and types of adverse effects associated with the AAPs in the pediatric population overall are not well known. Furthermore there are no published Detroit area specific data on use of psychoactive medication specifically the AAPs in children and adolescents.
Objectives: To estimate for a sample of children and adolescents receiving care in an urban pediatric hospital ED 1.) the frequency and type of psychoactive medication use 2.) the frequency and type of antipsychotic use and 3.) mental health and comorbid diagnoses.
Design/Methods: The WSU-IRB approved this descriptive retrospective electronic medical records (EMR) review. Eligible cases were males and females aged 2 to <18 years who received a psychiatric consult for any reason in the Children's Hospital of Michigan ED during 2005 –2009. Demographics, diagnoses, medications, and adverse reactions were abstracted from EMR. Chi-Square Fisher's Exact and regression analyses were used.
Results: A convenience sample (n= 608 cases) was 81% African American, 51% female, mean age 13 ± 3 years (4-17.5). Almost all (96%) from home. Common chief complaints were violence (30%), self-harm (21%) and sexual assault (8%). Mental health conditions included: ADHD (22%), depression (17%), bipolar (16%), substance abuse (9.4%), anxiety (6%) with 23% having a previous psych admission. Leading non-mental health conditions were asthma (12%), seizures (3.3%) ... diabetes (1%). Seven cases of antipsychotic - dystonia. Insurance type: 42 % Community mental health, 19 % private, 17% Medicaid. 22% were uninsured. Psychoactive medications were used by (239/608) 39.3% of children and adolescents. Of these (147/239) 61.5% received at least one prescription for an antipsychotic, the majority (88%) received an AAP. ADHD medications-CNS stimulants (41%) ... Antidepressants (33%) ... Mood stabilizers (33%) were also common. The proportion of male (66.7% v 59.2% ... p<.001) ... insured (92% v. 10% p<.001) ... with a history of ADHD (65% v 82% p< .001) were greater for children and adolescents receiving at least one AAP compared to those receiving at least one prescription for any other psychoactive medication. Conclusion: In this sample of urban youth receiving a prescription for an AAP is associated with male gender, a history of ADHD and having insurance. Use of stimulant-amphetamines may reflect the prevalence of diagnosis of ADHD during this time of development. Effects of urban environment on the mental health of children warrant further examination.

---

## Abstract No. 59 (Student_Graduate) (Clinical_Sciences)

**Title**

Electrolyte abnormalities in ICU patients receiving parenteral nutrition: incidence and associated outcomes

**Affilliations**

Wayne State University, Eugene Applebaum College of Pharmacy and Health Sciences ... Detroit Medical Center

**Authors**

Vera Vulaj, PharmD. ... Jennifer Froomkin, PharmD. Candidate ... William Arthur, R.Ph ... Steven Tennenberg, M.D. ... Bryan Dotson, PharmD.

**Abstract**

Purpose: Malnutrition is common in the intensive care unit (ICU). Oral or enteral feeding is preferred whenever possible, and parenteral nutrition (PN) is reserved for patients with a nonfunctional gastrointestinal tract. One common complication of PN is electrolyte imbalances. Although studies have shown an association between various electrolyte abnormalities during critical illness and increased mortality, none of these studies have focused on patients receiving PN. The primary objectives of this study are to determine the incidence of electrolyte abnormalities in ICU patients receiving PN and to assess if any electrolyte abnormalities are associated with increased mortality.

Methods: A retrospective study will be conducted in adult patients who received PN in the ICU for ≥ ... 48 hours at three Detroit Medical Center hospitals. Data to be collected include demographic and clinical characteristics, Acute Physiology and Chronic Health Evaluation II score, indication for PN, macronutrient doses, duration of PN in the ICU, electrolyte levels prior to starting PN (sodium, potassium, chloride, bicarbonate, calcium, magnesium, and phosphorous), lowest and highest value for each electrolyte while on PN in the ICU, mean blood glucose during PN, standard deviation of blood glucose levels, presence of hypoglycemia (blood glucose ≤ ... 40 and < 70), whether the patient required mechanical ventilation or vasoactive support, length of ICU stay, hospital length of stay, ICU mortality, and in-hospital mortality. The incidence of mild, moderate, and severe electrolyte abnormalities will be determined, and logistic regression will be used to determine if any electrolyte abnormalities are associated with mortality or length of stay. Univariate and multivariate analyses will be conducted. This study has been submitted to the Wayne State University Institutional Review Board for approval.

Results: N/A

Conclusion: N/A

---

## Abstract No. 60 (Student-Graduate) (Clinical_Sciences)

**Title**

Prevention of the Emergence of Vancomycin Resistance in S. aureus by combination Vancomycin and beta-lactams

**Affilliations**

Anti-Infective Reseach Laboratory
Eugene Applebaum College of Pharmacy & Health Sciences, Wayne State University

**Authors**

N Singh, J Yim and MJ Rybak

**Abstract**

Background

Vancomycin (VAN) is the primary therapy for MRSA infections. Unfortunately, vancomycin intermediate resistant Staphylococcus aureus (VISA) has emerged secondary to widespread use of this agent worldwide. Beta-lactams have been recently demonstrated to have antibiotic synergy with a number of lipopeptides and glycopeptides including vancomycin. However,

little to know data is available on whether beta-lactam combination with vancomycin could prevent the emergence if VISA. Our objective is to determine if beta-lactam combination VAN therapy would prevent the emergence of VAN resistance.

Methods

We chose a VAN susceptible (MIC = 0.5 mg/L) MRSA isolate (RN9120) that has an accessory gene knockout as our experimental organism to incorporate in a 1-compartment pharmacokinetic and pharmacodynamic (PK/PD) model. We then simulated suboptimal human VAN dosing ranging from 62.5-500 mg q 12 h over 72 hours to produce an VISA like organism (MIC = 4 mg/L). In vitro model simulations were repeated 2-3 times to ensure that the VISA like organism obtained was reproducible. If VISA was not noted within the first 72 h, the organism at the end of the experiment was cycled through an addition 72-144 h exposure. A side experiment using serial passage techniques VAN exposure was also attempted to produce a VISA like organism.

Results

After repeated PK/PD model experiments, a VAN dosage regimen of 200 mg q 12 h produced VISA (VAN MIC = 4 mg/L) within a 72-144h exposure. This organism maintained the VISA phenotype (MIC of 4 mg/L) despite 3 serial passages onto antibiotic free media and was considered stable resistance. The serial passage of the VAN susceptible RN9120 also produced a VISA like organism (VAN MIC 4-8 mg/L) after 23 days of VAN exposure.

Conclusions

Similar to what the literature has demonstrated, our simulated human suboptimal VAN exposure contributed to the emergence of VISA. Our next planned experiments will be to repeat the PK/PD VAN simulated suboptimal dosing in the presence of a beta-lactam antibiotic to see whether the addition of the beta-lactam can prevent the emergence of VISA.

# HEALTH AND BEHAVIORAL SCIENCES

## Abstract No. 61 (Student_Graduate) (Health_and_Behavioral_Sciences)

**Title**

INFLUENCE OF PEDALING CADENCE AND INCREMENTAL PROTOCOL ON THE ESTIMATION OF EMGFT

**Affilliations**

Physical Therapy Program and Integrative Physiology of Exercise Laboratory
Wayne State University
College of Pharmacy and Health Sciences
Department of Health Care Sciences
Detroit, MI 48201

**Authors**

Timothy M. Duff ... Hallie Fournier ... Orie B. Hopp ... Eli Ochshorn, PhD ... Eric S. Sanders ... Rachel E. Stevens ... and Moh H. Malek, PhD

**Abstract**

Theoretically, the electromyographic fatigue threshold (EMGFT) is the highest exercise intensity that an individual can exercise at indefinitely without an increase in EMG amplitude. This index is estimated from a single incremental test. There are, however, factors that may influence EMG amplitude such as pedaling cadence or the incremental protocol used. The purposes of this study were to determine if different pedaling cadences and/or incremental protocols influence the estimation of the electromyographic fatigue threshold (EMGFT). Eight healthy college-aged men performed incremental cycle ergometry on three separate visits. The participants exercised using the following combinations of pedaling cadences and incremental protocols in random order: 25 W at 70 RPM ... 13 W at 70 RPM ... and 25 W at 100 RPM. The EMGFT value was determined from the vastus lateralis muscle of each participant for each of the three conditions. Separate one way repeated measures ANOVAs were performed to determine mean differences for various outcome indices. The mean maximal power output for the 13 W at 70 RPM condition was significantly lower than the two other conditions. There were, however, no significant mean differences [$F(2,14) = 2.03$ ... $p = 0.169$] for EMGFT between the three conditions . The findings of the current study indicated that different pedaling cadences and incremental protocols did not influence the estimation of the EMGFT.

---

## Abstract No. 62 (Student_Graduate) (Health_and_Behavioral_Sciences)

**Title**

INFLUENCE OF PEDALING CADENCE AND INCREMENTAL PROTOCOL ON THE ESTIMATION OF EMGFT

**Affilliations**

Physical Therapy Program and Integrative Physiology of Exercise Laboratory

**Authors**

Timothy M. Duff, SPT Hallie Fournier, SPT Orie B. Hopp, SPT, Eli Ochshorn, PhD, SPT Eric S. Sanders, SPT Rachel E. Stevens, SPT and Moh H. Malek, PhD

**Abstract**

Theoretically, the electromyographic fatigue threshold (EMGFT) is the highest exercise intensity that an individual can exercise at indefinitely without an increase in EMG amplitude. This index is estimated from a single incremental test. There are, however, factors that may influence EMG amplitude such as

pedaling cadence or the incremental protocol used. The purposes of this study were to determine if different pedaling cadences and/or incremental protocols influence the estimation of the electromyographic fatigue threshold (EMGFT). Eight healthy college-aged men performed incremental cycle ergometry on three separate visits. The participants exercised using the following combinations of pedaling cadences and incremental protocols in random order: 25 W at 70 RPM ... 13 W at 70 RPM ... and 25 W at 100 RPM. The EMGFT value was determined from the vastus lateralis muscle of each participant for each of the three conditions. Separate one way repeated measures ANOVAs were performed to determine mean differences for various outcome indices. The mean maximal power output for the 13 W at 70 RPM condition was significantly lower than the two other conditions. There were, however, no significant mean differences [F(2,14) = 2.03 ... p = 0.169] for EMGFT between the three conditions . The findings of the current study indicated that different pedaling cadences and incremental protocols did not influence the estimation of the EMGFT.

---

## Abstract No. 63 (Student_Graduate) (Health_and_Behavioral_Sciences)

### Title

Facilitators and Barriers to Sustainable Global Rehabilitation Programming: Learning Lessons from the Past.


### Affilliations

1Department of Healthcare Sciences, Program in Physical Therapy, and 2Department of Healthcare Sciences, Program in Occupational Therapy, Wayne State University, Detroit, Michigan, 48201.

### Authors

H.F. Alvarez1, B.S., SPT, F.D. Pociask1, PhD, PT, and R. DiZazzo-Miller2, PhD, OTRL.



### Abstract

INTRODUCTION: Approximately one billion people worldwide are in need of rehabilitation services, the majority in low-income countries. Although the burden of disability is on the rise, an increase in global poverty has led to diminished access to quality healthcare. In response, many Global Rehabilitation Projects (GRPs) are conducted yearly to aid in medical care and rehabilitation in resource poor environments. However, there is currently a substantial gap in literature regarding factors that promote and hinder GRPs.

PURPOSE: The purpose of this study was to assess barriers and facilitators to sustainable GRPs and to identify factors to be used to develop a questionnaire to rank global rehabilitation factors. Research questions were: 1) What factors promote and hinder GRPs, and 2) what lessons have rehabilitation experts learned that will enhance future GRPs in resource poor environments? METHOD: Eleven GRP specialists with involvement in projects in three or more countries and a minimum of eight years of experience (mean = 21.00 and range = 9 - 37) were recruited on a voluntary basis using a peer nomination process ... those not meeting the above criteria were excluded. Participants completed a single 40 to 60 minute telephone interview conducted by the same trained researcher. Interview questions asked GRP specialists to identify factors they believe are absolutely critical for successful planning, implementation and sustainability of GRPs, as well as factors that are absolutely detrimental. Digital recordings were transcribed verbatim, independently reviewed for accuracy, and analyzed using a qualitative content analysis approach, as well as frequency analysis.

RESULTS: Four parallel themes, two unique themes and corresponding sub-themes

describing barriers and facilitators to sustainable GRPs emerged from analysis. The four parallel themes that emerged as barrier and facilitators were described by the presence or lack of 1) established processes and procedures, 2) government, health ministry and health organization support, 3) availability of trained local personnel and knowledge, and 4) long term funding, resources and equipment. Working within established standards was a distinctive facilitator and uncontrollable factors were a distinctive barrier. A resounding theme was involvement of the host country in all aspects of the process to ensure local leadership, the ability to take over the project when volunteers leave and long-term sustainability of the project. Frequency analysis provided the number of occurrences of all factors as identified for each respondent.

DISCUSSION AND CONCLUSION:
Qualitative findings from this study provide valuable insight into crucial factors that contribute to successful planning, implementation and sustainability of GRP's. Findings from frequency analysis provide particularly useful information beyond causal explanations. Improved understanding of factors that account for successful GRPs is essential to address the current gap in GRP literature and to improve access for individuals that are currently unable to receive proper care.

LIMITATIONS AND FUTURE RESEARCH:
This study utilized a small sample size and study finding cannot be generalized to other GRPs and GRP specialists. Data from this study will be used to construct a questionnaire to prioritize global rehabilitation factors for more effective and informed decision-making.

---

## Abstract No. 64 (Student_Graduate) (Health_and_Behavioral_Sciences)

### Title

Analysis of pharmacy student learning from a pilot interprofessional patient safety program

### Affilliations

Stephanie Everard, Nicole Pearl, Diane Levine, Mary Beth O'Connell – Wayne State University
Mary E. Burkhardt - Medication Safety Consultant

### Authors

Stephanie Everard, BS ... Nicole Pearl, BSc ... Mary E. Burkhardt, MS, RPh, FASHP, FSMSO ... Diane Levine, MD ... Mary Beth O'Connell, PharmD, BCPS, FASHP, FCCP, FNAP

### Abstract

Purpose:
Providing patient care that is safe and effective requires training student healthcare professionals in strategies to prevent, recognize, report, and resolve medical events. These students should receive the fundamentals of patient safety training during didactic and experiential learning. A pilot interprofessional education program was initiated to train medical and pharmacy students on patient safety and medical error analysis and prevention. The purpose of this study was to evaluate pharmacy student learning about patient safety and event analysis and to capture ideas to expand and improve the interprofessional pilot program.

Methods:
Seven third-year pharmacy and fifty third-year medical students completed a half-day long interprofessional patient safety pilot program that began with a pre-program survey. A physician led a real-life patient safety case discussion. An episode of Grey's Anatomy involving a patient's death from a patient safety error was played. Pharmacist and physician

instructors presented fundamental patient safety analysis tools and prevention strategies and concepts, such as Reason's Swiss cheese model, cause and effect diagramming, root cause analysis, and concepts for quality improvement. The principles of just culture, sentinel events, and human factors engineering were also reviewed. Interactive exercises were completed by teams of one pharmacy student and seven to eight medical students. Students completed post-assessment surveys that included self-reported learning and opinions. Descriptive statistics using Statistical Package for the Social Sciences (SPSS) program version 22 were used to summarize the surveys.

Results:
Before and after the program all students felt healthcare professionals need to understand principles of patient safety and disagreed that reporting near miss events is not important. Prior to the program, most pharmacy students agreed that reporting adverse events is important ... afterwards, all students agreed. Most pharmacy students (4 to 6 per topic) had no to minimal prior understanding of the Swiss cheese model, human factors engineering, a sentinel event, cause and effect diagrams, root cause analysis, concepts for quality improvement, and a just culture, however, after the program almost all students (3 to 6 per topic) had a basic understanding of these topics. Students felt more knowledgeable about patient safety (baseline 2, post 6 students) and medical error prevention (baseline 3, post 6 students). Since students listed very likely or somewhat likely to report near miss and adverse events before the program, no change in reporting likelihood occurred. More students strongly disagreed that healthcare professionals cannot do anything about medical errors (baseline 1, post 4 students). Ideas for program improvement were more pharmacy students per team, more interactive exercises, and dividing the program into two days.

Conclusion:
Completion of the pilot interprofessional patient safety education program resulted in improvement of pharmacy student knowledge deficits in patient safety, medical error analysis, and prevention of medical errors. Due to the pilot program's success, the program will be expanded to include all third-year pharmacy students to allow patient safety and interprofessional learning to have a larger presence in the pharmacy school curriculum. Interactive exercises will be expanded and changes made to the assessment tools to better capture learning.

---

## Abstract No. 65 (Student_Graduate) (Health_and_Behavioral_Sciences)

### Title

Anterior Pelvic Tilt and Pelvic Gait Asymmetries in Individuals with Trans-tibial Amputation, Case Series

### Affilliations

Wayne State University Physical Therapy Program. Wright and Fillipis

### Authors

Jaclyn Davis, SDPT. Leanne Lambros, SDPT. Tracy Newsom, SDPT. Kayleigh Reed, SDPT. Marie-Eve Pepin, PT, DPT, MSPT, OMPT. Diane E Adamo, OTR, MS, PhD

### Abstract

Introduction: Following a trans-tibial amputation, a properly fitted prosthesis may reduce the risks of developing abnormal gait patterns. Anterior pelvic tilt (APT) is one parameter used to determine proper fit. However, APT measurements are often taken in static positions which may not capture changes in APT during gait. The purposes of this study are to compare right and left limb differences in APT, to compare static and dynamic ATP and to compare APT to gait parameters in individuals who have a trans-tibial amputation.

Methods: Six participants [mean (SD) age 55 +/- 12.05 years], recruited from Wright and Filippis, participated in the study. The Prosthetic Evaluation Questionnaire was administered to assess quality of life and satisfaction of prosthesis. Static APT was measured after movement in 4 conditions (static standing, sit to stand, march in place, 10 meter walk) using the Palpation Meter device. Dynamic APT and gait parameters were measured while walking 10 m at ones' preferred pace using the BTS G-WALK.

Results: Static APT was greater than dynamic APT in 5 participants. There were no significant differences between the amputee side and sound side for both static and dynamic APT. Double limb stance time was increased with a reduction in single limb stance when compared to normative values. The ATP did not seem to influence stride length or gait speed.

Discussion: Findings here suggest that dynamic anterior pelvic tilt measurements be included in measurements of prosthetic fit following a trans-tibial amputation since it may be more representative of what truly occurs during gait. More studies are needed to investigate if prosthetic fit using dynamic measures may results in better prosthetic fit and decreased gait deviations.

---

## Abstract No. 66 (Student_Graduate) (Health_and_Behavioral_Sciences)

**Title**

VIDEO MOVEMENT ANALYSIS USING SMARTPHONES (VIMAS): A PILOT STUDY

**Affilliations**

**Authors**

Finkbiner M, Gaina K, McRandall M, Wolf M, Pardo V, Reid K, Adams B, Galen S.

**Abstract**

Introduction/Clinical Relevance: The use of smartphones in clinical practice is steadily increasing with the availability of low cost and sometimes freely available "apps" that can be used for assessing human movement during activities such as gait. Smartphone apps such as Dartfish and Ubersense allow clinicians to objectively measure human movement through video analysis. The primary aim of this study was to test the concurrent validity of kinematic measures recorded by the smartphone application known as Ubersense (Ubersense Inc, Boston, MA) by comparing them to measures recorded by a 3D motion capture system in the sagittal plane. The secondary aim of this study was to develop a protocol that will help clinicians to use a smartphone camera for video movement analysis using smartphone apps.

Methods: The concurrent validity of the Ubersense app was tested using 32 healthy adults. The knee angle in the sagittal plane was measured both during the heel strike and toe off events of the gait cycle using the Ubersense app and an Optotrak Certus 3D motion-capture system, while the subjects walked over a 10 meter walkway. Subjects completed a total of 6 walking trials during which the smartphone camera mounted on a tripod was randomly placed at a distance of 2.0m (near) for 3 walking trials and 4.0m (far) away for another 3 walking trials from the center of the walkway. The absolute measurement errors were calculated and an interclass correlation (ICC) was performed to establish the agreement between the two systems.

Results: All subjects completed the walking trials, however data from 6 individuals were not included in the analysis due to technical issues resulting in poor marker visibility. The absolute measurement errors of knee angle were least during toe off events (3.12+5.44 degrees) compared to heel strike (5.81+5.26 degrees). There were no significant ($p>0.05$) agreements between the Ubersense and Optotrak measures of knee angles. There were also no significant

($p>0.05$) differences between the absolute measurement errors between the two camera positions. Discussion: This study has established for the first time the absolute measurement errors that can be observed while performing video movement analysis using a smartphone app in the sagittal plane. The measurement errors averaged between 3 to 5 degrees in the measurements made during toe off and heel strike events of the gait cycle. The recommended height for the smartphone for both a near (only lower extremity) and far (upper extremity, trunk and lower extremity) camera placements can be estimated using the following regression equations

Far camera height (in meters) = (leg length (in meters) x1) – 0.23

Near camera height (in meters) = (leg length (in meters) x0.87) – 0.12

Conclusions: The use of smartphone apps can be a useful tool in the clinic for performing gait or human movement analysis. Further studies are needed to establish the accuracy in measuring movements of the upper extremity and trunk.

---

## Abstract No. 67 (Student_Graduate) (Health_and_Behavioral_Sciences)

**Title**

FALLS RISK IN PATIENTS DIAGNOSED WITH CRITICAL ILLNESS MYOPATHY

**Affilliations**

Physical Therapy Program, Wayne State University, Detroit, Michigan
Physical Therapy In-patient Rehabilitation Services, Beaumont Hospitals, Royal Oak, MI

**Authors**

Kypros M, Stempky E, Thornton K, Wilkewitz R, Weber K, Greene C, Mugarian L, Gray E, Kottoor J, Schiller M, Galen S

**Abstract**

Purpose/Hypothesis: Critical illness myopathy (CIM) is a muscular pathology acquired in the ICU. The exact pathophysiology of this condition is still not fully understood. The clinical findings associated with CIM are significant weakness affecting proximal muscles more than distal muscles. The financial burden of falls and fall related injuries continues to be an area of concern for the health care systems. Total economic cost has been estimated at $300,000 per patient per year in post discharge care for ICU acquired weakness. The aim of this study is to assess fall risk using spatio-temporal gait parameters and the modified gait efficacy scale (mGES) in patients diagnosed with CIM prior to discharge from inpatient rehabilitation.
Subjects: This study is an ongoing study with a cross-sectional study design. Participants are being recruited from the inpatient rehabilitation unit at William-Beaumont Hospital at Royal Oak MI. A total of 30 patients diagnosed with CIM will be recruited to participate in this study. To date 7 patients have been recruited (Male=4, Female =3, Age=69.3+6.4).
Materials/Methods: All seven subjects have had a single assessment of 4 gait parameters: gait speed, step length, stance time, and swing time, and the mGES were also administered during this single visit. Both of these outcome measures have been previously shown to be related to risk of falls and therefore were administered between 5 days to the day prior to discharge from inpatient rehabilitation. A follow-up phone call will be made 3 months post discharge in order to administer the mGES for a second time, and record any falls experienced within the past 3 months. All gait parameters were recorded using the wireless gait assessment tool (Wi-GAT) while the subjects walked 3 times over a 10-meter walkway using a self-selected walking speed.
Results: All subjects recorded slower walking speeds compared to age matched normative

data. Subjects 1,3,5,6,7 who were in their 60's had an average walking speed of 0.5+0.17 m/s while previously published normative walking speeds for 60 year old healthy adults were shown to be 1.36 m/s for men and 1.30m/s for women. All subjects also had a longer stance time, shorter swing time and shorter step lengths. The mGES scores recorded were as follows ... S1=86, S2= 49, S3= 53, S4=68,S5=37, S6 =34 and S7=49.
Conclusion: All subjects had substantially reduced walking speeds in comparison to the normative walking speeds reported previously for their age groups in healthy aging adults. Most subjects had mGES scores well below the normative values, indicating a low level of walking confidence during everyday activities, which has also been associated with increased risk of falls.
Clinical Relevance: This is the first study to our knowledge that has reported both the Spatio-temporal gait parameters and walking confidence in patients diagnosed with CIM. If this trend indicative of a greater risk of falls in patients diagnosed with CIM is observed in more patients, this may necessitate the need for a longer in-patient rehabilitation focused on preventing falls.

---

## Abstract No. 68 (Student_Graduate) (Health_and_Behavioral_Sciences)

### Title

Implementing an Interprofessional Student-Run Free Clinic: Lessons Learned


### Affilliations

Masters of Occupational Therapy Program, Diabetes Education Wellness Clinic

### Authors

Nancy V. Milligan, PhD, OTR, FAOTA ... Danielle Bresso ... Mara Monte ... Sherin Pennickara MOT Students



### Abstract

Introduction
- Diabetes, an epidemic which affects nearly 30 million Americans, depends on a persons knowledge and ability to perform self-management tasks. To educate the community of the risks for and management of diabetes, the Eugene Applebaum College of Pharmacy and Health Sciences runs the Diabetes Education Wellness (DEW) Clinic which is an inter-professional, student-run, free clinic. Consisting of seven health science disciplines, the students work inter-professionally educating persons with type- 2 diabetes. Clinic attendees are provided with proper resources and tools to manage their diabetes independently.
- There is a need for health professionals who function well in a dynamic team-based environment. Interprofessional education aims to meet this need by enabling health professional students to collaborate on teams while working toward common goals1
- To bridge from classroom to a complex healthcare environment, student learning must involve teamwork. The DEW clinic has been in operation for the last five years. To evaluate its effectiveness, a focus group was conducted with students, faculty, and mentors.

Objectives
- To understand the challenges and benefits of developing and sustaining an interprofessional student run clinic.
- To determine the perspective and attitudes of faculty and students toward interprofessional education and improvements to the DEW student run clinic.

Methods
- 24 staff and students participated in a focus group addressing perspectives and attitudes toward inter-professional education and improvements for the DEW clinic. A grounded theory approach was used to analyze the data to identify emerging themes.

Results
- There were five emerging themes ... 1. An

interprofessional collaboration allows for practical application of roles specific to diabetes 2. The DEW provides a practical application in a real life context 3. Interprofessional collaboration develops exposure to other resources allowing for a more comprehensive, whole approach to treating a patient with diabetes 4. Overall in favor of integrated team tables with complementary grouping of no more than 3 disciplines per table for best patient outcomes 5. A revised format with more organization and include realistic visual training would enhance orientation sessions

Conclusion
- All participants in the study felt that interprofessional collaboration was beneficial. The clinic provides students with invaluable first hand experiences: serving individuals with type- 2 diabetes, learning alongside health care workers, and taking the lead at problem solving.
- Students and faculty mentors were in consensus to integrate the team tables but recommended a maximum of three disciplines to a promote best practice outcomes.
- Recommendations for future student training included enhanced visual instruction through a mock DEW clinic demonstration and online tutorials.

---

## Abstract No. 69 (Student_Graduate) (Health_and_Behavioral_Sciences)

### Title

Feasibility and Minimum Detectable Change of the Lower Extremity Fugl Meyer Assessment in Acute Stroke

### Affilliations

Wayne State University, Detroit, MI

### Authors

Michelle Bendewald, SPT, Chelsea Casanova, SPT, Krista Kelly, SPT, Meagan Rekowski, SPT, Allon Goldberg, PT, PhD, Sujay Galen, PT, PhD, Victoria Pardo, PT, MHS, DHS

### Abstract

Introduction/Clinical Relevance: The Fugl-Meyer Assessment Scale (FMA) is a standardized quantitative outcome measure that assesses motor function following a stroke. The lower extremity subscale (FMA-LE) has been studied in chronic stroke and found to have good reliability and concurrent validity. The feasibility of using the FMA-LE in an acute stroke population has not been studied to date. The purpose of this study was to determine the feasibility (patient tolerance, duration of testing) and the minimum detectable change of the FMA-LE in individuals with acute stroke in an inpatient rehabilitation setting. Methods: Forty-three patients with acute stroke (mean 20.9 days post-stroke) resulting in unilateral hemiparesis were recruited from an inpatient rehabilitation setting in the Metro Detroit area. Participants were assessed using the FMA-LE, twice on the same day with at least a 5 minute rest in between assessments. The duration of each FMA-LE assessment was recorded. Blood pressure, heart rate, oxygen saturation, rate of perceived exertion (RPE) and pain were measured before, during the 5 minute rest, and after the two trials. The intraclass coefficient (ICC 2,1) was computed to assess the relative reliability of each test. Standard error of measurement (SEM), which quantifies measurement error in absolute values, was calculated as the standard deviation (SD)* √ ... (1-ICC). MDC at a 95% confidence level (MDC95) was calculated as z*SEM*√ ... 2 where z=1.96. Results: The mean time to complete the FMA-LE for each trial was 8.99 (SD 2.12) and 8.68 (SD 2.25) minutes. Mean changes in vitals were very small. Mean FMA-LE was 22.97 (SD 8.36, range 4-34) out of a possible 34 points, with an ICC of 0.98 (SEM was 1.32, MDC95 was 3.66). Measurement error and MDC95 expressed as a percentage of mean FMA-LE were 5.7% and 15.9% respectively. Discussion: The amount of time necessary to perform the FMA-LE (less than 9

minutes) in the acute stroke population demonstrates that this is an outcome measure that can be incorporated into the initial assessment of the inpatient rehabilitation population. The minimal changes in vitals, pain and RPE demonstrate that the FMA-LE is tolerated well by the acute stroke population in the inpatient rehabilitation setting. The high ICC for the FMA-LE suggests high agreement between assessors. The low SEM% is suggestive of low measurement error and good absolute reliability. The low MDC95% suggests that this test may be able to detect real change in physical performance in patients with acute stroke. Conclusions: This study has demonstrated that it is feasible to perform the FMA-LE in patients with acute stroke in an inpatient rehabilitation setting. Real change was computed to be > 3.66 points, which will assist clinicians and researchers in interpreting whether real change has occurred when comparing repeated measures of the FMA-LE. These preliminary results should be used to encourage clinicians to use the FMA-LE when assessing motor recovery in the acute stroke population.

Key words: stroke, Fugl-Meyer, feasibility, minimum detectable change

---

## Abstract No. 70 (Student_Graduate) (Health_and_Behavioral_Sciences)

### Title

HEALTH BEHAVIORS AND ROLE-MODELING ATTITUDES AMONG CLIENTS IN A PRO BONO THERAPY PHYSICAL THERAPY CLINIC

### Affilliations

Wayne State University, Detroit, MI

### Authors

Schwartz, M, Neda, R, Alqattan, H, Mhaid, D, Pysh, J, Schiller, M

### Abstract

INTRODUCTION: Physical activity, weight management, cigarette smoking and nutrition all impact a person's health and wellness. The impact of role modeling health behaviors by healthcare professionals is not known in a probono PT clinic setting. The purpose of this study was to describe the health behavior beliefs and role-modeling attitudes among individuals managed by physical therapists in a pro bono PT clinic. METHODS: This was a prospective descriptive study using a sample of convenience of patients referred to PT at the WSU SAY Detroit Pro Bono PT Clinic. After obtaining informed consent, patients completed a health behavior beliefs and role-modeling attitudes questionnaire. Demographic information was obtained and blood pressures were taken. Descriptive statistics were tabulated for all data using SPSS 21. RESULTS: 36 female subjects participated in the study ... 34 were African American. Of the 36 subjects, 22% smoked, 50% reported not meeting physical activity guidelines or consuming recommended fruits & vegetable, 72% were not managing a healthy weight. Most participants were contemplating or preparing to change behaviors with their physical activity (42%), weight management (72%), consumption of fruits/vegetables (45%) and smoking (17%). Suboptimal blood pressures were found in 75% of the subjects ... 56% with prehypertensive and 19% with hypertensive values. There was no significant correlation found between practicing health behaviors and suboptimal BP status. There was strong agreement among participants that physical therapists should practice what they preach (81%), should role model physical activity (92%), weight management (86%), eating fruits and vegetables (83%) and non-smoking (83%) behaviors. DISCUSSION: Many of the patients seen in the pro bono PT clinic were not engaged in positive health behaviors but were

contemplating or preparing for change. The suboptimal BPs points to the importance of PTs monitoring this as a standard of care. PTs have the opportunity to play an active role in educating, motivating and engaging patients in healthy behaviors as they typically see their patients on an ongoing basis. Role modeling of healthy behaviors by PTs was reported to being important to the subjects. As with physicians, PTs should be aware that the examples they set and share is important and may elicit greater compliance from their patients. Sample size, patient self-report and number of student data collectors are study limiting factors. CONCLUSIONS/CLINICAL RELEVANCE: The majority of patients in this sample are not practicing good health behaviors with respect to physical activity, weight management and consumption of fruits/vegetables however most were contemplating change and did regard role-modeling from their PT professionals as important. Identifying health behaviors and blood pressure screening in an outpatient pro bono clinic may identify clients that could benefit from health and wellness strategies or may be need referral for further medical management. AKNOWLEDGEMENTS: Special thanks to the SAY Detroit Health Clinic staff, patients and volunteers.

---

## Abstract No. 71 (Student_Graduate) (Health_and_Behavioral_Sciences)

### Title

Oncology EDGE Task Force on Colo-rectal Cancer Outcomes: A Systematic Review of Clinical Measures of Strength and Muscular Endurance

### Affilliations

### Authors

Francine Burgess, SPT ... Lindsay Galambos, SPT ... Alexis Howland, SPT ... Monica Yalamanchili, SPT ... Lucinda A. Pfalzer, PT, PhD, FACSM, FAPTA

### Abstract

Background: Patient reported weakness and decreased muscular strength are a common morbidity following treatment for colorectal cancer. Accurate clinical assessment of strength and muscular endurance following colo-rectal cancer treatments is essential to identify deficits and plan physical therapy intervention.

Purpose: To identify strength and muscular endurance outcome measures that have strong psychometric properties and are clinically useful for examination of individuals treated for colo-rectal cancer.

Methods: Multiple electronic databases were searched between December 13, 2014 and March 4, 2015. Studies of tools used to assess strength and muscular endurance were included if they reported psychometric properties, clinically feasible methods, were conducted on adults and published in the English language. Each outcome measure was independently reviewed and rated by two reviewers. A single Cancer EDGE Task Force Outcome Measure Rating Form was completed for each tool, and a recommendation was made using the 4-point Cancer EDGE Task Force Rating Scale.

Results: Of the original 4922 articles identified, 21 were reviewed. Six clinical measures of strength were identified: hand grip strength, hand-held dynamometry, isometric strength, manual muscle testing, trunk flexion strength/lower extremity (LE) dynamometry, and endurance. Hand grip strength using dynamometry and hand-held dynamometry were rated a 3 (recommended for clinical use), isometric strength testing and trunk flexion/LE dynamometry were rated a 2B (unable to recommend at this time due to poor psychometric properties). Manual muscle testing and muscular endurance testing were rated 2B and 1 respectively (1, unable to recommend at this time due to lack of

psychometric support).

Conclusions: Utilizing the objective measures of hand grip strength and hand-held dynamometry for muscle strength testing provides precise measurement to assess baseline status and monitor change among those being treated for colo-rectal cancer.

---

## Abstract No. 72 (Faculty) (Health_and_Behavioral_Sciences)

### Title

Kinematic adaptations during walking using a bionic exoskeleton in healthy individuals

### Affilliations

1. Physical Therapy Program, Wayne State University, Detroit, MI. USA
2. Rehabilitation Institute of Michigan, Detroit Medical Center, Detroit, MI. USA
3. Department of Physical Therapy, University of Michigan, Flit, MI. USA

### Authors

Galen S,1 Denes M,2 Pardo V,1,2 Devour A,1 Berndt L,3 Vanderweele H,3Larsen K,3 VanStrien L,3 Larson C2,3.

### Abstract

Introduction
Bionic exoskeletons such as the EKSO (ekso bionics, Richmond, CA) are enabling individuals with spinal cord injury(SCI) to attempt walking after they have either sustained a complete or incomplete injury. The primary aim of this study was to study the kinematic and EMG patterns in individuals without pathology while they walked over ground unassisted and with the full assistance of an exoskeleton. Data on the kinematics will inform Clinicians/Therapists on the kinematic patterns that they can expect to see while gait training with an exoskeleton.
Methods: Ten healthy participants (female: mean age:) were studied. The lower extremity kinematics were recorded using the Optotrak Certus 3D motion capture system (NDI, waterloo, Canada). A cluster marker system was used to record the kinematics. Each individual completed 6 trials of overground walking while wearing the exoskeleton and a separate 6 trials while walking without it at a self-selected walking speed. Kinematic data of the lower extremity from a single stride was recorded on each of the walking trials and averaged.
Results: The ankle ROM during the entire gait cycle was reduced to 10 degrees (dorsiflexion to plantarflexion) while walking with the exoskeleton. The hip and knee ROM remained were comparable, however the temporal pattern of cycling from flexion to extension in both hip and knee were greatly altered due to a longer stance duration and shorter swing duration observed while walking with the exoskeleton.
Conclusion: The temporal patterns of lower extremity kinematics were altered while walking with the exoskeleton.

---

## Abstract No. 73 (Faculty) (Health_and_Behavioral_Sciences)

### Title

The control of grasp force for individuals who suffered a stroke and age-matched controls.

### Affilliations

- Institute of Gerontology
- Rehabilitation Institute of Michigan
- Department of Healthcare Sciences, Physical Therapy Program, Wayne State University Physical Therapy

- Funding from Blue Cross Blue Shield of Michigan Foundation grant awarded to DA

- Physical Therapy Endowment Scholarship awarded to CA.

**Authors**

Charlie E. Anderson, SPT, Rajiv George, Vicky Pardo, PT, DHS, Diane E. Adamo, OTR, PhD

**Abstract**

Introduction

Stroke survivors have difficulty overcoming deficits associated with grasping ability that may differ for their right and left hand. The purpose of this study was to determine right and left hand differences in control of grasp force for right handed individuals who suffered a stroke and compare findings to age-matched right handed controls.

Methods

Three groups of participants (25 right hemisphere damage, 22 left hemisphere damage and 26 controls) completed clinical assessments and performed hand-grasp tasks using Instrumented Strain Gauges embedded with force sensors. Pre / post stroke hand preference scores were obtained using the self-reported Edinburgh Handedness Inventory (EHI). A right and left hand reference force was based on 20% of the respective right and left maximum grasp force and provided the reference when matching with the same and opposite hand. Visual feedback, represented by a horizontal line on a computer monitor, displayed the 20% reference force. The matching force, performed without visual feedback, indicated whether the participant overshot or undershot the reference force and this value quantified the Constant Error.

Results

Pre and post EHI scores for individuals with right hemisphere damage were 0.87 / 1.00 and 0.82 / 1.00, respectively indicating they continued to use the right hand for most tasks. Pre and post EHI scores for individuals with left hemisphere damage were 0.88 / 1.00 and 0.50/ 1.00, respectively indicating less right hand use post stroke. For grasp force matching, the ANOVA showed a significant three-way interaction for matching hand *condition* group, $F(4,138) = 5.9$, $p < 0.05$) for constant error. Individuals with right hemisphere damage showed left hand matching undershoots for right hand reference forces ($p < 0.05$) and right hand matching overshoots for left hand reference forces ($p < 0.05$). Similar directional differences were found in the control group. However, those individuals with left hemisphere damage showed right and left hand overshoots for opposite hand matching ($p > 0.05$).

Discussion

Shifts in handedness scores and the magnitude of directional differences in force matching performance were dependent on lesion location. The control group performed in a manner similar to individuals with right hemisphere damage. Those with right hemisphere damage also continued to use their right hand to perform everyday tasks post stroke. However, those with left hemisphere damage showed significantly less right hand use and consistently overshot right and left reference forces. From a clinical perspective, stroke survivors may not be aware of how shifts in hand use or changes in the control of grasp force influence their ability to perform everyday tasks. Further investigation is warranted.

---

## Abstract No. 74 (Student_Graduate) (Health_and_Behavioral_Sciences)

Graduate Student (actually the presenting author will be Amina Ammar, a pre-pharmacy student (SURF 2015)

**Title:**

Texting, Driving and Drugs:  Driving Simulator Studies

**Affilliations:**

Pharmaceutical Sciences and Occupational Therapy

**Authors:**

Amina Ammar, Ashley Blanchette, Theresa Palumbo, Aaron Swift, Doreen Head and Randall Commissaris

**Abstract**

The Eugene Applebaum College of Pharmacy and Health Sciences (EACPHS) fixed base full-size driving simulator is public health research resource that is not typically available for research with pharmacy or health sciences students. Our research group has involved graduate students, pharmacy and health care professional students and pre-pharmacy students in research studying the problem of texting while driving and drugs while driving. Initial studies examined the influence of driver age on the disruption of driving while texting. Typically, more mature drivers perform better in distracted driving situations, but it turned out that was not the case when the distraction was texting; although drivers of all ages were prone to driving errors when asked to text while driving, the magnitude of this disruption increased with increasing driver age (Rumschlag et al, 2014). The results of this study clearly debunked the argument that experience offers protection from the dangers texting while diving. In a second study we examined the effects of vision impairment produced by 'beer goggles' on the disruption of diving while texting. Not surprisingly, mimicking the visual impairment associated with being drunk resulted in greater driving impairment by texting, and this texting was associated with a dangerous reduction in the time that subjects ' eyes were on the road during texting (Palumbo et al, 2015).

Having demonstrated the utility of the EACPHS driving simulator as a research tool, we are planning studies in several new directions: (1) OTC drugs and texting while driving; of particular interest are comparisons like Benadryl (diphenhydramine) v the 'non-sedating' antihistamine loratidine (Claritin) v placebo; (2) Rx medications (pain meds, antidepressants, antipsychotics, anti-epilepsy drugs, medical marijuana) and texting and driving; subjects in these studies will be patients who are receiving the meds;

The results of these studies will provide for a better understanding of the public health risks associated drugs and texting alone on driving behavior. More important, these studies will allow us to better understand – and hopefully prevent – the 'imperfect trifecta' of drugs, texting and driving.

(Supported in part by EACPHS FRAP awards to Drs Head and Commissaris).

# POSTDOCTORAL RESEARCH

## Abstract No. 75 (Post_Doctoral_Fellow) (Postdoctoral_Research)

### Title

Risk Assessment and Severity Analysis in Acute Bacterial Skin and Skin Structure Infections (ABSSSIs)


### Affilliations

1. Wayne State University Eugene Applebaum College of Pharmacy and Health Sciences, Detroit, MI
2. Wayne State University School of Medicine, Detroit, MI

### Authors

Kimberly Claeys, PharmD, BCPS (1)
Evan Zasowski, PharmD, BCPS (1)
Adalhamid Lagnf, MPH (1)
Donald P. Levine, MD (2)
Susan L. Davis, PharmD (1)
Michael J. Rybak, PharmD, MPH (1, 2)



### Abstract

Background: ABSSSIs are among the most common infections seen in hospital and ambulatory care settings. There is little evidence-based guidance regarding the appropriate level of care for ABSSSIs. We sought to develop a clinical decision support tool to aid in the treatment of ABSSSIs.

Methods: Retrospective single-center cohort of adult ABSSSI patients in EDs, OUs, and inpatient setting. A series of multinomial regression models was used to derive a predictive model to determine patient disposition in the "appropriately treated" subgroup. Based on American College of Emergency Physician Guidance, patients were determined to be "appropriately treated" if care was: ED < 6 hours, OU < 24 hours, inpatient admission > 24 hours, no 96-hour ED revisit/hospitalization. Coefficients of the final regression model were assigned integer-valued, weight-adjusted values. Bootstrapping was used for internal validation. Receiver Operator Curve (ROC) analysis used to determine overall accuracy of the new scoring tool and compared to previously published tools – the CREST Class and the Standard Early Warning Score (SEWS).

Results: A total of 665 patients were collected, 506 were appropriately treated – 230 (45.4%) ED, 65 (12.8%) OU, and 211 (41.7%) inpatient admission. Patients with advanced age, higher Charlson score, prior hospitalization, acute kidney injury (AKI), chronic kidney disease (CKD), or peripheral vascular disease (PVD) were treated at a higher level of care (OU/inpatient) ($p < 0.05$). Inpatients were more likely to have at least SIRS criteria, particularly elevations in WBC count or body temperature alterations ($p < 0.001$). CREST Class I was the most common for both ED and OU patients (70.4% vs. 60.0%, respectively). Class II was the most common for inpatients (59.2%). The median ED SEWS was 0 (IQR 0 – 1), compared to 1 (IQR 0 – 1) in OU and 1 (IQR 0 – 3) in inpatients. CREST and SEWS were not accurate in ED versus OU disposition (ROC CREST 0.527 [95% CI 0.460 – 0.594], ROC SEWS 0.609 [95% CI 0.545 – 0.673]). They performed better in determining ED/OU versus inpatient (ROC CREST = 0.678 [95% CI 0.630 – 0.725], ROC SEWS 0.693 [95% CI 0.645 – 0.740]). A scoring system from 0 – 10 points was derived form clinical presentation and comorbid condition parameters (WBC, temperature, liver disease, PVD, AKI, CKD, leg infection). The accuracy of the newly derived model was 0.675 [95% CI 0.611 – 0.739] ED versus OU and 0.787 [95% CI 0.746 – 0.829] ED/OU versus inpatient.

Conclusions: The remains significant room for improvement in the disposition of patients being

treated for ABSSSIs. The derived clinical decision support tool needs to be validated in a multi-center cohort of patients.

---

## Abstract No. 76 (Post_Doctoral_Fellow) (Postdoctoral_Research)

### Title

Ceftaroline Fosamil (CPT) for the Treatment of Methicillin-Resistant Staphylococcus aureus (MRSA) Pneumonia (PNA)

### Affilliations

Wayne State Univ., Detroit, MI ... Husson Univ., Bangor, ME ... Univ. of Florida Hlth. Shands Hosp., Gainesville, FL

### Authors

Evan Zasowski, Pharm.D. ... Kimberly Claeys, Pharm.D. ... Anthony Casapao, Pharm.D. ... Noor Sabagha, B.Pharm. ... Kenneth Klinker, Pharm.D. ... Susan Davis, Pharm.D. ... Michael Rybak, Pharm.D., M.P.H.

### Abstract

Background: Although CPT is active against MRSA and is FDA approved for community-acquired bacterial pneumonia, culture-confirmed MRSA PNA was excluded from published trials. Despite availability of Vancomycin (VAN) and linezolid (LZD) for MRSA PNA, clinical failure and toxicity of these agents underscore the need for alternative therapies. This study describes the clinical characteristics and outcomes of patients who received CPT for MRSA PNA.
Methods: Retrospective, multi-center, observational study from 1/2011 - 5/2015. Inclusion: age ≥ ... 18 yr ... ≥ ... 1 respiratory culture positive for MRSA ... given CPT for ≥ ... 72 h for MRSA PNA. Primary outcome: clinical success - cessation of signs/symptoms of PNA by end of therapy/discharge and alive at 30 days. Secondary outcomes: 30-day mortality, microbiologic eradication in patients with follow up cultures ... hospital length of stay (LOS).
Results: 43 patients were included. Demographics/clinical characteristics: mean (SD) age 56 (17.5) ... 58.1% male ... 41.9% African American ... CABP 36.6% ... 27.9% intensive care unit ... concurrent bacteremia 27.9%. Median (IQR) APACHE II and Charlson Comorbidity score were 11 (7,15) and 2 (1,5) respectively. Reasons to use CPT: 53.5% prior therapy failure ... 27.9% cover multiple pathogens/sites of infection ... 9.3% prior therapy toxicity. VAN was prior therapy in 83.7% of patients. CPT was administered Q8H in 23.3% of patients. Median (IQR) duration of prior therapy 4 (3,9) days. Microbiology: MRSA - 65.1% VAN minimum inhibitory concentration (MIC) 2 mg/L ... CPT MIC range 0.5-1 mg/L (11 isolates) ... LZD MIC range 2-4 mg/L ... 11.6% concurrent gram-negative respiratory isolate with all susceptible to CPT. Outcomes: clinical success 83.7% ... 30-day mortality 14% ... microbiologic eradication 90% ... median (IQR) hospital-LOS 24 (11,43) days.
Conclusion: CPT produced high rates of clinical and microbiologic success in patients with culture-confirmed MRSA PNA, including many cases with perceived failure of prior therapy. Comparative analyses are needed determine CPT's place in the therapy of MRSA PNA.

---

## Abstract No. 77 (Post_Doctoral_Fellow) (Postdoctoral_Research)

### Title

Parenterally administrable nano-micelles of 3,4-difluorobenzylidene curcumin for treating pancreatic cancer

### Affilliations

Use-inspired Biomaterials & Integrated Nano Delivery (U-BiND) Systems Laboratory, Department of Pharmaceutical Sciences, Eugene

Applebaum College of Pharmacy and Health Sciences, Wayne State University, 259 Mack Ave, Detroit, MI 48201, USA

**Authors**

Prashant Kesharwani (PhD), Rahul Deshmukh (PhD), Arun K. Iyer (PhD)

**Abstract**

Pancreatic cancer remains one of the most devastating diseases in terms of patient mortality rates for which current treatment options are very limited. 3,4-Difluorobenzylidene curcumin (CDF) is a nontoxic analog of curcumin (CMN) developed in our laboratory, which exhibits extended circulation half-life, while maintaining high anticancer activity and improved pancreas specific accumulation in vivo, compared with CMN. CDF however has poor aqueous solubility and its dose escalation for systemic administration remains challenging. We have engineered self-assembling nano-micelles of amphiphilic styrene-maleic acid copolymer (SMA) with CDF by non-covalent hydrophobic interactions. The SMA-CDF nano-micelles were characterized for size, charge, drug loading, release, serum stability, and in vitro anticancer activity. The SMA-CDF nano-micelles exhibited tunable CDF loading from 5 to 15% with excellent aqueous solubility, stability, favorable hemocompatibility and sustained drug release characteristics. The outcome of cytotoxicity testing of SMA-CDF nano-micelles on MiaPaCa-2 and AsPC-1 pancreatic cancer cell lines revealed pronounced antitumor response due to efficient intracellular trafficking of the drug loaded nano-micelles. Additionally, the nano-micelles are administrable via the systemic route for future in vivo studies and clinical translation. The currently developed SMA based nano-micelles thus portend to be a versatile carrier for dose escalation and targeted delivery of CDF, with enhanced therapeutic margin and safety.

## Abstract No. 78 (Post_Doctoral_Fellow) (Postdoctoral_Research)

**Title**

Hyaluronic acid-conjugated polyamidoamine dendrimers for targeted delivery of 3, 4-difluorobenzylidene curcumin to CD44 overexpressing pancreatic cancer cells

**Affilliations**

Use-inspired Biomaterials & Integrated Nano Delivery (U-BiND) Systems Laboratory, Department of Pharmaceutical Sciences, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, 259 Mack Ave, Detroit, MI 48201, USA

**Authors**

Prashant Kesharwani (PhD), Hashem O Alsaab (M. Pharma.), Arun K Iyer (PhD)

**Abstract**

The current study was aimed to develop a targeted dendrimer formulation of 3, 4-difluorobenzylidene curcumin (CDF) and evaluate its potential in CD44 targeted therapy for pancreatic cancer. Using amine terminated fourth generation poly(amidoamine) (PAMAM) dendrimer nanocarrier and hyaluronic acid (HA) as a targeting ligand, we engineered a CD44-targeted PAMAM dendrimer (HA-PAMAM) formulation of CDF. The resulting dendrimer nanosystem (HA-PAMAM-CDF) had a particle size and surface charge of 9.3 ± 1.5 nm and − ... 7.02 ± 9.53 mV, respectively. When CD44 receptor overexpressing MiaPaCa-2 and AsPC-1 human pancreatic cancer cells were treated with HA-PAMAM-CDF, a dose-dependent cytotoxicity was observed. Furthermore, blocking the CD44 receptors present on the MiaPaCa-2 cells using free excess soluble HA prior to treatment with HA-PAMAM-CDF nano-formulation resulted in 1.71 fold increase

in the IC50 value compared to non-targeted formulation (PAMAM-CDF), confirming target specificity of HA-PAMAM-CDF. Additionally, HA-PAMAM-CDF formulation when compared to PAMAM-CDF, displayed higher cellular uptake in MiaPaCa-2 cancer cell lines as shown by fluorescence studies. In summary, the novel CD44 targeted dendrimer based nanocarriers appear to be proficient in mediating site-specific delivery of CDF via CD44 receptors, with an improved therapeutic margin and safety.

---

## Abstract No. 79 (Post_Doctoral_Fellow) (Postdoctoral_Research)

### Title

Design, Synthesis of Enzalutamide-Histone Deacetylase Inhibitor Hybrid Drugs to Downregulate Androgen Receptor and to Inhibit Proliferation of Castration Resistant Prostate Cancer Cells

### Affilliations

Department of Pharmaceutical Sciences, Eugene Applebaum College of Pharmacy and Health Sciences, 259 Mack Ave, Detroit, MI, 48201
Department of Oncology, Barbara Ann Karmanos Cancer Institute, 4100 John R, Detroit, MI, 48201

### Authors

Bailing Chen, Ph.D.
Rayna Rosati,
Siyu Ou,
Manohar Ratnam, Ph.D.
Zhihui Qin, Ph.D.

### Abstract

Although the early stage, localized prostate cancer (PCa) is manageable, prognosis of castration resistant prostate cancer (CRPC), the relapsed/metastatic late stage of PCa, is extremely poor. Because the sustained androgen receptor (AR) signaling has been recognized as a major driving force of PCa, the past decade has witnessed the discovery of several potent non-steroid AR antagonists for PCa therapy, exemplified by the approval of enzalutamide (Enz) in 2012 for post-chemo and in 2014 for chemotherapy-naïve CRPC patients. However, drug resistance mechanisms inevitably developed and survival benefits of Enz in CRPC patients are limited (4~6 months versus placebo). Innovative treatment options are urgently needed. Herein, we have designed and synthesized a series of Enz-histone deacetylase inhibitor (HDACi) hybrid drugs aimed for CRPC treatment. Because of AR binding activity conveyed by Enz scaffold, we hypothesized that Enz-HDACis can be effectively directed to AR-overexpressing CRPC cells and to AR-localized cellular compartments, such as cytosolic AR-Hsp90-HDAC6 complex and AR- regulated genes in the nucleus. AR binding directed-HDAC inhibition may lead to AR downregulation via proteasome mediated protein degradation, enhanced suppression of AR target genes and effective growth inhibition in CRPC cells meanwhile avoiding typical side effects induced by non-selective HDACis (either isoform non-selective and/or gene non-selective).

In our experiments, Enz-HDACis inhibited enzymatic activities of recombinant cytosolic HDAC6 and nuclear HDACs from a Hela cell nuclear extract. Drug treatments also effectively decreased expression of AR-regulated genes, suggesting that AR binding affinity was retained by the new chemical scaffolds. A binding mode of Enz-HDACi 2-75 to AR was proposed using molecular docking methodology. Intriguingly, Enz-HDACis were able to induce AR degradation, which may be attributed to HDAC6 inhibition, Hsp90 acetylation, AR dissociation from Hsp90 chaperone and proteasome-mediated protein degradation pathway. Enz-HDACi 2-75 and 1005 suppressed the growth of CRPC C4-2 cells, more effectively than Enz, SAHA (a HDACi) and the combination of Enz and SAHA at 1:1 ratio, suggesting that the observed

antiproliferative effects of 2-75 and 1005 were due to Enz-directed HDACi activity. Collectively, these promising results warrant further investigations on Enz-HDACis as a novel class of anti-PCa agent.

---

## Abstract No. 80 (Post_Doctoral_Fellow) (Postdoctoral_Research)

### Title

Global protein profiling of visceral fat and subcutaneous fat from obese non-diabetic and obese T2D subjects


### Affilliations

Wayne State University, Detroit, MI

### Authors

Danjun Ma,Ph.D ... Alemu Fite,Ph.D ... Xiangmin Zhang,Ph.D ... Yue Qi,BS ... Michael Howard Wood,MD ... Rebecca Tagett,BS ... Sorin Draghici,Ph.D ... Berhane Seyoum,MD ... Zhengping Yi,Ph.D


### Abstract


The prevalence of diabetes is increasing globally over the last 20 years. More than 90% diabetic cases are type 2 diabetes (T2D), which is characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency. Adipose tissue has been characterized as a major endocrine organ in the pathogenesis of the disease. Visceral fat is associated with increased risks of a number of health problems including type 2 diabetes other than subcutaneous fat. Proteomic analysis of visceral fat and subcutaneous fat from obese non-diabetic (Non-T2D) and obese T2D subjects will identify the adipose tissue-derived factors linked to diabetes, especially in visceral fat. It will increase our understanding of the pathogenesis of type 2 diabetes and insulin resistance.

Here, we used a straightforward label-free quantitative proteomics approach to analyze the human subcutaneous fat and visceral fat tissue. A total of 18 biopsies, including 9 Non-T2D and 9 T2D, were homogenized. Samples were analyzed with Orbitrap-Elite after trypsin digestion. A total of 1606 protein groups are identified in our study with FDR at 0.01 and minimum 2 unique peptides. Two-hundred and forty-three protein groups show at least 2-fold differences between Non-T2D visceral fat and subcutaneous fat, including 116 protein groups with significant change ($p<0.05$) ... while 397 protein groups show at least 2-fold differences between T2D visceral fat and subcutaneous fat, including 220 protein groups with significant change ($p<0.05$). A total of 204 protein groups show at least 2-fold differences between Non-T2D subcutaneous fat and T2D subcutaneous fat, including 71 protein groups with significant change ($p<0.05$) ... while 133 protein groups show at least 2-fold differences between Non-T2D visceral fat and T2D visceral, including 53 protein groups with significant change ($p<0.05$). Of particular interest, vacuolar protein sorting-associated protein 29 (VPS29), one of three core proteins in the trans-Golgi network, has been related to T2D. In our study, VPS29 is 2.6-fold in T2D visceral fat comparing with non-T2D visceral fat. It implicated that insulin resistance may be caused by VPS29-dependent endosomal trafficking. Pathway analysis indicated that several pathways are significantly enriched for the proteins with a significant change between T2D visceral fat comparing with non-T2D visceral fat, such as Integrin Signaling, Protein Ubiquitination Pathway, Actin Cytoskeleton Signaling, EIF2 Signaling, etc.. Other proteins and pathways with differences fat tissues from these participants were also identified. In summary, we have performed the 1st quantitative proteomics analysis on subcutaneous and visceral fat tissues in non-T2D and T2D subjects. We have identified multiple proteins and pathways that are may contribute to the pathogenesis of T2D.


---

## Abstract No. 81 (Post_Doctoral_Fellow) (Postdoctoral_Research)

### Title

Comparison of risk factors and clinical outcomes in polymicrobial versus monomicrobial enterococcal bloodstream infections


### Affilliations

1. Anti-Infective Research Laboratory, Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit Michigan, USA
2. Department of Medicine, Division of Infectious Diseases, School of Medicine, Wayne State University, Detroit, MI, USA
3. Department of Pharmacy Services, Detroit Medical Center, Detroit, MI, USA

- Change in address: Husson University College of Pharmacy, Bangor, Maine

Corresponding Author: Michael J. Rybak, Pharm.D., M.P.H.
259 Mack Ave, Detroit, MI, USA 48201
Phone: 313-577-4376
Fax: 313-577-8915
E-mail: m.rybak@wayne.edu

### Authors

Abdalhamid M. Lagnf, M.P.H.1
Evan J. Zasowski, Pharm.D., BCPS1
Kimberly C. Claeys, Pharm.D., BCPS1
Anthony M. Casapao, Pharm.D. 1*
Michael J. Rybak, Pharm.D., M.P.H.1,2,3


### Abstract


Objective: Enterococcal bloodstream infections (EBSI) are frequently polymicrobial but little data compare the outcomes of polymicrobial and monomicrobial EBSI or examining risk factor for polymicrobial infection. This study examined the risk factors and outcomes of polymicrobial versus monomicrobial EBSI.

Design: Single center, retrospective, matched case-control study.

Methods: Patients with monomicrobial EBSI (MEBSI) were matched 1:1 to polymicrobial EBSI (PEBSI) by: age ± 10 years, source, Pitt bacteremia score, and enterococcal species. Multivariable logistic regression was performed to explore factors predicting incidence of polymicrobial EBSI and 30-day all-cause mortality.

Results: Of 715 patients eligible for inclusion, 284 were matched. Mortality was 20.0% in monomicrobial versus 24.0% in PEBSI (p = 0.551). Through multivariable regression, Charlson Score (aOR, 1.2 ... 95% CI, 1.1-1.4 ... p = 0.001), Pitt bacteremia score (aOR, 2.4 ... 95% CI, 1.3-4.5 ... p = 0.007), prior antibiotics (90 days) (aOR, 2.2 ... 95% CI, 1.1-4.1 ... p = 0.021), and presence of decubitus ulcer (aOR, 2.4 ... 95% CI, 1.1-5.3 ... p = 0.027) were significantly associated with 30-day all-cause mortality. Chronic hemodialysis was significantly associated with MEBSI (aOR, 0.48 ... 95% CI, 0.29-81 ... p = 0.006) while prior antibiotic (90 days) aOR, 1.8 ... 95% CI, 1.2-3.0 ... p = 0.013), diabetes (aOR, 1.6 ... 95% CI, 1.0-2.6 ... p = 0.048), and chemotherapy/radiotherapy (30 days) (aOR, 2.7 ... 95% CI, 1.0-7.4 ... p = 0.048) were significantly associated with PEBSI.

Conclusion: PEBSI were not an independent predictor of mortality ... importantly Charlson co-morbidity index and Pitt bacteremia score were. Risk factors for PEBSI identified in this study should be further evaluated for clinical intervention.

Keywords: E. faecalis, E. faecium, bacteremia, mortality, and polymicrobial, renal disease

## Abstract No. 82 (Post_Doctoral_Fellow) (Postdoctoral_Research)

### Title

Development of a novel iron(II) preferring multifunctional iron chelator for the symptomatic and neuroprotective therapy of Parkinson's disease

### Affilliations

1. Department of Pharmaceutical Sciences, Wayne State University, Detroit, MI 48202
2. Department of Pharmacology and Department of Neurology, Wayne State University, Detroit, MI 48201

### Authors

1Banibrata Das, 1Liping Xu, 2Gnanada Joshi, 1Ashoka Kandegedara, 1Timothy L. Stemmler, 2Sokol Todi, 1Aloke K. Dutta

### Abstract

Parkinson's disease (PD) is a major neurodegenerative disorder affecting 1-2% of the elderly population, causing profound motor impairments that include tremors at rest, rigidity, bradykinesia, and postural instability along with non-motor symptoms such as autonomic, cognitive and psychiatric problems. Although the etiology of PD is still not completely understood, recent research has provided more insights into the basic pathogenic factors of PD such as aggregation of alpha-synuclein (α ... SN) protein, oxidative stress, and nigral iron dysregulation. Current therapies for PD are focused mainly on the symptomatic aspect of the disease process and consequently, the disease progression continues. Thus, there is a great unmet need for development of disease modifying symptomatic agents which will provide great benefit and a paradigm shift over the current treatment options. It is increasingly evident that for a complex disease such as PD, a drug targeting only a single site will only partially address the therapeutic need of the disease. In our overall goal to develop multifunctional drugs as neuroprotective treatment agents for PD, we designed and developed a novel dopamine D2/D3 agonist molecule, D-607, with a capacity to address some underlying pathological factors in PD including chelating iron to reduce oxidative stress and reducing α ... SN-induced toxicity. Binding and functional assays at dopamine D2/D3 receptors indicate the potent agonist activity of D-607. The molecule displays strong antioxidant and efficient preferential iron (II) chelation properties, accompanied with potent in vivo efficacy in a reserpinized PD animal model, which indicates efficient brain penetration. D-607 also rescued neuronal PC12 cells from toxicity induced by iron in a dose-dependent manner. Finally, we used a unique GFP-based Drosophila model of PD where pathogenic alpha-synuclein is expressed in the eyes to produce detectable and quantifiable toxicity. Our lead compound D-607 significantly reduced synuclein-dependent toxicity at two different doses compared to the vehicle control. These observations strongly support the notion that D-607 might be a promising multifunctional lead molecule for a viable therapy of PD. This work is supported by grants from NINDS (NS 047198, AKD).

## Abstract No. 83 (Post_Doctoral_Fellow) (Postdoctoral_Research)

### Title

Effects of Dapagliflozin on Energy Intake and Appetite in Healthy Subjects: A Clinical Research Study in Progress

### Affilliations

All authors: Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University

**Authors**

Nour Ghamrawi, BHS ... Aaron Nixon, BHS ... Rommel-Edward Reyes, BS ... Heba Sobh, BS ... Lama Wehbi, BS ... Elizabeth A. Bertran, PharmD ... Helen Berlie, PharmD ... Linda A. Jaber, PharmD

**Abstract**

Introduction:
The new sodium-glucose cotransporter (SGLT) 2 inhibitor, dapagliflozin, prevents glucose reabsorption in the proximal tubules of the kidney, thus reducing blood glucose levels. Dapagliflozin's insulin-independent mechanism of action improves glycemic control while avoiding hypoglycemia and weight gain. Dapagliflozin has been shown to reduce weight ... however, the actual weight reduction observed in clinical studies is less than expected based on the caloric loss from drug-induced glucosuria. It has been suggested that a potential mechanism for this finding is a compensatory increase in energy intake in individuals taking dapagliflozin.

Purpose:
The purpose of this study is to evaluate the effects of dapagliflozin relative to placebo on energy intake and appetite ratings in healthy individuals, and to identify individual-level characteristics that predict the change in caloric balance in response to dapagliflozin. Our hypothesis is that dapagliflozin increases caloric intake, in response to caloric loss, which results in less than expected weight loss.

Methods:
This is a randomized, single-blinded, placebo-controlled, crossover study. Participants will receive a 2-week supply each of dapagliflozin and placebo over a four week period. Assessments will be conducted at baseline and at weeks 2 and 4. For 24 hours prior to assessment days, participants will refrain from alcohol and strenuous exercise and will be instructed to fast at 8 PM starting the night before assessment. On each assessment day, participants will receive a pre-load standardized breakfast to be consumed within 15 minutes. Appetite ratings including feelings of satiety, hunger, fullness, and desire to eat will be measured with 100 mm visual analog scales (VAS) immediately before and after breakfast and every 30 minutes for 4.5 hours thereafter. Energy intake and meal duration will be measured at a subsequent ad libitum lunch. The lunch will consist of the same commercially-available, pre-packaged meal with fixed macronutrient content at each assessment. Energy intake, appetite responses, fasting blood glucose, and body weight measurements will be assessed at baseline and at the end of each 2-week study period. The between- and within-differences in outcome measures from baseline will be assessed by ANOVA with repeated measures.

---

## Abstract No. 84 (Post_Doctoral_Fellow) (Postdoctoral_Research)

**Title**

Outcomes associated with methicillin-resistant Staphylococcus aureus (MRSA) pneumonia and concurrent bloodstream infections (BSI)

**Affilliations**

Anti-Infective Research Laboratory, Eugene Applebaum College of Pharmacy & Health Sciences, Wayne State University, Detroit MI

**Authors**

Trang D. Trinh, Pharm.D. ... Evan J. Zasowski, Pharm.D. ... Michael J. Rybak, Pharm.D., MPH

**Abstract**

INTRODUCTION
Methicillin-resistant Staphylococcus aureus (MRSA) remains a predominant pathogen in critically ill patients causing serious healthcare-acquired infections including pneumonia. Similar to other MRSA invasive infections, pneumonia has significant health care cost burden with mortality rates between 10% and 30%. Pneumonia is often complicated by secondary BSI and shown to be an independent risk factor for mortality. A recent study with MRSA pneumonia reported a 12% prevalence of concurrent BSI but did not find mortality differences. We sought to further characterize the epidemiology and outcomes of MRSA pneumonia with concurrent BSI.

METHODS
We conducted a multicenter retrospective cohort study (2011 to 2015) including adult patients hospitalized with MRSA pneumonia and treated with ceftaroline for at least 72 hours. Pneumonia cases were confirmed by one positive MRSA respiratory culture, and categorized as either community-onset (≤ ... 2 days after admission) or hospital-onset (>2 days after admission). We compared the bacteremic and non-bacteremic groups based on their demographic and clinical characteristics and outcomes.

RESULTS
Among 85 patients with MRSA pneumonia, 51 (60%) had concurrent BSI. Both groups were similar based on demographic and clinical characteristics except for frequencies of COPD (43.1% bacteremic and 17.6% in non-bacteremic, p = 0.01), chronic liver disease (21.6% bacteremic and 2.9% in non-bacteremic, p = 0.02), and chronic kidney disease (60.8% bacteremic and 29.4% in non-bacteremic, p = 0.005). The frequencies of hospital-acquired pneumonia, APACHE II scores, and in-hospital mortality were also higher in the bacteremic group (Table 1).

Table 1. Clinical outcomes.
Concurrent BSI, N (%) No concurrent BSI, N (%) P value
N = 51 N = 34
HCABP, HABP, VABP 26 (81.3) 19 (55.9) 0.03
APACHE II, 19 [14,25] 12 [7,17.5] <0.001
median [IQR]
In-hospital mortality 13 (25.5) 2 (5.88) 0.02
30-day mortality* 12 (23.5) 4 (11.8) 0.26
Length of stay, 22 [14,34] 20 [9.75,42.3] 0.56
median [IQR]

- From date of index culture.

CONCLUSIONS
The prevalence of concurrent BSI with MRSA pneumonia was higher in our cohort. We did not detect a significant difference in 30-day mortality between the two groups, but did find an increase in in-hospital mortality in the bacteremic group. Although these results should be interpreted with caution based on the retrospective nature of the study, further research is warranted to describe the risks associated with MRSA pneumonia and concurrent BSI.

---

## Abstract No. 85 (Post_Doctoral_Fellow) (Postdoctoral_Research)

### Title

Colonic Neurotoxicity in Rats that Self-Administer Methamphetamine

### Affilliations

Wayne State University
Rush University Medical Center

### Authors

Amanda Flack Ph.D., Amanda L. Persons Ph.D., Sharanya M. Kousik Ph.D., Jickssa M. Gemechu Ph.D., T. Celeste Napier Ph.D., and Anna Moszczynska Ph.D.

### Abstract

Methamphetamine (METH) is a highly abused psychostimulant that is associated with an increased risk for developing Parkinson's disease (PD). This enhanced vulnerability may relate to the known neurotoxic effects of METH that are also observed in PD pathology. High-dose METH increases α ... -synuclein levels and decreases the E3 ligase parkin in the striatum of rats, and in PD, α ... -synuclein is increased in the substantia nigra. Peripheral factors may contribute to central nervous system (CNS) pathology. α ... -Synuclein levels in the enteric nervous system are increased in PD patients, as well as in rats that self-administered (SA) METH prior to tyrosine hydroxylase (TH) deficits in the striatum. As in PD patients and rats that SA METH, gut α ... -synuclein pathology precedes brain pathology, and we hypothesized that a similar pattern would occur with gut monoamines (i.e., dopamine and norepinephrine). Thus, the aim of the present study was to measure the levels of α ... -synuclein, TH and dopamine-β ... hydroxylase (Dβ ... H), a noradrenergic marker, at different times following withdrawal from self-administered METH in the distal colon of rats. Male Sprague-Dawley rats were allowed to self-administer METH for 3h per day for 14 days (d) while yoked controls received saline. Colon tissue was harvested at 1d, 14d, and 56d after cessation of the operant task. As compared to their saline-yoked counterparts, METH exposed rats showed a trend for an increase in α ... -synuclein immunoreactivity at 1d that returned to baseline levels by 14d. At 1d, significant deficits in both TH and Dβ ... H immunoreactivity were observed ... the deficit in Dβ ... H persisted at least up to 14d. Our results, coupled with those from our previous studies, indicate that the colon demonstrates an early onset neurotoxicity that may predispose human METH users to develop PD.

Supported by DA034783, DA024923 and the Center for Compulsive Behavior and Addiction.

## Abstract No. 86 (Post_Doctoral_Fellow) (Postdoctoral_Research)

### Title

Alterations in phospho-Ser-129-α ... -synuclein in the striatum in rats after binge METH may provide clues to understanding the link between METH abuse and PD

### Affilliations

Department of Pharmaceutical Sciences, Eugene Applebaum College of Pharmaceutical Sciences, Wayne State University, Detroit, MI 48201

### Authors

Jickssa M. Gemechu, Ph.D. ... Amanda Flack, Ph.D. ... Bin Liu, Ph.D. ... Aundrea Albrech ... Anna Moszczynska, Ph.D.

### Abstract

Methamphetamine (METH) is a psychostimulant drug which is widely abused in the US and worldwide. At high doses, it causes neurotoxicity in rats, non-human primates, and humans. Previous studies have shown that exposure to METH in earlier stages of life increases the likelihood of developing Parkinson's disease (PD) later on. PD and METH neurotoxicity share several hallmarks of neurodegeneration. For example, in both conditions, tyrosine hydroxylase (TH), a dopamanergic (DAergic) marker, is decreased while α ... -synuclein is increased in the brain. The most frequent modification of α ... -synuclein in PD patients is its aggregation and phosphorylation at Ser-129. Previous studies have found that approximately 90% of α ... -synuclein deposits found in Lewy bodies have been phosphorylated at Ser-129. It is not

currently known how neurotoxic doses of METH change the levels of phospho-Ser-129-α ... -synuclein in striatal compartments (matrix or striosome). The matrix contains higher DAergic innervation than the striosomes, but a previous study has shown that TH losses are more dramatic in the striosomal patches. Therefore, we examined alterations in TH as well as examined the levels of α ... -synuclein and phospho-Ser-129-α ... -synuclein after binge METH in the matrix and in the striosomes of striatal tissue from rats. We have hypothesized that METH binge will increase the immunoreactivity of phospho-Ser-129-α ... -synuclein in striatal matrix and striosome compared to saline (SAL) treated controls. To test our hypothesis, rats were treated with 4x7.5mg/kg METH-HCl, euthanized at 7 d after the binge, and striatal tissue was examined for changes in immunoreactivity of TH, α ... -synuclein, phospho-Ser-129-α ... -synuclein in the striatum. Consequently, our findings suggest that aggregated phospho-Ser-129-α ... -synuclein mediates METH neurotoxicity and potentially also susceptibility of human METH users to develop PD later in life.

---

**ABSTRACT NO. 87**
**(POST_DOCTORAL_FELLOW) ()**

### Title

An Evaluation of Synergistic Antibiotic Combinations to Treat Persistent Enterococcal Bloodstream Infection (BSI)

### Affilliations

1Division of Infectious Disease, Department of Medicine, 2Anti-Infective Research Laboratory, Department of Pharmacy Practice, Euguene Applebaum College of Pharmacy and Health Sciences and School of Medicine, Wayne State University, Detroit, MI

### Authors

1Miriam T Levine, MD ... 2Jordan R Smith, PharmD ... 2Juwon Yim, PharmD ... , 1Donald P Levine, MD ... 1,2 Michael J Rybak, PharmD, MPH

### Abstract

Background:
Daptomycin (DAP) is often used for vancomycin-resistant Enterococcus (VRE) BSI. Prolonged BSI has been associated with human cationic peptide resistance development and cross-resistance to DAP. We present a case of VREF BSI treated with DAP and DAP combination therapy.
A 53YO man with AIDS and ESRD presented with VRE faecium BSI. DAP 4mg/kg was started but increased to 10mg/kg on day 5 along with initiation of gentamicin (GENT). On day 10, GENT was switched to ceftaroline (CPT) 200mg Q12h for continued bacteremia. Work-up for the infection source was negative. Persistent BSI prompted synergy testing with minimum inhibitory concentration (MIC) and kill-curve analysis (TKA). Two-hour survival analysis with human cathelicidin LL37 was also done to determine isolate susceptibility.

Methods:
DAP MICs were performed on blood isolates from days 1 and 14. MICs were also performed in broth supplemented with subinhibitory CPT, ampicillin (AMP), and CPT + AMP. 24-hour TKAs were done to detect synergy between DAP and CPT, AMP, or AMP/CPT. Isolates were also grown overnight in Luria broth (LB) and exposed for 2 hours to LL37 in RPMI-5% LB. The percentage of surviving bacteria was calculated by plating on brain heart infusion agar.

Results:
DAP MICs on days 1 and 14 were 1 and 4 μ ... g/mL, respectively. The greatest synergy was with DAP + CPT + AMP compared with all other regimens ($p<0.05$). This regimen was

chosen for the patient's therapy ... though not synergistic, linezolid (LNZ) was added as assurance to clear the bacteremia. BSI cleared 5 days later. However, LNZ was switched to tedizolid (TED) due to thrombocytopenia, with subsequent resolution. LL37 survival analysis showed significantly increased survival at day 14.

Conclusions:
Either initial suboptimal DAP dosing or prolonged bacteremia resulted in DAP resistance. Prolonged exposure of bacteria to cathelicidins can select for resistant strains that, due to cross reactivity, are DAP-resistant. LL37 survival analysis supports both explanations. In vitro testing of novel antibiotic combinations may be lifesaving when a therapeutic regimen fails. Further research should investigate the relationship between cathelicidin exposure and DAP resistance.

---

## Abstract No. 88 (Post_Doctoral_Fellow) (Clinical_Sciences)

### Title

Rapid Diagnostic Testing for Hepatitis C Virus: Pilot Study in an Urban Ambulatory Care Setting

### Affilliations

1 Department of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University

2 Division of General Internal Medicine, Wayne State University School of Medicine

### Authors

Abdulbaset Salim1, MBChB, MPH, Prateek Lohia2, MD, MHA, Muhammad Daniayl Shamim2, MD, Paul Kilgore1, MPH, MD

### Abstract

Background: In 2011, US national data showed that an estimated 2.7 million persons are living with hepatitis C virus (HCV) infection. HCV screening is now a national priority and interest in HCV has accelerated with the availability of HCV testing and effective therapies. The aim of this study is to evaluate use of a rapid point-of-care HCV test among primary care patients in Detroit.
Methods: in the University Health Center (Detroit Medical Center), ambulatory internal medicine clinic, we prospectively enrolled patients aged 18 to 70 years who had not previously undergone testing for HCV. Following informed consent, patients were reviewed for eligibility and enrolled if inclusion criteria were met. Upon enrollment, a fingerstick and oral swab specimen was collected from each patient. Specimens were processed for HCV testing using a commercial assay (HCV OraQuick®, OraSure, Inc, Bethlehem, PA). While waiting for test read out (~20-40 minutes), patients were interviewed to gather additional demographic and risk factor information. An electronic study database was assembled for study data analysis.
Results: From May 22 to October 6, 2015, a total of 123 patients aged 18 to 69 (mean age: 48.3 years ... 61% female) were enrolled during their regular clinic visit. Oral swab testing detected three HCV-positive patients while fingerstick blood testing identified four HCV-positive patients (including 3 patients detected by oral swab). Among the four HCV+ patients identified, 2 (50%) were female. The four HCV+ patients identified were referred for confirmatory testing and all four were RT-PCR positive using an HCV genotyping assay.
Conclusion: In the ambulatory care setting, rapid HCV testing proved feasible and provided accurate and actionable information for newly identified HCV+ patients. Future studies will evaluate scaled-up testing with the rapid HCV test in urban populations who have traditionally suffered from health disparities.

---

# Author Index