Welcome Guests, Faculty, Staff and Students,

Research Day has become an annual tradition at Touro University California and it is my honor to welcome you to this festive event. We showcase today the most recent work of our faculty and students and celebrate as a university the contributions of our researchers to science, clinical practice, education and public health.

As a university heavily invested in graduate and professional education, we need to create an environment which values and nurtures intellectual curiosity and the development of new knowledge which contributes to professional practice. Your presence here today demonstrates your understanding of this worthy goal and your support for faculty and students who are presenting their research.

I look forward to working with you and other members of the campus community as we build a dynamic research environment at TUC.

Sincerely,

Marilyn Hopkins, PhD
Provost and Chief Operating Officer
Touro's Annual Research Day has become a campus tradition that provides an opportunity for students, faculty and staff to share their research efforts with the campus community and local guests. The program encourages the development of joint research projects and increases the student body awareness of the quality and range of research conducted on campus. With that being said we would like to thank everyone who have participated in this year’s Research Day, without the students, faculty, and staff who have spent countless hours doing their research projects, submitting their abstracts, and creating their posters to present, this event would not be possible.

We are very proud to say that Research Day is continuing to grow every year; in 2015 the number of abstracts has grown 45%!

We would like to thank Mrs. Mallory Davis for her spotless work in the creation of this Abstract Book and together with Ms. Lilibeth Tabas, for taking care of every detail that makes the program successful,. We are very grateful to the staff of the Research Department for their impeccable work to support our research and for help in the event. We thank the following Touro University California staff for their support: Ms. Amy Crivello, Mr. Ralph Cuberos, Mr. Alex Perez, and all the members of the Facilities crew who helped with set-up for this event, Mrs. Renee Morris for her expert guidance with event planning, the Information Technology and the Food Services Departments who provided us with the delicious food and refreshments.

Alejandro Gugliucci, MD, PhD

Associate Dean for Research-COM, Professor, Director of Sponsored Programs

*Editorial Disclaimer: The Editor (COM Research and Office of Sponsored Programs) makes no representations as to accuracy, completeness, correctness, suitability, errors, omissions or validity of any information on this abstract book, which lies on the authors.*
14th ANNUAL RESEARCH DAY

TIMELINE OF EVENTS
APRIL 29th, 2015:
Landen Hall, Lecture Hall A

1:00-1:10 Introductions:
Dr. Alejandro Gugliucci, Associate Dean

1:10-1:30 Keynote Address:
“Metabolic Alchemy: Clinical Studies of the Conversion of Sugar to Fat”
Kathleen Mulligan, PhD (UCSF-TUCOM)

1:30-1:45:
"Corporate Influences on What We Eat: The Sugar Industrial Complex"
Elena Lingas, MPH DrPH (MPH program, TUC-CEHS)

1:45-2:00:
“Is fructose toxic?”
Jeffrey Ritterman, MD (Joint PA/MPH program, TUC-CEHS)

2:00-3:30
Nutrition & Lifestyle: Current Community Service and Future Service

Moderated by: Grace Marie Jones, PhD (TUCOM faculty) and
Arpita Sinha (DO-MPH Candidate)

• Several students will present their community outreach programs
• Discussion on future service

Farragut Inn

3:30-6:00 Poster session:
Hors d’oeuvres and wine
KEYNOTE

ADDRESS

1:10 p.m. – 1:30 p.m.

LANDER HALL, LECTURE HALL A
Biographical information

Kathleen Mulligan, PhD, is a member of the faculties of both UCSF and TU. Since completing her PhD in Nutritional Biochemistry at UC Berkeley, Dr. Mulligan has performed NIH-funded research in the nutritional and metabolic effects of obesity, fatty liver disease, and type 2 diabetes, as well as HIV infection and its therapies, with a focus on changes in body composition, glucose and lipid metabolism, endocrine function, and bone metabolism; and a strong emphasis on treatments and mechanisms. Her research experience has ranged from serving as principal investigator for intense inpatient metabolic ward studies to chairing multicenter outpatient trials through consortia such as the adult and pediatric AIDS Clinical Trials Groups and Adolescent Trials Network. In addition to her own clinical research, for eight years Dr. Mulligan directed the Body Composition, Exercise, and Metabolism Core of the UCSF Clinical and Translational Science Institute. In that role, she oversaw the assessment of body composition, energy metabolism, and functional performance for clinical studies at UCSF, as well as advised other investigators on study design, implementation, and data analysis. Dr. Mulligan is currently a principal investigator or co-investigator with Dr. Jean-Marc Schwarz on two active NIH-funded projects focusing on the effects of fructose on insulin sensitivity, lipogenesis, and fat distribution that will be the focus of her lecture.

Description of talk

The prevalence of obesity, diabetes, and non-alcoholic fatty liver disease is increasing worldwide. The potential contribution of diets high in sugar, including fructose, has received considerable attention, and recent studies have led to recommendations to limit sugar consumption. However, it has been argued by some that the deleterious effects of simple sugars occur only in the context of weight gain. This presentation will focus on the results of recent controlled feeding studies to examine the effects of fructose feeding and fructose restriction on fat synthesis and storage, lipid metabolism, and insulin sensitivity, both in healthy adults and obese children. These studies employed sensitive stable isotope tracer studies and advanced imaging technology to demonstrate that short-term fructose restriction is associated with metabolic improvements that, if sustained, could reverse the harmful effects of high sugar intake.
FACULTY PRESENTATIONS

1:30 p.m. – 2:00 p.m.

LANDER HALL, LECTURE HALL A
Elena Lingas, MPH DrPH (MPH program, TUC-CEHS)

"Corporate Influences on What We Eat: The Sugar Industrial Complex"

Prior to her appointment at Touro University California, Dr. Lingas was a postdoctoral scholar at the Center for Tobacco Control Research and Education at the University of California, San Francisco. Immediately preceding her time at UCSF, Dr. Lingas was a Research Scientist at the Berkeley Media Studies Group, where she analyzed media content on a variety of topics, including intimate partner violence, paid family leave, pesticides, tuberculosis, immigration, racial discrimination, and food and beverage marketing. Before commencing her doctoral studies, Dr. Lingas served as an epidemiologist in the AIDS/STD Control Program for the San Bernardino County Health Department. Dr. Lingas holds a doctorate in public health from the University of California, Berkeley, an MPH in Infectious Disease Epidemiology from Yale University, and a BA, cum laude and Phi Beta Kappa, in Spanish from the University of Oregon. Research interests: corporate activities as a determinant of health; intersection of news media and public health policy; health equity; infectious diseases.

Jeffrey Ritterman, MD (Joint PA/MPH program, TUC-CEHS)

“Is fructose toxic?”
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BASIC SCIENCES
Influenza vaccine formulation from plant expressed Hemagglutinin (from influenza virus) by TMV conjugation

Hardeep Kaur, Janet Lee and Alison McCormick
Touro University California, College of Pharmacy

**Background:** Influenza is continually emerging and causes seasonal epidemics and global pandemics due to introduction of different strains from animal reservoirs. The novel influenza H7N9 virus emerged in China in 2013 (1), and both H7N9 and H5N1 (2) human infections have been associated with exposure to poultry. The host immune response against influenza virus mainly directed to HA (viral surface protein) and the antibodies against HA can prevent infection. Though the currently available methods for vaccine production (eggs or cultured mammalian cells based) are effective in preparing virus based vaccines but require prolonged process to produce sufficient amounts of the key vaccine antigen, hemagglutinin (HA). So there is an imperative need to develop an alternative approach to produce sufficient HA vaccines against influenza.

**Hypothesis and Aims:** Our hypothesis is that the hemagglutinin (surface virus protein) can be expressed in plants, and protein subunit vaccines can be effectively formulated to replace live virus vaccines. The aim of current study is to express the influenza proteins (from H5N1 and H7N9) in plants, and fuse the purified HA to the surface of the plant virus Tobacco Mosaic Virus (TMV) to impart antiviral responses after vaccination and improve anti-HA immunity and virus neutralization.

**Methods:** HA5 and HA7 protein sequences were optimized for plant codon usage and amplified to add a plant leader sequence known to improve protein accumulation. DNA sequencing was used to confirm HA codon identity; HA5/HA1 (hybrid HA5) and HA7 were cloned into a plant expression vector (DN15). TMV-H5/H1 and TMV-HA7 DNA was used as a template to express infectious viral RNA, which was encapsulated using TMV coat protein. The encapsulated product was rubbed gently on the leaves of *Nicotiana benthamiana*. Plants were observed for visual signs of infection and expression was checked by western blotting on day 10 post infection. Expressed proteins were purified by metal affinity chromatography and conjugated to TMV to form vaccines formulations.

**Results:** H5A/HA1 (hybrid HA5) and HA7 proteins are expressed well in plants as tested by SDS-PAGE and western blotting. Proteins are purified using metal affinity chromatography and analyzed by SDS-PAGE. Vaccines are formulated by conjugating the purified proteins to the surface of TMV. The conjugated products are analyzed by SDS-PAGE. We are in the process of scaling up and testing these vaccines in mice for immunity against relevant virus strains.

**Conclusions:** Our goal is to express HA7 and H5PXA proteins in plants, and formulate an effective vaccine against virus infection. Future studies will test the antigenicity and efficacy of vaccines in mice.

Visualization of Morphogenesis with the Processing Programming Language
Avik Patel¹, Amar Bains², Richard Millet³, Mung Lar Lam⁴, and Tamira Elul¹
¹Touro University California; ²Department of Molecular and Cellular Biology, UC Berkeley, ³Mellon Foundation, UC Berkeley, ⁴New School, Parsons School of Fashion, New York.

Background: The field of biovisualization could benefit from the use of artistic tools to enable more aesthetic and realistic modeling of biological phenomena. In particular, morphogenesis—the development of form and shape in embryos—could be modeled effectively with programming languages designed for visual analysis.

Hypothesis and Aims: We hypothesized that the programming language Processing, developed at MIT Media lab for visual artists to develop programming skills, would enable us to aesthetically and realistically model the cell dynamics underlying morphogenesis in the developing nervous system.

Methods: Based on, and inspired by, previously published time-lapse videos, we made visualizations of the cell motility underlying convergent extension of the neural ectoderm, and of branch dynamics underlying optic axon branching in Xenopus embryos.

Results: We first visualized cell motility to mimic that observed in time-lapse videos of neural convergent extension in explants from Xenopus embryos. Six geometric and mechanical parameters including conservation of area and springiness and damping were used to realistically simulate neural cell motility. We then visualized optic axon branching with an iterative geometric model that included three parameters such as number of branches, branch angle and branch number.

Conclusions: These models show that with a minimum number of parameters one can adequately and aesthetically model cell motility driving neural tube morphogenesis and optic axon branching that establishes visual connectivity. Future work could focus on establishing parameters to visualize interactions between the cells, and comparing the computational properties needed to simulate cell dynamics driving neural development in other cell types and species.
Examination of Pattern Recognition Receptor-Induced Activation of B Lymphoblastoid Cell Lines in African-American Lupus Patients
Angadpreet Sidhu\textsuperscript{1}, Ryan Cook\textsuperscript{1} Hattie Pearson\textsuperscript{2} and Evan Hermel,\textsuperscript{1,2}
\textsuperscript{1}Masters of Science in Medical Health Sciences Program, College of Osteopathic Medicine, Touro University California.

\textbf{Background:} Systemic lupus erythematosus (SLE) is a severe immune complex-mediated autoimmune disease. Between 300,000 to 4 million people are estimated to suffer with SLE in the US. SLE may not be considered a single disease but rather a single syndrome, which is defined by a set collection of signs and symptoms occurring together. Uric acid crystals directly promote macrophage and T cell activation, and are a cause of inflammation in gout. We sought to extend these findings to B cells in order to determine if B lymphoblastoid cell lines (BLCL) from patients might be used as surrogates for patient blood cells to allow for more rapid identification of biochemical pathologies.

\textbf{Hypothesis and Aims:} We hypothesize that uric acid can activate BLCL to produce inflammatory cytokines, including interleukin-2 (IL-2), interferon-gamma (IFN-\gamma), and tumor necrosis factor (TNF). To test this, treated BLCL with the NALP3 activator monosodium urate (MSU) crystals and TLR-7, -8 and -9 agonists and assayed for the production of IL-2, IFN-\gamma, TNF. We also hypothesize that there will be a difference in signaling cascade between MSU-treated and untreated cell populations.

\textbf{Methods:} BLCL and the control THP1, U937 (both monocyte lineage), and Jurkat (helper T) cell lines; were treated with the MSU crystals and incubated for time periods of 24 and 72 hours. Supernatants from the treated cells were assayed via ELISA to test for the relative amounts of TNF, IL-2 and IFN-\gamma produced.

\textbf{Results:} After a 24 hour incubation with MSU crystals, negative control cells showed no difference between the different amounts of MSU) in terms of IL-2 and TNF production. No significant changes were noted after treatment of cells with Imiquimod (a TLR7 agonist), or ssRNA40 (TLR8). However, the TLR9 agonist ODN2006 appeared to increase TNF production from patient \textit{CASP12}-positive BLCL, whether heterozygous or homozygous.

\textbf{Conclusions:} A 24 hour incubation showed no difference in IL-2 and TNF production for MSU-treated vs untreated cells. However, \textit{CASP12} stimulates TLR9-mediated production of TNF in patient-derived BLCL. Future plans also include western blotting analysis of lysates from treated cell lines, in order to examine if and what differences in intracellular cytokine production and signal cascades exist. We will also extend incubation times of cells with MSU.
The mechanism of swapped domain constructs as fusion inhibitors of HIV infection
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Background: Infection by the Human Immunodeficiency Virus (HIV) relies on the fusion of viral to host cell membranes. This process is facilitated by the extracellular domain of the HIV transmembrane protein gp41, which consists of NHR and CHR domains linked together in a hairpin structure. It is purported that these domains interact with each other in a complex of trimers during the fusion process. Fusion inhibitors like Enfuvirtide are constructs that mimic the CHR domain and are believed to interrupt the formation of these complexes. Unfortunately, Enfuvirtide use rapidly leads to the development of resistant viral strains in the patient. Alternative fusion inhibitors with a different mechanism of action would be a welcome addition to our therapeutic arsenal. We have prepared gp41 swapped domain constructs that present the NHR domain, utilizing residues in a known hydrophobic pocket for activity, and determined that they are nM inhibitors of HIV-1 fusion. In this study we are examining detailed properties of these inhibitors by mutagenesis experiments aimed at elucidating the kinetics of the NHR – CHR interaction and the hairpin fold in inhibitor potency.

Hypothesis: Fusion occurs at or near the membrane boundary, and the membrane is likely to play a role in structure and interactions of gp41 and in the active state of the swapped domain constructs. We propose that the constructs form a trimeric hairpin structure that unfolds in membranes to expose a full length NHR domain for activity.

Methods: We are using mutagenesis to alter the strength of the interaction between NHR and CHR and determine the effect on potency and structure. We are generating cysteine mutants that can be used to investigate the protein fold and kinetics of unfolding, and its correlation to activity in the presence and absence of membranes. We will use fluorescence, NMR and cell biology to evaluate the mutants.

Results: CD and analytical ultracentrifugation studies of WT and mutants indicate that they are in the trimer state, including in a membrane-mimetic solvent. Mutant Q652L with an increased affinity of CHR to NHR demonstrated slower folding kinetics and correspondingly lower potency against HIV fusion. We have successfully mutated both WT and Q652L mutants with cysteine in two positions, and will express the proteins to evaluate their fold and kinetics.
Interactions of extracellular potassium, calcium, magnesium and hydrogen with the outer pore of the cardiac potassium channel HERG.
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Background: The human ether a-go-go related gene (HERG) encodes a cardiac potassium channel that is important in the repolarization of the action potential. A reduction in the number of HERG channels has been implicated in long QT syndrome, which in some cases can degenerate into the lethal arrhythmia Torsades de Pointes. Many patients present with abnormal serum electrolyte levels due to a variety of conditions including gastrointestinal dysfunction, renal and endocrine disorders, diuretic use, alcoholism, and also with aging. Extracellular electrolytes have also been shown to alter HERG function by either altering HERG channel gating or by reducing current through HERG channels. It is thought that extracellular electrolytes exert these two different effects by interacting with the HERG channel at two different sites on the channel.

Hypothesis and Aims: The cardiac potassium channel HERG is blocked by calcium at a site near the outer mouth of the channel.

Methods: Divalent block of HERG as well as extracellular Ca$^{2+}$ effects on HERG channel gating were measured using two-electrode voltage clamping of Xenopus oocytes expressing either wild-type HERG or the HERG mutants S631A, and G628CS631C. G628C is thought to be located at the outer end of the selectivity filter and S631 is thought to be located in the outer pore of the HERG channel.

Results: Changing extracellular potassium from 0 mM to 20 mM resulted in a greater decrease in WT HERG current by extracellular calcium, as well as by a number of other divalent ions (Mg$^{2+}$, Co$^{2+}$ and Mn$^{2+}$). In addition, current reduction of WT HERG by calcium was voltage dependent, with increased current reduction at negative voltages. There was little or no block of the HERG double mutant G628CS631C by calcium at all voltages tested, whereas there was increased block of the HERG mutant S631A by calcium at negative voltages. Alterations in HERG channel gating kinetics by Ca$^{2+}$ are expected to be independent of changes in extracellular potassium.

Conclusions: 3 results suggest that calcium blocks HERG by physically occluding the pore of the channel: 1) Extracellular calcium effects on channel gating are independent of extracellular potassium whereas current reduction of HERG by extracellular calcium depends on extracellular potassium. 2) The lack of block of G628CS631C by Ca$^{2+}$ 3) the altered voltage dependence of block of S631A by Ca$^{2+}$. This study has implications for an increased risk of cardiac arrhythmias with hypokalemia as well as for patients with acute promyelocytic leukemia treated with arsenic, a trivalent ion that might block HERG at the same site as calcium.
Art of Observation: Using Visual Arts to Enhance Cultural and Gender Competency in Medical Students
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**Background**: Cultural competency has emerged as a key concept in medicine, signifying the phenomenon that by understanding and respecting the cultural background of patients, physicians will be better able to treat their patients in healthcare settings. Analogously, gender sensitivity in medicine implies that life conditions, positions in society, and societal expectations based on ‘femininity’ and ‘masculinity’ are to be considered along with biology in professional encounters. Many medical schools enhance cultural and gender awareness through courses and seminars such as global health programs and diversity shuffles. Electives that involve observation of fine art provide a unique avenue for students to enhance their observational skills as well as to be exposed to different cultures and gender. Using creative arts in medical education may open up learner’s worldview by encouraging them to seek an understanding of the perspectives, feelings and experiences of patients and their families.

**Objective**: To evaluate the Art of Observation elective course’s effect on gender and cultural competency in clinical skills by performing a quantitative and qualitative assessment of medical students’ observations in these areas.

**Methods**: Art of observation students participated in seven sessions spread over five months. During each of these sessions students were presented with three pieces of artwork, which included paintings and photographs of men and women from different cultural backgrounds. Students were requested to observe the portraits and to write down their observations and associated interpretations. In addition, an extra on campus session was held in which five non- AOO students and five AOO students participated. During this session, the students were again requested to use observations to dictate their interpretations of the three pieces of artwork.

**Results**: Quantitative analysis showed that AOO students more frequently mentioned gender or culture compared to non-AOO students. Image 1: 80% of the AOO students mentioned gender characteristics whereas only 20% of non-AOO student mentioned gender. There was no mention of culture from either group. Image 2: 40% of AOO students mentioned culture traits whereas 0% of non-AOO students mentioned culture. There was no mention of gender from either group. Image 3: 60% of AOO and 60% of non-AOO students mentioned culture. There was no mention of gender from either group. Additional qualitative analysis showed that AOO students focused on different characteristics that defined male vs female and expressed a better understanding of different cultural customs, traditions and history. AOO students also hesitated to immediately jump to conclusions about individuals’ gender and culture, and spent time analyzing certain features that contributed to each.
Conclusions: Based on a comparison of AOO and non-AOO students, we conclude that the Art of Observation elective effectively improved gender and cultural awareness among medical students. Students who participated in the elective were more inquisitive and questioned certain gender and cultural characteristics more often than students who had not taken the elective. This suggests that by using visual arts to expose students to diverse genders and cultures, medical students broadened their understanding of different customs and became more aware of their own biases. This could better help future physicians observe their patients as a whole – including their cultural and gender identity, thereby reducing gender or cultural bias that could hinder appropriate care.
Differential Utilization of Glucose and Fructose for *De Novo* Lipogenesis (DNL) in Intestinal Epithelial Cells and Liver Cells

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**Background:** Dietary glucose and fructose (ingredients of sugar-sweetened beverages) cause hypertriglyceridemia, and probably contribute to obesity and insulin resistance. While the liver is the primary producer of triglycerides (TG), we have recently demonstrated DNL in the intestines in humans.⁴ However, little is known about the substrate(s) of DNL in the gut.

**Hypothesis and Aims:** Dietary fructose may contribute to DNL in the gut. Our aim was to determine utilization of glucose and fructose for *de novo* lipogenesis (DNL) in intestinal epithelial cells and liver cells, used as models for the respective tissues.

**Methods:** For hepatocytes, human-derived HepG2 cells were used. For gut cells, human-derived Caco-2 cells differentiated into intestinal epithelial cells were employed; substrates were added to the apical (luminal) side of the cell layer. To approximate postprandial conditions, cells were incubated with a mixture of glucose and fructose (10 mmol/L each), where either glucose or fructose was labeled with ¹³C.

**Results:** In the intestinal cells, the contribution to DNL⁴ of ²-C¹³-glucose was 2.2 ± 0.7 % per 6 h (mean ± S.D, n=5), while the contribution of ²-C¹³-fructose was undetectable. In contrast, preliminary results with HepG2 cells showed that fructose was slightly preferred to glucose as a DNL substrate, as expected.

**Conclusions:** According to our results, intestinal DNL is supported by glucose but not fructose, provided that the Caco-2 culture is an adequate model of intestinal epithelium. Though fructose is well absorbed when ingested with glucose, it is uncertain whether it is phosphorylated and metabolized in the gut. Both glucose and fructose are substrates for hepatic DNL.

Optimization of Semi-automated Imaging System for Big-data Analysis of Alzheimer’s Risk Factor Genes in *C. elegans*

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**Background:** Previously, we have developed a semi-automated imaging system using the Multi Worm Tracker (MWT) (Machino *et al.*, 2014. Front. Genet. 5:202. doi: 10.3389/fgene.2014.00202). The semi-automated system identified a defect in locomotion behavior that is similar to human Alzheimer’s disease (AD). However, there is a limitation in the system for more precise analysis. Here, we expand the semi-automated system that has an improved capability to a more systematic analysis of behavioral profiles. It tracks worms through analysis of variables including worm position, speed, body area, and omega bend detection.

**Hypothesis and aim:** Our hypothesis is that the AD strain shows a reduced profile of locomotion compared to the wild type *C. elegans* strain. Our aim is to determine the locomotion variables altered in the Alzheimer’s strain.

**Methods:** All strains will be maintained in a Nematode Growth Media (NGM) spotted with *Escherichia coli* type OP50 as described previously (Machino *et al.*, 2014). Using the strain, we capture video imaging of worm behaviors. WormLab program is implemented to the semi-automated system previously described. We analyze behavioral variables. Data will then be exported to excel for collection and NCSS for analysis.

**Results:** The AD strain shows significantly slower locomotion than the wild type strain, N2. Our imaging system shows similar results in accordance with previous research observing. The AD strain is being tested and analyzed for more detailed behavioral variables, which are presented in the poster.

**Conclusions:** AD is characterized by plaques and neurofibrillary tangles that are in part caused by abnormal buildups of toxic proteins in the central nervous system. Previous research indicates that *C. elegans* has been shown to suffer locomotion deficits in the AD strain. However, it is unclear about details of the locomotion defects. Our current research should reveal details as to which behavioral parameters are defective. Future studies will include the modulation of *C. elegans* Alzheimer’s disease risk genes that are presented in another poster (Phong *et al.*).
**Vaccine protection in three pathogen models: Influenza, Tularemia and Plague.**
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**Background:** Vaccine protection against viral and bacterial pathogens has typically used killed attenuated pathogen as the primary immune stimulus. However, production of attenuated viral and bacterial strains can be slow, costly, and in some cases not very effective. We have taken the approach of producing subunit vaccine proteins that are known to be involved in the immune response to pathogen exposure, and in immune protection, and associating those proteins to the surface of a non-pathogenic plant virus, Tobacco Mosaic virus (TMV). TMV is an ideal subunit vaccine carrier, because it stimulates uptake to associated proteins, interaction and activation of antigen presenting cells like dendritic cells (DCs) and stimulation of antiviral immunity. We used TMV as a subunit protein carrier in three different pathogen models of disease, and show efficacy in all three.

**Hypothesis and Aims:** Our hypothesis is that 1) subunit protein immunity can be improved by TMV conjugation and 2) Improved immunity will support survival in challenge models of three different diseases, Influenza H5N1, Tularemia, and Plague.

**Methods:** Subunit proteins HA from H5N1 Influenza A, LcrV from Yersinia pestis (Plague) and OmpA, Tul4 and dnaK from Francisella tularensis (Tularemia) were purified and chemically conjugated to TMV. TMV-Ag conjugates and were used to vaccinate mice, and immune responses were measured by serum Ig titers. Mice vaccinated with each different pathogen-specific TMV-Ag conjugate were challenged with a lethal dose of each pathogen, and monitored for survival.

**Results:** In all three pathogen models, TMV-Ag vaccines protected mice from lethal challenge. For Influenza, two doses of TMV-H5HA were 100% protected from lethal challenge. For Tularemia, which is more virulent, three different TMV-Ag vaccines were combined, and protected 50% of mice after three vaccinations. Protection against plague was also partial, but greatly improved compared to subunit antigen alone. In all cases, mice were protected without the use of additional adjuvants.

**Conclusions:** TMV has shown to be an effective carrier for subunit vaccines, improving potency and protection in three different animal models of infectious disease. Improvements in protection, by using additional TMV-Ag combinations for Plague and Tularemia, and by varying dose and route of administration to optimize immune response, and potential for protection.
Development of a multi-subunit vaccine against *Mycobacterium tuberculosis* using tobacco mosaic virus as a carrier
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1. Touro University California

**Background:** Tuberculosis (TB) is an infectious, airborne, bacterial infection that mainly affects the lungs. It is estimated that 1/3 of the world’s population is currently infected with the causative agent of tuberculosis, *Mycobacterium tuberculosis* (*Mtb*), and causes 1.5 million deaths annually worldwide. Once inside the lung, *Mtb* is able to avoid eradication by the host immune response and either survive in an inactive form know as latent TB or progress to active TB disease. Currently there is only 1 vaccine available against *Mtb*, Bacille Calmette-Guerin (BCG), an attenuated strain of *Mycobacterium bovis*. BCG has shown the ability to control TB infection in the infant to young adult population, however its protection in adult pulmonary TB is highly varied. Due to the staggering number of newly diagnosed cases and deaths each year, a new vaccine strategy is of utmost importance. Several current clinical trial vaccines have shown promise, but they too have limitations, especially that they do not include antigens for latent TB, which accounts for 90-95% of all TB cases. To combat this issue, our laboratory is working on developing a multi-subunit *Mtb* vaccine that includes both active and latent TB antigens. We are using Tobacco Mosaic virus (TMV) as an antigen carrier to augment antigen presentation and stimulate anti-TB immunity. With its ability to display more than 2,100 copies of a protein antigen on its surface, TMV serves as a promising viral vector for TB vaccine development.

**Hypothesis and Aims:** Our hypothesis is that TMV-*Mtb* antigen vaccines will promote both humoral (IgG) and cellular (cytotoxic T lymphocyte) immunity that we can measure after vaccination in mice.

**Methods:** *Mtb* antigens 85A, 85B, Cfp10, Esat6, Hrp1, and HspX were expressed in bacterial culture and purified by metal affinity chromatography. Proteins were verified by western blot and concentrations were determined by BCA. Proteins were conjugated to TMV using EDC and sulfo-NHS, and optimized by testing different incubation concentrations and times. Mice were vaccinated once with 20ug antigen or 20ug antigen linked to TMV. Serum was collected on days 14 and 28 to determine IgG immune response titer by ELISA. Mice were boosted once at day 30, and serum was collected at day 45. On day 48, spleens will be removed, made into single cell suspensions, and tested for cellular immunity by Interferon gamma secretion after antigen stimulation (ELISpot).

**Results:** Vaccine proteins were made in mg quantities, at ~90-95% purity using one-step metal affinity chromatography. TMV-*Mtb* conjugates were successfully prepared at mg scale, as determined by the absence of free protein by SDS-PAGE visualization. Mice were immunized and serum was collected at scheduled intervals. IgG immune response results will be presented. Significant improvements in immune responses were seen after one dose of TMV-Ag in 5 out of 6 vaccine groups.
Conclusions: We were successful in achieving our aims, to prepare *Mtb* antigens, make TMV-*Mtb* conjugates, and test for immunogenicity in mice. Further studies will include combining individual TMV-*Mtb* vaccine for multi-antigen potency testing, as well as testing vaccines for functional immunity in a pathogen challenge setting in collaboration with Dr. Jeffery Schorey (U. Notre Dame).
Examination of Toll-like receptor activity in B-lymphoblastoid cell lines via IgG and inflammatory cytokine production as surrogates for African American lupus patients.

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Background: Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease with a heterogeneous clinical presentation, in which patient tissues undergo damage from immune complex formation. Ninety percent of patients at diagnosis are women of childbearing years; however, all genders, ages, and ethnic groups are susceptible, with prevalence being highest within female Americans of recent African descent. SLE is a multifactorial disease with genetic components influencing abnormal immune responses, defective suppression of the immune response, excess inflammation, in addition to environmental components. Pathogenic insults to the body are recognized by pattern recognition receptors such as toll-like receptors (TLR) that serve to initiate immune responses, many of which are implicated in SLE.

Hypothesis: We hypothesized that TLR-mediated responses are different in selected B-lymphoblastoid cell lines (BLCL) from SLE patients vs controls, dependent upon stimulatory factors given. Furthermore, that we surmise that the CASPASE-12 (CASP12) gene either in a heterozygous state or a homozygous state will influence TLR responses to stimuli when compared against the CASP12 pseudogene.

Methods: Following incubation with TLR agonists such as Poly IC -(a TLR 3 agonist) Imiquimod (TLR7), ssRNA40 (TLR8) and ODN2006 (TLR9), as well as the pan-specific mitogen PMA, supernatants from treated and untreated BLCL were assayed via ELISA testing for the relative amounts of IgG production. Analyses were performed on patients vs controls with or without the influence of CASP12 genotype.

Results: PMA treatment of BLCL resulted in decreased IgG production from patient BLCL versus controls. The CASP12p1 pseudogene influenced the highest IgG responses to PMA. For BLCL treated with specific TLR agonists, we found that the BLCL from patients homozygous for CASP12 had higher overall responses.

Conclusions: We found increased production of IgG from BLCL of African-American SLE patients relative to controls in a CASP12 genotype-specific manner. Following these experiments, we will be performing western blotting to dissect TLR pathways at the biochemical level.
Influence of Factors Secreted by Senescent Cells on Mitochondrial Bioenergetics of Pancreatic β-Cells
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Background: Today it is estimated that 29 million people in the U.S have Type II Diabetes Mellitus. Type II diabetes mellitus is the most prevalent form of diabetes and is characterized by insulin resistance and dysfunction of pancreatic β-cells. It has become increasingly clear that key to the normal function of pancreatic β-cells is intact mitochondrial function, which is responsible for connecting the levels of circulating glucose with insulin secretion. Furthermore, the prevalence of type II diabetes increases with age, perhaps the result of both systemic inflammation surrounding β-cells and increased oxidative stress inside of β-cells. Aging is also associated with the accumulation of senescent cells throughout the body, which are formed in response to DNA damage. Some senescent cells have also been shown to secrete a compliment of signaling factors known as the Senescence-Associated Secretory Phenotype (SASP). Many of these secreted factors are pro-inflammatory cytokines or chemokines; their accumulation is deleterious to neighboring tissue and, in some contexts, can promote tumorigenesis. What might connect accumulation of senescent cells, secretion of SASP factors, and β-cell dysfunction? Because the mitochondria play such an essential role to β-cell function, we considered the possibility that SASP factors produced by senescent cells could send signals to β-cells that would result in disrupted capacity to detect and respond to changes in glucose levels. Were this to be the case, it would help to explain the age-related decline in β-cell function, and onset of type II diabetes.

Hypothesis and Aims: Our hypothesis is that SASP factors can cause disruption to the normal metabolic activity of mitochondria in pancreatic β-cells.

Methods: To test this hypothesis, we collected SASP factors produced by X-ray irradiated mouse embryonic fibroblasts. We then measured the complete mitochondrial bioenergetics profile via respiratory control assay (Seahorse XF24) of mouse β-insulinoma cells with and without SASP-containing media.

Anticipated Results: These experiments are ongoing, but we expect that by measuring oxidative ATP production, proton leak and maximal spare respiratory capacity, that we will be able to pinpoint which aspect of mitochondrial function, if any, might by disrupted when β-cells are exposed to SASP factors.

Conclusion: This study is important because it could, for the first time, make the connection between accumulated senescent cells in aging tissue and disruption of pancreatic β-cell function, thus helping to explain the link between aging and type II diabetes.
Studies of novel resveratrol analogs on hormone-responsive and hormone-refractory prostate carcinoma cells
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Prostate cancer is the second leading cause of cancer death among American men. Studies indicated that prostate cancer cells are slow growing and androgen-dependent (ADPc) initially; ADPc patients can remain subclinical for an extended period of time. The disease ultimately progresses to an androgen-independent state (AIPc), characterized by greater proliferation of cells, lack of responsiveness to androgen blockade, and high fatalities. Resveratrol (3,4´,5-trimethoxystilbene) is a grape-derived polyphenol, which possesses a wide range of health-promoting activities, including anticancer properties. However, its low potency, limited bioavailability and rapid biotransformation to metabolites counteract its potential use for cancer prevention and therapy. Therefore, it is important to synthesize novel analogs of resveratrol with better solubility and improved potency to investigate their chemopreventive effects and mechanisms.

A series of 2-phenyl benzimidazole structures as analogs of resveratrol were designed and synthesized. Human prostate cancer cells LNCaP, CWR22Rv1, DU145 and PC-3 were selected for our in vitro studies. LNCaP are androgen responsive cells considered to be a model of the androgen-dependent state of prostate cancer, whereas CWR22Rv1, DU145 and PC-3 may be considered as representative of prostate cancer in its advanced stages. The synthesized compounds were first screened for their antiproliferative activity in these human prostate cancer cell lines. Out of these, compound GZN144A caused the most pronounced loss of proliferation and cell viability at concentrations that were significantly better than the parent chemical resveratrol, in both ADPc and AIPc models. Compounds GZN120C1 and GZN120C2 with improved solubility had activity better than that of resveratrol in certain cell lines, but not in others. Further studies are in progress.
Cellular senescence of stromal cells produces soluble factors that promote proliferation and potency of neighboring stem cells.
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**Background:** Trophic support for adult stem cells is provided by the niche microenvironment. This function of the niche declines with advanced age resulting in dysregulation of stem cells.

**Hypothesis and Aims:** We hypothesized that accumulation of senescent cells within the niche could be a contributing factor to niche destabilization because senescent cells have been shown to influence neighboring cell function through cell non-autonomous mechanisms.

**Methods:** To test this hypothesis, we reevaluated a simple in vitro model of the stem cell niche: co-culture of mouse embryonic fibroblasts (MEFs) with pluripotent stem cells (PSCs).

**Results:** We show that mitomycin C exposure, commonly used to inactivate MEFs in this system, is a potent inducer of cellular senescence and the senescence-associated secretory phenotype. Surprisingly, many molecules known to promote PSC maintenance are induced by senescent MEFs.

**Conclusions:** The connection of these findings to declining stem cell health with age will be discussed.
Roles of APC N-terminal and central domains in optic axon pathfinding and arborization \textit{in vivo}
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Touro University California, COM

\textbf{Background:} Formation of neuronal circuits involves axons navigating specific paths to their targets in the brain, where they then elaborate terminal arbors required for functional visual connectivity. Wnt ligands regulate axon pathfinding and arborization but the mechanisms of their downstream factors are not well defined. APC (Adenomatous Polyposis Coli) is one important downstream factor of Wnt signaling that can regulate $\beta$-catenin stability as well as actin and microtubule organization.

\textbf{Hypothesis and Aims:} We hypothesized that the APC regions that bind $\beta$-catenin (central repeat region) and that regulate the cytoskeleton differentially sculpt growth cones of optic axons in the optic tract, and shapes their developing arbors within the optic tectum.

\textbf{Methods:} We overexpressed a truncation of APC that binds to $\beta$-catenin in one to ten optic neurons in developing eyebuds of \textit{Xenopus} embryos. We then examined the effect of this mutant on the pattern and organization of optic axons and their growth cones in the optic tract, as well as the shape of their nascent arbors within the optic tectum, of whole brains taken from young tadpoles. We also constructed a mutant of the N-terminal domain of APC that can regulate microtubule organization.

\textbf{Results:} Overexpression of an APC truncation that can bind $\beta$-catenin (APC$\beta$-cat) but not microtubules, resulted in disordered optic axons in the optic tract. Growth cones of these optic axons were also malformed, with smaller, narrower shapes and very long filopodia. In addition, in the optic tectum at a later stage, APC$\beta$-cat expressing optic axons developed arbors with significantly fewer branches than controls.

\textbf{Conclusions:} These data suggest that the APC binding domain for $\beta$-catenin and microtubules differentially regulate pathfinding and arborization of optic axons required to establish functional visual connectivity \textit{in situ}. 
Calcium block of the HERG pore mutant G628
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Background: The human ether a-go-go related gene (HERG) encodes a cardiac voltage-gated potassium channel that has been implicated in long QT syndrome. Long QT syndrome can lead to the potentially lethal arrhythmia Torsades de Pointes. In addition, patients can acquire abnormal serum electrolyte levels due to a number of conditions such as alcoholism, aging, gastrointestinal dysfunction, renal disorders, and endocrine disorders. Previous studies have suggested that calcium blocks the pore of the HERG channel. However the location of the calcium-binding site is currently not known. The goal of this study is to determine if a point mutation located in the selectivity filter sequence GFG in HERG will alter block of the HERG by calcium.

Hypothesis and Aims: Residue G628 at the outer end of the selectivity filter forms part of the binding site for the pore blocking divalent cation Ca$^{2+}$, and possibly for other divalent, trivalent, and monovalent ions as well.

Methods: Site directed mutagenesis using the QuikChange kit from Agilent technologies will be used to create a point mutation at residue G628 on the HERG channel. G628 corresponds to the other glycine in the highly conserved selectivity filter sequence GFG (or GYG in other potassium channels). The glycine at the position 628 will be mutated to an alanine, serine, cysteine, glutamine, and proline. Calcium block of these pore mutants will be tested using two-electrode voltage clamping of Xenopus oocytes.

Results: It is expected that all point mutations will be successfully generated using the QuikChange kit. Based on mutations in the Shaker potassium channel previously made in the outer glycine in the selectivity filter, it is expected that the above mutations will form functional channels in oocytes (Heginbotham et al., Biophys J 1994 Vol 66, p1061). In addition, G628C in HERG has been shown to make a functional channel in Xenopus oocytes, although non-physiological conditions are required in order to measure ionic currents (Zeineb et al, Biophys J. 2011 Vol 101, p662-670).

Conclusions: Considering previous results that indicate that the HERG double mutant G628CS631C is not blocked by calcium, alterations in calcium block of any of the single pore mutants at G628 will suggest that G628 is the location of the calcium-binding site. The study has implications for an increased risk for cardiac arrhythmia via long QT syndrome due to abnormal serum electrolytes.
Characterizing the Distribution of Proteins in the Mitochondrial Inner Membrane
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Background: Knowing the protein distribution of sub-organelar compartments is essential to understanding the connection between cellular morphology and function. The mitochondrion, in particular, has shown to have a strong relationship between protein distribution and function. Mitochondria are composed of 3 main regions: outer membrane (MOM), inner membrane (MIM), and matrix. The inner membrane has deep invaginations called “cristae” and the part of the membrane closest to outer membrane is called the inner boundary membrane (IBM). For this project, we are investigating the protein compositions of these different parts of the mitochondrial inner membrane in order to better understand what proteins may be differentially distributed, and what implications these distributions have for mitochondrial function. Our results to date suggest that mechanical separation of the inner boundary membranes from the cristae is an effective way to isolate these membranes, and will allow future analysis of their respective compositions.

Hypothesis and Aims: The aim of this project is to look at protein distribution in the mitochondrial inner membrane and investigate the relationship between protein distribution and function by effectively separating the cristal and inner boundary membrane fractions of rat liver mitochondria. This protocol can be used to look for where a specific protein resides in the mitochondrial inner membrane.

Methods: The liver of a 5 month old female Wistar rat was placed in STE (250mM sucrose, 5mM Tris, 2mM EGTA) containing 1% bovine serum albumin (BSA) at pH 7.4 at 4°C. Liver was homogenized in a Dounce homogenizer, and spun in Beckman JA25.50 centrifuge to obtain crude mitochondria. Crude mitochondria was then sonicated 6 x 20 seconds, with 1 minute in between sonications. The crude mitochondria was layered on top of a Percoll gradient and spun in Beckman JA25.50 centrifuge. Fractions were collected and immunoblotting was performed using anti-ATP synthase β-subunit and anti-Tim50 antibodies.

Results: Using a crude preparation of rat liver mitochondria, we developed a method to separate inner boundary and cristal membrane regions through extensive sonication followed by density gradient centrifugation. Using immunoblotting against the ATP synthase β-subunit as an indicator of the cristal membrane, we found an enrichment of this signal in the initial (less dense) fractions collected from the Percoll gradient column. Immunostaining for the ATP synthase was decreased in later (more dense) fractions of the Percoll gradient. At the same time, immunoblotting against Tim50, an indicator of the inner boundary membrane, was absent in the low-density fractions but increased sharply in the higher-density fractions. Together, these results indicate that successful fractionation of the mitochondrial inner membrane into cristal and IBM fractions was achieved, and will allow the discovery and analysis of other proteins that may be differentially distributed along the mitochondrial inner membrane.
Conclusions: Mapping interorganellar protein distribution will increase our understanding of why certain proteins reside in specific places, and can answer questions regarding specific protein mechanisms. This project aims to show that proteins are differentially distributed in the MIM, and that these potential distributions may be functionally meaningful. Mitochondrial dysfunction is already associated with disease, but a better understanding of differentially distributed proteins may lead to new avenues for disease prevention and treatments.
Effect of Resveratrol and Resveratrol Derivatives in Chemo-Resistant Human Melanoma Cells
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Background: In the developed world, we are facing an increased occurrence of cancers during aging. Therapeutic intervention largely relies on inducing cell death; however, this method is highly toxic to normal tissues. There is thus a great need to identify alternative effective anticancer therapeutic strategies. A less toxic tumor suppression mechanism, which has gained increasing interest in the field, is through induction of senescence in tumor cells. Studies have shown that many dietary substances have anti-cancer properties. The polyphenol compound resveratrol (RES) is one of them. It is found in various fruits, such as red grapes. Recent literature indicates that RES has dose-dependent antiproliferative and apoptotic effects in certain cancer cell lines. In addition, RES can downregulate DNA methyltransferase leading to re-expression of certain tumor suppressor genes. Among tumor suppressors, CST6 encodes a cystatin (a member of the cysteine protease inhibitors) known to be silenced in various types of cancers via DNA hypermethylation. Another gene of the cystatin family, CST1, has recently been coined a putative senescence biomarker. This study is aimed at investigating and contrasting the roles of RES and its derivatives (122C1 and 144a) on human cancer cells. To understand the mechanisms of drug action, molecular changes (including changes in CST6 and CST1 expression) in drug-treated cells will be analyzed. It is anticipated that results obtained from this study will help further our understanding of cancer biology and may lead to the development of novel cancer therapeutic strategy.

Hypothesis/Aim: This study is designed to test the hypothesis that RES and its derivatives (122C1 and 144a) will exhibit dose-dependent cytostatic or cytocidal effects on human cancer cells. It is also hypothesized that the treatment will lead to altered expression of molecules relevant to tumor suppression.

Materials and Methods: A highly chemo-resistant human melanoma cell line, MDA-MB-435S was used in this experiment due to its lack of CST6 expression. Drug sensitivity assays were carried out using RES and its derivative compounds. RT-PCR analysis was conducted to assess mRNA expression in drug-treated cells.

Result & Conclusion: Preliminary results show that MDA-MB-435S cells treated with RES and 122C1 exhibit dose-dependent cytostatic response up to 50μM. In contrast, cells treated with 144a exhibit cytocidal response at doses lower than 12.5μM. Expression of CST6 or CST1 showed little to no change in drug-treated MDA-MB-435S cells for 8 days. The molecular mechanism is currently being further analyzed. To our knowledge, this is the first study of the effect of RES and its derivatives on a highly chemo-resistant melanoma cell line. The results obtained from this study may impact the development of novel therapeutic intervention for cancers.
Comparative Analysis of Cell Signaling Mediated by Ras Isoforms
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Background: Cancers are genetic diseases that account for the leading causes of mortality worldwide. Approximately 30% of all human cancers involve mutations in the Ras proto-oncogenes. The Ras gene family includes three closely related Ras isoforms (H-Ras, N-Ras, and K-Ras) which encodes for GTP-binding proteins that are crucial in mediating various cell signaling pathways. A single mutation on codon 12, 13, or 61 in the Ras gene respectively is sufficient to confer a constitutively active state of the Ras protein and its tumorigenicity. Interestingly, however, while these three Ras proteins are believed to share similar signaling pathways, they have also been observed to activate different effector molecules in various model systems. These observations may help explain the prevalence of mutations of specific Ras isoform in certain cancer types. However, most of the studies have been done in immortalized rodent or human cells that contain known or unknown gene mutations, which might complicate the interpretation of results obtained. Furthermore, little is known if specific codon mutations of the Ras gene lead to differential signaling outcomes. Further investigation of specific Ras signaling is thus necessary to help advance our understanding of cancer biology.

Hypothesis and Aims: The aim of this study is to help delineate the cell signaling pathways mediated by the Ras isoforms through the use of normal human fibroblasts that do not contain any known genetic alterations. It is anticipated that results obtained from this study will help advance our understanding of Ras signaling and will have important implications towards targeted cancer interventions and therapeutics. It is hypothesized that Ras isoforms share similar signaling pathways, but each can trigger unique signaling mechanisms.

Materials & Methods: Normal human diploid lung fibroblasts IMR90 (ATCC) were transduced with H-RasV12, N-RasV12, K-RasV12, K-RasL61, MEKQ56P, or an empty vector control via retroviral gene transfer. Data mining was performed using results previously obtained from the GeneChip Human Genome U133 Array Analysis of the transduced cells. Relevant research articles on cancer biology and molecular mechanisms on PubMed focused the search interest. Images of transduced cells were analyzed using the computer software ImageJ (NIH). Parameters for the image analysis were width, length, and angle of cells. RT-PCR analyses with gel electrophoresis were used to validate changes in gene expression in the transduced cells.

Results & Conclusions: Preliminary studies identified distinct signaling pathways shared by all three Ras isoforms, and uncovered unique signaling pathways associated with each Ras isoform. Additionally, mutations on codon 12 and codon 61 in the K-Ras gene lead to differential biology and signaling, respectively. Potential therapeutics can exploit these differences to produce more effective cancer interventions.
Solid microneedles for transdermal delivery of amantadine hydrochloride
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Background: Parkinson’s disease (PD) is a neurodegenerative disorder that is characterized by tremor, bradykinesia, postural instability, and rigidity. The disease is associated with the loss of dopamine in the nigro-striatal system. In advanced stages of Parkinson’s disease, speech, gait, and balance disorders often become poorly responsive to levodopa. Amantadine is a nonselective N-methyl-D-aspartate (NMDA) receptor antagonist that improves gait in PD patients. Amantadine is mostly utilized to treat peak-dose levodopa-induced dyskinesias in advanced stages of PD. The drug has a log P value of 2.4 and permeates the skin poorly. Enhanced transdermal delivery of this drug would be beneficial for advanced stage PD patients.

Hypothesis and Aim: In this project we will use microneedles to deliver amantadine. We hypothesize that microneedle delivery of the drug may lead to increased flux. The aim of this project was to study the influence of microneedles on transdermal delivery of amantadine across porcine ear skin in vitro.

Methods: An LC-MS/MS technique was developed for quantitative determination of amantadine. HPLC/DAD-ESI/MS/MS analysis was performed using an Agilent series 1200 HPLC with diode-array and Agilent 6320 Ion Trap mass spectrometer detector (Agilent Technologies, Palo Alto, CA). Chromatographic separation was carried out on the reverse-phase Agilent Zorbax Eclipse Plus C18 (100×2.1 mm, 3.5 micron) analytical column, which was protected by a guard column with the same stationary phase (12.5×4.6 mm, 5 micron) (Agilent Technologies, Palo Alto, CA). HPLC/DAD-ESI/MS/MS analysis was performed using an Agilent series 1200 HPLC with the diode-array and Agilent 6320 Ion Trap mass spectrometer detector (Agilent Technologies, Palo Alto, CA). Chromatographic separation was carried out on the reverse-phase Agilent Zorbax Eclipse Plus C18 (100×2.1 mm, 3.5 micron) analytical column, which was protected by a guard column with the same stationary phase (12.5×4.6 mm, 5 micron) (Agilent Technologies, Palo Alto, CA). The column temperature was set at 40 °C, and the autosampler temperature was set at 4° C. The mobile phase consisted of 0.1% formic acid in water (solvent A), and 0.1% formic acid in methanol (solvent B). The solvent gradient was performed at 0.4 mL/min with an initial condition of 5% of mobile phase B. Mobile phase B was increased to 95% at 2 min and held at 95% B until 6 min at which Mobile phase B was then reduced to 5% at 7 min. A post run time of 2 min for mobile phase equilibration was used after each sample run. MS/MS transition was 152>135. Limit of detection was 0.1ppm. Using the LC/MS/MS technique, we carried out skin permeation studies to quantify the influence of solid microneedles on transdermal delivery of amantadine. Pig ear skin was used since it is a representative model of human epidermal membrane.

Results: Transdermal flux of amantadine through porcine skin was determined from the steady-state portion of the cumulative amount versus time curve. The flux of amantadine, determined using the developed LC-MS/MS technique, was 68.8µg/cm²/hr while the flux following the use of a stainless steel microneedle roller was 27.1µg/cm²/hr. Statistical analysis was carried out with the Student’s t-test.
Conclusions: Although there was a 2.53-fold increase in flux, the difference in flux value following the use of solid stainless steel microneedle roller was not significant. Future studies will examine combined techniques such as microneedles in conjunction with sonophoresis or chemical penetration enhancers.
Comparative Analysis of Human Alzheimer’s Risk Factor Genes from GWAS and Linkage Analyses.
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Background: Alzheimer’s disease (AD) is the major cause of dementia. AD has two types, early onset AD (EOAD) and late onset (LOAD). The vast majority of AD patients have LOAD that has been becoming more problematic as people continue to age and the average lifespan of the population increases. Genome-wide association studies (GWAS) and linkage analyses have identified genes with possible risk susceptibility to LOAD and other neurological diseases. How these genes are involved in the molecular mechanism of Alzheimer’s disease is still not well understood.

Hypothesis and Aims: Our hypothesis is that human LOAD risk factor genes have orthologs in the nematode Caenorhabditis elegans. The primary aim of this study is to identify their C. elegans orthologs (referred to as AD genes).

Methods: C. elegans genome data (~20,000 genes) and four ontology databases have been used to identify C. elegans orthologs (i.e., genes with conserved functions) for AD genes. We use a list of human genes responsible for development of AD and searched for their ortholog counterparts in C. elegans. A new list of genes was created by comparing with multiple databases of human and C.elegans ortholog genes. Matching registry test was performed on these genes to find their ortholog counterparts in C.elegans (Wormbase). The results were confirmed by using homology search (BLAST/BLAT). The selected genes were then divided based on their number of Wormbase ID matches with four databases. We used the ensembl ID of the human genes and locus ID of the C.elegans to compare our list of genes with four different search engines and determined how many of our selected genes matched with the new search engines.

Results: The 695 human risk factor genes for AD shares risk susceptibility with other neurological disorders, including Schizophrenia, Parkinson’s disease, Multiple Sclerosis, and Amyotrophic lateral sclerosis. In addition, 93 genes were found to have ortholog counterparts in C. elegans. Of 93 genes, 94% were identified in an ontology database, 85% were identified in two databases, 75% were identified in three databases, and 55% were matched by all four search engines. The last group should provide a reasonable pool for further assays.

Conclusion and Perspective: The study generated a list of AD genes including human genes and C. elegans orthologs. The next step in this research will be to determine distribution of the gene functions using ontology analysis. The genes identified with high confidence levels will be subjected to functional analysis.
Background: An effective anticancer drug therapy should aim at killing or decreasing the growth of cancer cells with minimal cytotoxicity to normal cells. SHetA2 is one such novel heteroarotinoid (Flex-Hets) compound in preclinical trials that has shown promising anticancer effects on various cancer models. In order to maximize the yield, minimize the number of synthetic steps as well as improve the physicochemical properties, various SHetA2 analogs were synthesized and tested in breast and prostate cancer cells at Touro University CA-College of Pharmacy in a collaborative approach. Of the ten analogs tested, SL-01-18 was found to be the most effective growth inhibitor of both prostate and breast cancer cells. Further experiments in our lab showed that SL-01-18 differentially inhibited the growth of androgen dependent prostate epithelial cell lines, LNCaPs, while minimally affecting the growth of androgen independent prostate cancer cell lines.

Hypothesis and Aims: The aim of this project was to further characterize the growth inhibitory effects of SL-01-18 on LNCaPs and compare it with PWR-1E, a normal prostate epithelial cell-line. We hypothesize that the growth inhibitory and pro-apoptotic effects of SL-01-18 are due to inhibition of androgen receptor (AR) signaling in LNCaP cells.

Methods: All experiments were performed on LNCaP and PWR-1E cell lines grown in media conditioned for cell growth in response to androgens alone and bicalutamide, a non-steroidal AR antagonist, was used to compare our results. Cell viability and nuclear staining experiments with Hoechst 33342 were performed after 24, 48 and 72 hours exposure, to evaluate growth inhibitory and pro-apoptotic properties of SL-01-18. AR levels in cell lysates were measured using Western Blot analysis and ELISA was performed to monitor levels of both secreted and cellular prostate specific antigen (PSA) levels in the two cell lines after exposure to either SL-01-18 or bicalutamide.

Results: The SHetA2 analog, SL-01-18, was found to be more potent in inhibiting the growth of LNCaPs than PWR-1E cells. Hoechst 33342 live nuclear staining showed chromatin condensation and nuclear fragmentation, a hallmark of apoptosis, in LNCaP cells. Both secreted and cellular PSA levels were significantly lowered in LNCaPs by 72 hours. Finally, a significant reduction in cellular AR levels in LNCaP cells was observed after treatment with SL-01-18.

Conclusion: These results confirm that SL-01-18 selectively inhibits growth of androgen dependent prostate cancer cells and may eventually induce cell death via apoptosis. Our preliminary results indicate that SL-01-18 does cause inhibition of AR signaling. Further investigations SL-01-18’s mechanism of action in prostate cancer cells is ongoing.
Interaction of HERG and beta-catenin in an oocyte expression system.
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**Background:** The HERG (human ether-a-go-go-related gene) channel is a K+ selective voltage gated ion channel most important in the repolarization of ventricular cardiac myocytes. Studies have shown that drug-induced blocking of HERG or mutations in the HERG channel may be associated with delayed cardiac repolarization, which may lead to Long QT syndrome and the development of the potentially lethal ventricular arrhythmias called Torsades de Pointes. Beta-catenin is a multifaceted protein that is involved in cell-to-cell adhesion, signal transduction, cancer, and neuronal development. Recent evidence suggests that beta-catenin upregulates the number of HERG potassium channels expressed in Xenopus oocytes (Munoz et. al. 2012 PLoS One 7(8)43353).

**Hypothesis and Aims:** The goal of this research is to confirm that beta-catenin upregulates HERG channels in the plasma membrane of Xenopus oocytes and to determine if the gating properties of HERG (i.e. channel open and closing and channel inactivation and recovery from inactivation) are altered by beta-catenin.

**Methods:** Electrical recordings to assess HERG function will be performed using two-electrode voltage clamping of Xenopus oocytes expressing either HERG alone, beta-catenin alone, or HERG coinjected with beta-catenin. cRNA will be injected into enzymatically defolliculated oocytes and currents recorded 1-5 days after injection.

**Results:** It is expected that beta-catenin will upregulate the number of HERG channels in the Xenopus oocytes. This upregulation may involve changes in channel activation, deactivation, inactivation and recovery of activation.

**Conclusions:** Beta-catenin upregulates HERG channels by changing ion channel kinetics. This may have implications for the development of the embryonic nervous system.
Fragment-based and structure-aided discovery of HIV-1 glycoprotein 41 fusion inhibitors
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**Background:** Despite significant progress being made, the HIV virus spread has not halted and a definitive cure remains elusive. There is clearly a need for exploring new therapeutic options. Entry of HIV into cells is mediated by its two envelope glycoproteins: gp120 and gp41. Upon gp120 binding to the cellular receptors, gp41 undergoes a series of conformational changes from a non-fusogenic to a fusion-active conformation. The fusogenic core of gp41 is a trimer of helical hairpins in which three C-terminal helices pack against a central coiled coil formed by three N-terminal helices. The formation of this fusogenic structure brings the viral and cellular membranes close together, a necessary condition for membrane fusion to occur. Currently no effective small molecule fusion inhibitors exist.

**Hypothesis and Aims:** Well-crafted molecules that bind to the gp41 coiled coil may prevent formation of the fusogenic structure, thus inhibiting membrane fusion and HIV-1 entry.

**Methods:** A fragment-based approach was used to facilitate gp41 inhibitor discovery. A screening assay was specifically designed for gp41 and a fragment library was screened by using ligand-based NMR spectroscopy.

**Results:** Using WaterLOGSY (Water Ligand Observed via Gradient SpectroscopY) NMR experiments, we identified several fragment hits that bind to a well-known conserved hydrophobic pocket on the NHR coiled coil of gp41, or to an adjacent C-terminal sub-pocket. Further paramagnetic relaxation assisted docking was used to identify possible binding modes of ligands in each pocket.

**Conclusions:** A fragment-based approach was successfully employed to find new hits with novel scanfolds that bind to the HIV-1 gp41. The fragment hits were also used to characterize novel gp41 protein constructs developed in our lab to form stable trimers with exposed binding surfaces for small molecules. Putting the fragment-based screening and protein structure results together, we are developing strategies to grow the fragments into a larger, more active inhibitor.
Novel swapped domain structures of the gp41 ectodomain
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Background: HIV-1 glycoprotein-41 (gp41) mediates viral membrane fusion and represents an ideal target for the development of novel HIV entry inhibitors. The conformational rearrangement of N-and C-heptad repeats (NHR, CHR) of the HIV-1 gp41 ectodomain into a trimer of hairpins triggers virus–cell fusion by bringing together membrane-spanning N- and C-terminal domains. Peptides derived from the NHR and CHR inhibit fusion by targeting a prehairpin intermediate state of gp41. Typically, peptides derived from the CHR are low nM inhibitors, while peptides derived from the NHR are low μM inhibitors. Low potency of NHR peptides is believed to be a result of aggregation and failure to form the trimer state. Additionally no detailed structural data exist for gp41 NHR: small molecule complexes, a limiting factor for structure-based drug design.

Hypothesis and Aims: By swapping the NHR and CHR domains of gp41, a new construct has been designed to stabilize NHR grooves as a unique gp41 model for inhibitor discovery and mechanism studies.

Methods: We designed and prepared a series of new gp41 ectodomain reverse hairpins, with the CHR domain preceding a four-residue loop and the NHR domain. Constructs were characterized using biophysical methods, including CD, NMR, and analytical ultracentrifugation, and in cell–cell and virus–cell fusion experiments.

Results: Biophysical characterization of the new gp41 constructs confirmed that the proteins formed stable trimers in solution with exposed binding surfaces for small molecules. The effect of DPC on the structure of the hairpins was also investigated, in order to mimic the membrane environment of gp41. Constructs were nM inhibitors of HIV-1 fusion by virtue of their stabilized NHR domain.

Conclusions: The swapped domain design of HIV-1 gp41 resolves the problem of unstable and weakly active NHR peptides, provides a unique model for gp41 inhibitor discovery, and suggests a different mechanism of action from that of CHR peptides in inhibition of HIV-1 fusion.
Evaluation of long-term culturing techniques of airway epithelium to provide genotype-specific treatments for cystic fibrosis.
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\textbf{Background:} Cystic Fibrosis (CF) is an autosomal recessive genetic disease that is caused by a mutation in the cystic fibrosis gene. Cystic fibrosis affects about 30,000 adults and children in the United States and about 70,000 adults and children worldwide. Recently, a new cell culturing technique has been developed called conditionally reprogrammed cells (CRCs) for use in drug testing and responsiveness in human bronchial epithelial cells. We are testing this cell culture model on bronchial epithelial cells to see whether it can be used to passage and maintain bronchial epithelial cells in culture for longer times and whether these cells keep their phenotypic properties with serial passaging. Currently two drugs are leading research, VX-770 (Kalydeco), which has been FDA approved for the G551D mutation, and VX-809 (Lumacaftor), which is in phase III trials. This new cell culture model can offer many possibilities for personalized medicine and possible drug discoveries for the CF population as well as other diseases.

\textbf{Hypothesis and Aims:}

- Develop a cell culturing technique/model for passaging primary bronchial epithelial cells that would produce more cells from the desired cell of study.
- Test if the CRC method is a good model for passaging bronchial epithelial cells by using Ussing assays, and to test if these cells keep their phenotypic properties after multiple passaging.

\textbf{Methods:} Transepithelial resistance ($R_t$), ENaC-mediated currents, CFTR-mediated currents, and ATP-stimulated currents were measured and analyzed.

\textbf{Results/Conclusions:}

- We have extensively tested conditionally reprogrammed airway cultures. We found that the CRC method is a good technique to maintain the airway epithelial phenotype for up to 10 passages. Our data indicate that the CRC cultures can be used for research and drug testing. By using patient specific cultures, we found that we can predict a drug response in a patient from in vitro experiments, which can ultimately provide a means for personalized medicine in the clinical setting.
- We found that the pre-treatment of CF CRC cultures with VX-809 restored about 10-30% CFTR currents in the F508del CFTR tissues.
- We were successful in using the CRC method to culture bronchial epithelial cells for up to passage 10. We have tested that these cells do retain their phenotypic properties although some decay is seen with drug response in some of the subjects.
The effects of diarylthiourea analogs on triple negative breast cancer cell growth
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Background: Breast cancer is the second leading cause of cancer death in women after lung cancer. Breast cancer is often classified at the molecular level in terms of whether the cancer expresses the estrogen receptor, progesterone receptor and human epidermal growth factor 2 receptor. Hormone receptor positive breast cancer accounts for 75-80% of all breast cancer and the remaining 20-25% accounts for the most aggressive types of cancer which are negative for all three receptors—known as triple negative breast cancer (TNBC). One of the treatments used to manage TNBC is chemotherapy, surgery or radiation therapy. Although chemotherapy has been effective in improving patients’ prognosis, a significant number of patients either relapse or develop resistance to these drugs. There is a significant interest in developing new therapeutic drugs aimed at improving outcomes in TNBC patients. Many studies have shown that flexible heteroarotinoids (flex-het) are a promising new class of drugs due to their ability to regulate growth, differentiation and apoptosis in a variety of cancer cells without activating the nuclear retinoic acid receptors. Previous studies have shown ShetA2 as the leading flex-het anti-cancer drug with the greatest efficacy in treating various types of cancer cells Some of the limitations of the ShetA2 is its high lipophilicity, its side effects and the low yields associated with the laborious synthesis. Therefore, efforts have been made to develop 2nd generation diarylthiourea compounds that retain anti-cancer activity, but with minimal side effects.

Objective: To evaluate the effects of two 2nd generation drugs SL1-18 and SL1-09 on various TNBC cell lines including MDA-MB-453 and MDA-MB-231.

Methods: Two TNBC cell lines, MDA-MB-453 and MDA-MB-231, were treated with varying concentrations of the drugs and their effects on growth, gene expression and protein expression.

Results/Conclusion: Data from our proliferation assays indicate that exposure of 5uM of SL1-18 and SL1-09 effectively inhibited growth of both TNBC cell lines (P=0.04 and P=0.03). Western blot analysis suggests that SL1-18 and SL1-09 decreased the expression several of the cell cycle regulators including cyclin D1 and cyclin E. Furthermore, results from our BrdU incorporation assay demonstrate that SL1-18 decreased the number of cells entering S phase in comparison to mock treated cells by 13% (P=0.01). Collectively, these results indicate that the SL-1-18 and SL-1-09 do exhibit anticancer activity against TNBC, but further research is necessary to fully understand their mechanism of action.
A Novel LC-MS/MS Method using MIDA to Investigate the Impact of DNL on VLDL Profile.
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Background/Objectives: Dietary sugars have been shown to increase liver fat which contributes to dyslipidemia and increased risk for cardiovascular disease (CVD). Hepatic fatty acids are produced from carbohydrates through de novo lipogenesis (DNL). Newly synthesized fatty acids are assembled into triglycerides (TG) and packaged into very low density lipoproteins (VLDL) for export from the liver. The effect of newly synthesized fatty acids on the types of VLDL produced by the liver has not been investigated.

Hypothesis and Aims: We hypothesize that DNL will increase the relative abundance of less dense VLDL and alter the profile of VLDL produced by the human liver. To investigate the profile of VLDL produced by the human liver following DNL, we must first separate VLDL according to density, before subsequent mass spectrometry and mass isotopomer distribution analysis (MIDA). Separation of VLDL by density produces fractions with low TG abundances, which are challenging for analysis by gas chromatography with mass spectrometry (GC/MS). We have developed a novel LC-MS/MS method with sufficient sensitivity to measure newly synthesized fatty acids in four sub-fractions of lipoproteins containing TG.

Method: Subjects were dosed with stable isotopes and fed either a high-fat or high-carbohydrate diet. Triglyceride rich lipoprotein (TRL) was prepared from plasma using a fixed-angle rotor centrifuge. TRL at δ=1,035 was sequentially layered with solutions of, δ=1.02, δ=1.01 and δ=1.00, and centrifuged with a swing bucket rotor. The top four fractions containing VLDL of increasing density were sampled.

VLDL was extracted from each fraction using immuno-affinity with an α-apo-B100 immuno-affinity column. Triglycerides were extracted from each VLDL fraction and transmethylated to form fatty acid methyl ester (FAME) derivatives. The isotopomer ratio of methylpalmitate was measured by GC/MS, and the fractional synthetic rate of palmitate (%DNL) was measured using MIDA. Each sample was then re-derivatized to form palmitate pyrrolidide and re-analyzed by LC-MS/MS. VLDL from unfractionated TRL was also analyzed by both GC/MS and LC-MS/MS to measure total VLDL %DNL.

Results: Pyrrolidide palmitate analysis by LC-MS/MS allows for MIDA analysis at 50 fold lower concentrations than GC/MS analysis of methylpalmitate. Precursor pool enrichment (P) and fractional synthetic rate of palmitate (%DNL) were in good agreement (r = 0.986, p < 0.05) between each method.

Conclusion: A novel LC-MS/MS analytical method was developed that allows for MIDA in samples with insufficient abundances of fatty acid for GC/MS analysis. This method is currently being applied to VLDL fractionated by density, and total VLDL. This technique has further applications for MIDA of DNL in samples with limited amounts of lipid, such as Lipoprint® or cell cultures.
Isocaloric Fructose Restriction for 10 Days Reduces Hepatic De Novo Lipogenesis and Liver Fat in Obese Latino and African American Children
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Background: Previous studies have shown that high sugar (specifically fructose) consumption is associated with liver fat accumulation and/or hypertriglyceridemia, which may increase risk for Type 2 diabetes and cardiovascular disease. The conversion of sugar to fat in the liver (hepatic de novo lipogenesis, DNL) may be an important pathogenic mechanism.

Aim: To determine the effect of 10 days of a fructose - but not calorie- restricted diet on DNL in obese Latino and African American children with high habitual dietary sugar intake.

Methods: Latino (14F, 11M) and African American (12F, 3M) children (ages 9-18; BMI z-score 2.3), who were high dietary sugar consumers at baseline (average fructose intake >50 g/day), had all meals provided for 10 days with the same caloric and macronutrient composition as their standard diet, but with other carbohydrate substituted for sugar. Subjects were weighed daily and diets adjusted to maintain baseline weight. Fractional DNL and DNL under the curve (DNL-AUC) were measured over 8 hours of test meal feeding on Day 0 (high fructose) and Day 10 (low fructose). Test meals contained 1-13C sodium acetate tracer. Post-prandial blood samples were analyzed by gas chromatography mass spectrometry, and DNL calculated by mass isotopomer distribution analysis. Liver fat percentage was determined by magnetic resonance spectroscopy.

Results: DNL during feeding was significantly reduced with fructose restriction, beginning 50 minutes after initiation of tracer/feeding (2.1±0.2 vs. 1.3±0.1% on days 0 and 10, respectively, P<0.001 by paired t-test) and continuing throughout the tracer/feeding procedure 15.7±0.1 vs. 7.2±0.6% at 8 hours on days 0 and 10 respectively, P<0.001). Integrated DNL-AUC decreased be 56% from 70.4±5.1 on day 0 to 31.1±3.0 on day 10 (P<0.001). The decrease in DNL-AUC over only 10 days of fructose restriction was accompanied by a 22% reduction in liver fat from 11.2±9.1% on day 0 to 8.8±1.7% on day 10 (P<0.001; n=36). These effects remained statistically significant after adjusting by ANCOVA for minor weight loss over the 10 days (1.1±0.2 kg, P<0.001).

Conclusions: Isocaloric dietary fructose restriction after 10 days decreased hepatic DNL and liver fat in Latino and African American children irrespective of weight loss. These results suggest that hepatic DNL is an important mechanism leading to liver fat accumulation in children, which can be revered by short-term fructose restriction. These data support public health efforts to reduce sugar consumption.
Determining the Kinetics of Chylomicron and Very Low-Density Lipoprotein by Measuring the Incorporation of Leucine in Apolipoprotein B-48 and Apolipoprotein B-100.
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Background: Lipoproteins are macromolecular complexes, composed of lipids and proteins, which transport lipids around the body in the blood and originate in either the intestines or the liver. Chylomicrons are produced in the intestines where dietary fats are packaged as triglycerides with apolipoprotein B-48 (apo B-48). Very Low-Density Lipoproteins (VLDL) are formed in the liver where triglycerides are packaged with apolipoprotein B-100 (apo B-100).

Aim: To determine how a fructose restriction diet affects the kinetics of post-prandial chylomicrons and VLDL.

Methods: Obese children, ages 8 to 18, that consumed >50g/day fructose were recruited for the study. Participants were placed on a 10 day fructose restriction diet in which ≤4% of caloric intake came from fructose. Each participant received a bolus containing the stable isotope D₃-leucine pre- and post-intervention. Multiple blood samples were taken throughout each study day. ApoB100 immunoaffinity columns were used to separate chylomicrons and VLDLs. The large apo-B proteins from the lipoproteins were then separated from the lipids and hydrolyzed. Leucine was then derivatized using the FMOC derivatization method, resulting in a FMOC-leucine derivative. The enrichment of D₃-leucine was analyzed by liquid chromatography tandem-mass spectrometry (LC-MS/MS). Enrichment of leucine in the plasma was also measured using a solid phase extraction method followed by the FMOC derivatization method previously mentioned and analyzed by LC-MS/MS.

Results: After the 10-day fructose restriction dietary intervention the data showed that there was a decrease in the amount of labeled leucine that was incorporated in both apoB-48 and apoB-100.

Conclusions: Decreasing the amount of fructose consumption will decrease the rate of production of lipoproteins contained in chylomicrons and VLDLs.
Separation of Apolipoprotein Particle Species by Density Gradient Ultracentrifugation
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Background: Density gradient ultracentrifugation is used to isolate and purify cellular organelles, DNA, and RNA. Similarly, it can be used to separate lipoproteins. The use of this methodology and stable isotope tracers allows for the investigation of the maturation and the kinetics of hepatic lipoproteins.

Aims: We aim to 1) isolate triglyceride rich lipoproteins (TRL) from human plasma and 2) to fractionate TRL into different species. Specifically, very low-density lipoproteins (VLDLs) of different size; and chylomicrons from chylomicron remnants.

Methods: Density solutions were made from Sodium Bromide and kept at 4°C to reduce the likelihood of density change as a result of evaporation and to facilitate the formation and definition of layers. An ultracentrifuge tube was filled with 3 mL of fresh human plasma and adjusted to a d= 1.035 kg/m³. The samples were centrifuged in a TFT 45.6 fixed-angle rotor for 20 hours at 40,000rpm in a Beckman L8-70M or L8-80M ultracentrifuge. The ultracentrifuge tubes were then cut and the top 1.8mL of TRL were extracted. A swing-bucket ultracentrifuge tube was filled with 1.3 mL of TRL and 3.2 mL of d= 1.035 kg/m³ solution to yield 4.5mL. This was then sequentially layered with: 1) 3mL d= 1.020 kg/m³ solution, 2) 3mL d= 1.010 kg/m³ solution and 3) topped off with d= 1.000 kg/m³ solution. The samples were centrifuged for 6 hours at 40,000 rpm in a SW41Ti swing bucket rotor. A control tube with layered density solutions was spun as well. Following the 6 hour centrifugation 12-one mL aliquots were transferred using a “bubbling” technique; where half of the tip is submerged in the liquid, and the other half pulls air in across the surface of the sample. This technique reduces the probability of mixing layers, which contain different apolipoprotein sizes, and allows the aspiration of the topmost layer. The density of the 12 fractions taken from the control tube were measured using an Anton Paar DMA 4500 M Densitometer.

Results: Preliminary results show that the layers maintain their definition throughout the ultracentrifugation with minimal mixing. Results also show that the “bubbling” technique is effective at removing the topmost layer. Density measurements from the control tube confirm proper layering, ultracentrifugation and aliquots of fractions.

Conclusions: We have successfully applied the density gradient ultracentrifugation methodology to fractionate TRL samples. This method will allow for the investigation of newly synthesized fatty acids in different sized VLDL particles.
Ultrasound used as Point of Care at the bedside is bringing imaging to the patients at the site of need. This is especially true in areas where other imaging is not readily available, such as in underserved rural areas in third world. We present a case of skull fracture identified by use of Ultrasound in a rural clinic in Langue, Honduras. This fracture is corroborated with a plain film X-ray of the skull which was performed in a hospital 1.5 hour drive from the site of injury. The ramifications of Ultrasound use for skull fracture evaluation, far out way mere convenience and use just in underserved areas. Performing this exam in an emergency room setting in our country would preclude radiation exposure to a significant part of the population.
Adipose Triglyceride Lipolysis Following Consumption of Different Types and Amounts of Dietary Sugar.
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**Background:** Dietary intake of added sugars has increased in the typical American diet over the last 40 years. These added sugars, specifically fructose and high fructose corn syrup (HFCS), have been associated with the development of a metabolic disease state, and thus an increased risk of cardiovascular disease, diabetes, obesity, and fatty liver disease.

**Hypothesis and Aims:** This study aims to examine the effects of fructose and HFCS consumption on lipolysis, the breakdown of triglycerides into fatty acids. From previous studies, we expect that consumption of fructose and HFCS sweetened beverages will result in an altered release of free fatty acids (FFAs) from adipose.

**Methods:** Patients from the UC Davis Clinical Research Center were recruited to consume beverages sweetened with glucose, fructose, or HFCS three times daily over the course of two weeks, with an otherwise uncontrolled diet. During an initial baseline inpatient stay and a post-treatment inpatient stay, patients were given 26-hour infusion of \([1,2,3,4-^{13}\text{C}]\) palmitate (to measure FFAs release by adipose tissue) and given oral dosing of glyceryl tri-[\(\text{D}_3\)]hexadecanoate (to assess dietary triglycerides) with each meal. Blood samples were drawn hourly over the course of inpatient stay and stored for analysis. Upon analysis, plasma samples were thawed, protein precipitated, and FFAs derivatized with iodomethane Methylated FFAs were analyzed by Gas Chromatography-Mass Spectrometry (GC/MS).

**Results:** Fasting lipolysis was 1.19 mg/kg/min \((n=3)\) before intervention and decreased to 0.88 mg/kg/min \((n=3)\) after dietary sugar intervention. Suppression of lipolysis by the lunch was blunted (from 41% before vs 18% after the dietary sugar intervention).

**Conclusions:** These preliminary results suggest that adipose tissue insulin sensitivity is reduced after a sugar dietary intervention.
Kinetics of triglyceride-rich lipoprotein (TRL) turnover using a single label stable isotope tracer
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Background: Excess fructose and sugar consumption is linked to obesity and associated metabolic disorders. Recent studies suggest that the hepatic conversion of sugar to fat or de novo lipogenesis (DNL) is a key mechanism. Newly synthesized fatty acids assembled into triglycerides (TG) in the liver are packaged in very low density lipoproteins (VLDLs) and secreted into blood. Elevated plasma TG concentrations are a risk factor for cardiovascular disease. Therefore, measuring VLDL-TG turnover and kinetics will allow us to better understand the physiological implications of diet on the metabolic syndrome.

Hypothesis and Aims: In this study we aim to analyze the kinetics of TRL-TG turnover using the stable isotope [2-13C] glycerol in conjunction with mathematical modeling. We hypothesize that an isocaloric fructose restriction diet will lead to a reduction in postprandial TRL turnover and plasma triglyceride levels.

Methods: Overweight adolescents who habitually consumed high levels of fructose (≥50 g/day) were recruited for a 10-day dietary intervention study. The fructose restriction diet differed in carbohydrate quality, where complex carbohydrates substituted for fructose during the intervention period. Each subject was his/her own control. Subjects received an IV bolus of [2-13C]-glycerol for the determination of TRL turnover pre- and post-intervention. Blood was drawn at multiple time intervals on both study days. ApoB-100 immunoaffinity columns were used to separate lipoproteins. Enrichment of TRL-TG glycerol in these fractions was measured as the tracer-to-tracee ratio using a standard curve by liquid chromatography tandem mass spectrometry (LC-MS/MS) or gas chromatography mass spectrometry (GC/MS). Enrichment of TRL-TG glycerol in the plasma was also assessed using a solid phase extraction method. Total serum triglycerides in the TRL and chylomicron fractions were measured using an in vitro enzymatic assay kit from Wako (Richmond, VA).

Results: Both fasting (98.6±11.5 versus 67±7.8) and postprandial serum total triglycerides decreased after 10 days of fructose restriction (See figure 1). The change in chylomicron-TG glycerol enrichment increased slightly after the intervention period (pre-intervention, 0.10±0.01 versus post-intervention, 0.13±0.01). There was no significant change in VLDL-TG glycerol enrichment. Kinetic data were consistent with the decrease in triglyceride levels.

Conclusions: Preliminary data suggests that a 10-day fructose restriction leads to a decrease in plasma triglyceride levels. Compartmental modeling of TRL-TG turnover kinetics in response to diet suggests a decrease in the production of triglycerides.
The Association of Psychosocial Risk Factors with Subclinical Atherosclerosis in South Asians
Bijal Shah B.Pharm, Ph.D., Shriraj Shah B.S., Namratha Kandula MD, MPH, Alka Kanaya MD

**Background:** South Asians (individuals from India, Pakistan, Bangladesh, Nepal, and Sri Lanka) are at higher risk of cardiovascular disease (CVD) than other ethnic groups, however this increased risk cannot be explained by traditional risk factors.

**Hypothesis and Aims:** We investigated the association of psychosocial risk factors with carotid intima media thickness (cIMT), a measure of subclinical CVD, in a community-based cohort of South Asians living in the United States.

**Methods:** A total of 906 individuals from the Mediators of Atherosclerosis in South Asians Living in America (MASALA) Study, aged 40-83, were included in this cross-sectional analysis. High resolution B-mode ultrasonography was used to measure right and left common cIMT (CCA) and internal cIMT (ICA). Linear regression analyses were done to test the associations of the following psychosocial variables: anger and anxiety (Spielberger Trait Anger and Anxiety Inventory (STAXI)), depressive symptoms (Center for Epidemiologic Studies (CES-D) scale), current and prior 6-month life stress (Chronic Burden scale), social support index, and everyday hassles scale with CCA and ICA. In a multivariable model, results were adjusted for the following traditional CVD risk factors: age, sex, systolic blood pressure, hypertension medication use, education, physical activity, diabetes, BMI, smoking, and total/HDL cholesterol ratio. Interaction effects between sex and psychosocial variables were also tested.

**Results:** In age- and sex- adjusted analyses, current life stress and life stress over the past 6 months were positively associated with CCA [mean difference per 1-SD increase (CI) was 0.014 (0.001-0.028; p=0.042) and 0.015 (0.001-0.029; p=0.031), respectively], but was no longer significant after adjusting for other CVD covariates. There was a significant sex interaction with anxiety (p=0.044). Among men, anxiety was positively associated with CCA [mean difference per 1-SD increase (CI) was 0.021 (0.001-0.041; p=0.04) in age-adjusted analyses, and 0.022 (0.002-0.042; p=0.031) in a fully adjusted model]. ICA was not associated with any psychosocial factor.

**Conclusions:** Compared to results in other ethnic groups, there was no significant association between trait anger and cIMT in South Asians. Anxiety was associated with CCA independent of traditional CVD risk factors in men alone.
**Background:** As of 2012, Solano County, California has the highest rate of Type 2 Diabetes Mellitus (T2DM) among the 58 California counties. Over 1 in 10 people in Solano County have T2DM. In addition to high rates of T2DM, as of January 2015, 14.3% of Solano County residents are unemployed. Technology is increasingly utilized for teaching diabetes self-management education (DSME) to T2DM patients. Smart phones, e-mails, and interactive websites have been used in other research studies to effectively teach DSME. However, many lower socio-economic status and older patients may not have the access or skills to benefit from this type of technology.

**Aims:** The purpose of this descriptive study is to assess patient preferences in diabetic education opportunities at Solano County Family Health Services Clinic (FHS). With this information, we will better tailor future diabetic education programs at FHS.

**Methods:** Selection criteria for this study included English-speaking patients at FHS in Vallejo 18 years or older with a diagnosis of T2DM. Participants were identified at the time of clinic visit and offered a five-dollar cash stipend. Demographics information and education preferences were read aloud to each participant. Their answers were entered into the computer by a study investigator using Qualtrics software.

**Results:** The study population (N=16), 50% self-identified as male, 50% as female, ranging in ages 39-90 years old (mean age of 61). The average number of years since diagnosis of T2DM was 6.9±4.6 years. Fifty-six percent of participants had never attended formal diabetes education programs since their diagnosis. Twenty-five percent of the study participants had a smart phone and 13% had an iPad or Android tablet. Fifty-eight percent had a computer at home and half reported Internet access. Out of 11 options, the top three preferred methods for receiving diabetic education in order were: individually with a clinician, group visits with other diabetics, and individually with a diabetic educator. Utilizing technology was less favorable and the least preferred way to receive education social media. The top two topics patients wanted more training included nutrition/diet (n=14) and reducing diabetes complications (n=13). Stress reduction ranked the lowest (n=6) of nine potential topics.

**Conclusion:** This preliminary data demonstrates the need for more individual and group diabetes education opportunities at FHS. The utilization of technology including social media would not be an effective option in this study population due to the lack of access. More access to information on reducing diabetes complications and nutrition would be favorable to this study group.
Diabetes literacy, numeracy, & food insecurity in people with Type 2 diabetes at Solano County Family Health Services (Preliminary Report).
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1Touro University College of Osteopathic Medicine, 2Touro University College of Education and Health Sciences

Background: As of 2012, Solano County, California has the highest rate of Type 2 Diabetes Mellitus (T2DM) among the 58 California counties. Over 1 in 10 people in Solano County have T2DM. In addition to high rates of T2DM, as of January 2015, 14.3% of Solano County residents are unemployed. Food security, health literacy and numeracy have been shown to effect diabetes outcome measures including hemoglobin A1c. Food insecurity is defined by the USDA as “having limited availability of nutritionally adequate and safe foods or limited or uncertain ability to acquire acceptable foods in in socially acceptable ways”. Previous studies demonstrated that those with very low food security are more likely to have T2DM. Food insecurity often forces people to purchase lower quality, higher-calorie foods possibly contributing to weight gain and poor control of T2DM. Health literacy is the ability to understand basic health information. Limited levels of health literacy can influence reading prescription instructions, glucose monitoring, and healthy eating. The United Stated Department of Education reports nearly half of adult Americans have limited health literacy. The Vanderbilt 10-item Spoken Knowledge in Low Literacy in Diabetes Scale (SKILLD) is a validated scale to measure diabetes knowledge. Previous studies showed an average score of 49% in a low-literacy indigent population. Diabetes numeracy assesses if a person has the mathematical skills to effectively self-manage diabetes. Diabetes numeracy skills are necessary for diabetics to count carbohydrates, read food labels, adjust insulin levels and administer prescriptions. Those with lower diabetes numeracy scores have poorer health outcomes including higher A1c levels. The Vanderbilt Diabetes Numeracy Test (DNT)-5 is a validated 5-item scale to assess diabetes numeracy.

Aims: The purpose of this descriptive study is to assess patient’s food insecurity, diabetes literacy and numeracy using validated surveys at Solano County Family Health Services Clinic (FHS). With this information, we will better tailor future diabetic care and education programs at FHS.

Methods: Selection criteria for this study included English-speaking patients at FHS in Vallejo 18 years or older with a diagnosis of T2DM. Participants were identified at the time of clinic visit and offered a five-dollar cash stipend. Demographics and the USDA 6-question food insecurity survey were utilized to characterize the patient population. The 10-item Vanderbilt SKILLD scale was used to assess diabetes literacy. The Vanderbilt DNT-5 was used to assess diabetes numeracy skills. The surveys were read aloud to each participant and their answers were entered into the computer by a study investigator using Qualtrics software.

Results: The study population (N=16) self-identified 50% as male, 50% as female with an age range was 39-90 years old (mean age of 61). The average number of years since diagnosis of T2DM was 7±5 years. Fifty-six percent of participants never attended formal diabetes education programs. The majority (n=10) of participants had marginal or high levels of food security per the USDA food insecurity questionnaire. The median score was 2 of 5 and the
mean score was 1.65 of 5 for the DNT-5. The median score was 75% and the mean score was 69% for the SKILLD scale. The item asking what a normal A1c was most frequently missed on SKILLD scale, 75% responded incorrectly. The majority of participants could correctly identify hyperglycemia (n=11) and hypoglycemia symptoms (n=12). One participant did not know how to correct for hypoglycemia.

**Conclusion:** This preliminary data demonstrates the need for more formalized diabetes education programs at FHS. Low numeracy scores from the DNT-5 could have implications for type of treatments utilized in this population. The average SKILLD score at FHS is slightly higher compared to previous research. The DNT-5 and SKILLD scales could be used to help clinicians identify patients in need of additional diabetes interventions. Further research is needed to assess the correlation of food insecurity, DNT-5 and SKILLD scores on patient outcomes at FHS.
Effects of valerian on the standardized field sobriety tests and driving performance.
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Background: The availability of herbal medicines over-the-counter (OTC) has increased the use of natural products for self-treatment. Valerian has been used to treat generalized anxiety disorder and insomnia. Although the active constituents of valerian are not fully understood, studies have discovered that valerenic acid may increase gamma-aminobutyric acid (GABA) levels in the brain. Increased GABA levels have been associated with sedation, which could explain the therapeutic effects of valerian. Many OTC valerian products are standardized to contain 0.8% valerenic acid extracted from the valerian root. There have been contradictory findings regarding valerian’s sedative effects, but it is important to determine if valerian impairs driving performance.

Hypothesis and Aims: The purpose of our study is to determine the effects of a one-time valerian dose on the standardized field sobriety tests (SFSTs) and driving performance utilizing a driving simulator. We hypothesize that a one-time administration of valerian 1600 mg may cause impairment in driving simulator performance and increase SFSTs failure rates.

Methods: This study is a randomized, repeated measures, cross-over, double-blind, placebo-controlled design. After initial assessment, potential participants go through two separate sessions. For each session, participants take a dose of valerian or placebo, allowing 1 hour for absorption. The outcome measures include a simple visual reaction test, subjective sleepiness scales, SFST performance scores, and driving simulator performance measures.

Results: There were no significant differences in the simple visual reaction test or sleepiness scales between placebo and valerian exposures. SFST total and individual test failure rates were also not significantly different between the two exposures. There were no differences on any driving simulator performance parameter between the two groups.

Conclusions: Valerian OTC doses, used for insomnia, have no effect on sleepiness, SFST failure rates or driving performance within 2 hours after ingestion.
The Effects of Regular Marijuana Use on Driving Performance
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Abstract Type: Original Research

Purpose: The 2007 National Roadside Survey reported marijuana as the most common illicit drug quantified in drivers’ blood and oral fluid. Marijuana has been decriminalized in 19 states and Washington DC if recommended by a physician or for any use in 4 states. Therefore it is vital to understand the effects of chronic medical marijuana use on driving performance to protect public safety. This study compared the Standardized Field Sobriety Test (SFST) failure rates and driving simulator performance parameters between chronic medical marijuana users and nonusers.

Methods: The driving performance of 25 marijuana nonusers were compared to 25 medical marijuana users (marijuana use ≥4 days/week). Subjects were adults between the ages of 18-45 years with a valid California driver’s license. A saliva drug screen test was administered to ensure the absence of other drugs of abuse and verify medical marijuana user status. Participants’ driving ability was tested with both the SFST and a driving simulator task using the STISIM Drive® software program (Hawthorne, CA).

Results: There were significant differences between the nonusers and medical marijuana users for baseline characteristics of age, height, weight, and body mass index (BMI). The medical marijuana users were older, taller, heavier, and had a higher BMI than the nonusers. Failure rates for the horizontal gaze nystagmus (HGN) test were 0% for the nonusers and 56% (p<0.0001) for medical marijuana users; walk and turn (WAT) test failures were 8% for nonusers and 52% (p=0.0015) for medical marijuana users, and combined SFST failures were 16% for nonusers and 80% (p<0.0001) for medical marijuana users. There was no difference in any of the driving simulator performance parameters between the two groups.

Conclusions and Future Directions: SFST failure rates were higher for regular medical marijuana users, suggesting they may be more likely to be arrested for “driving under the influence.” In contrast to this finding, no significant differences were observed for STISIM driving simulator performance. Previously, SDLP parameters were significantly different in STISIM studies using acute marijuana exposure. These discrepant results suggest that SFST may potentially overestimate regular marijuana users’ actual driving impairment, which was indistinguishable from nonusers.
Point of care ultrasound training of medical students and primary care physicians for atherosclerotic cardiovascular disease screening.
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As ultrasound use becomes more prevalent in the primary care setting, little resources are available to determine the level of training necessary to prove competency. This study set out to establish a specific training protocol for medical students and primary care physicians with little to no prior ultrasound experience. The training protocol developed represents the first program to train and quantitatively assess competency for abdominal aortic aneurysm (AAA) screening in medical students and primary care physicians. Participants were first introduced to the AAA ultrasound screening procedure by an experienced radiologist and medical student (the authors) using a SONOSIM Export and GE VSCAN portable ultrasound device on several patients. Participants were then allowed time to practice using both the traditional export ultrasound machine and portable VSCAN devices, during which they were guided through the screening procedure. To prove competency, participants completed an online training module, virtual ultrasound simulator cases an online assessment tool, virtual OSCE and performed the full AAA ultrasound exam on three patients that were reviewed by the authors.
Paraoxonase 1 lactonase activity in familial hypercholesterolemia: a pilot study
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Background: The beneficial effects of PON1 on the inhibition of atherosclerosis might be more pronounced in a population that is prone to develop atherosclerosis than the general population. For this reason, we studied the role of PON1 in patients with familial hypercholesterolemia (FH). These patients are characterized by substantially increased serum low density lipoprotein-cholesterol (LDL-C) concentrations and sharply increased CVD risk. The few studies in the literature concentrate on polymorphisms and those that measured activity did not compare with a polygenic hyperlipidemia control population nor they measured the physiological lactonase activity of PON.

Aims: To investigate PON1 esterase and lactonase activity and its distribution in HDL subclasses in a population of FH patients treated with statins.

Methods: Heterozygous FH patients (n=19) and age-matched hyperlipidemic subjects (n=21) also treated with statins were recruited at the lipidology clinic in Jichi Medical School. PON1 arylesterase and lactonase activities were analyzed using phenylacetate or dihydrocoumarin as the substrate, respectively. Lipid profiles were measured using standard methods. PON1 distribution in HDL subclasses was analyzed with our recently published method (1-2): native lipoproteins from serum were separated in a 4-12% gradient gel and PON1 activity was detected in situ using para-nitro-phenylacetate, scanning and densitometry. The study was approved by the Ethics Committee of Jichi and Touro University.

Results: Controls and case did not differ in their TC, LDL-C, HDL-C or TG values. PON1 arylesterase was on average 13 % higher and lactonase was 79% higher in FH patients as compared to controls. The zymogram did not show a different distribution of PON1 in HDL subclasses.

Conclusions: Our pilot data show FH patients seem to have increased levels of a PON1 protein and even higher of its activity: they have more PON1 and it is far more active. We believe that the chance of finding effects of PON1 on CVD increased in a population at high risk for developing atherosclerosis and CVD. Indeed our pilot data suggest that enhanced lipoperoxidation in this condition induces PON1 expression and activity, probably as a protective measure. This difference is not due to statin treatment nor to redistribution within HDL subclasses.

**HMGB1 as a marker for monitoring the postoperative course of patients with colorectal cancer: Preliminary data.**

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**Background:** High-mobility group box 1 (HMGB1), a ubiquitous nuclear protein, has been shown to play a crucial role in several pathophysiological states, such as inflammation and cancer. Even when the incidence of colorectal cancer is increasing there have been only a few studies that focus on HMGB1 and this disease. Overexpression of HMGB1 in cancer tissues is reported to be associated with a poor prognosis in patients with colorectal cancer. No reports exist about whether serum HMGB1 can be a marker suitable for monitoring the postoperative course of patients with colorectal cancer.

**Hypothesis and Aims:** In view of this gap in our knowledge we hypothesized that HMGB1 excursions after colorectal survey are useful for monitoring postoperative recovery. The current study aimed to characterize the postoperative behaviour of serum HMGB1 levels in patients with colorectal cancer, and compare it to other conventional markers used postoperatively, such as blood white blood cell (WBC) counts, C-reactive protein (CRP), and serum amyloid A (SAA).

**Methods:** A total of 18 patients were enrolled in the current study. Patients who required surgery due to advanced colorectal cancers were included. Patients for whom blood examinations could not be conducted at four-time points (pre-surgery, and postoperative day 1, week 1 and week 3) were excluded. Blood was sampled at the above four time points. Peripheral blood WBC counts, serum CRP and SAA levels were measured by standard techniques. Serum HMGB1 levels were measured by an ELISA method (Shino-Test Corp., Kanagawa, Japan). To compare the patients’ levels with control levels, CRP, SAA, and HMGB1 (except for WBC count) levels were measured in age- and sex-matched control subjects.

**Results:** The changes in HMGB1 were significant, with peak levels observed on postoperative day 1 and at postoperative week 1. The HMGB1 levels at pre-surgery, postoperative day 1, and postoperative week 1 (P < 0.01 for all) were significantly higher than those at postoperative week 3. The highest WBC levels occurred on postoperative day 1. Unlike the WBC levels, the peak CRP and SAA levels occurred at postoperative week 1. They were then lower at postoperative week 3.

**Conclusions:** The present study confirmed significant changes in serum HMGB1 levels after colorectal surgery in colorectal cancer patients, with the peak serum HMGB1 level observed on postoperative day 1 and postoperative week 1. The changes differed from those of the other conventional markers (WBC, CRP, and SAA). The findings suggest that HMGB1 may be a unique marker for monitoring the postoperative course in such patients with colorectal surgery. Future work is warranted to establish the applications of serum HMGB1 to colorectal surgery practice.
Low protective PON1 lactonase activity in an Arab population with high rates of coronary heart disease and diabetes

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**Background:** Recent studies showing that high density lipoproteins (HDL) can effect plaque regression indicate that recent trial failures do not exclude an atheroprotective role of HDL. Instead, they highlight differences between HDL function and measured HDL-cholesterol (HDL-C). PON1 is one key functional activity of HDL. Urban Palestinians have lower HDL-C and a higher incidence and mortality from coronary heart disease than Israelis.

**Hypothesis and Aims:** We hypothesized that the cardioprotective PON1 lactonase and arylesterase activities and PON1 functional genotype may differ between Palestinians and Israelis.

**Methods:** We measured PON1 activities in a cross-sectional population-based study of Palestinian (n=960) and Israeli (n=694) residents of Jerusalem, 1654 participants in all.

**Results:** Palestinians had high prevalences of obesity and diabetes and low mean concentrations of HDL-cholesterol (0.97 mmol/l in men and 1.19 mmol/l in women). Lactonase and arylesterase activities were lower by 10.8% (p=1.2*10^{-14}) and 2.7% (p<0.0005), respectively, in Palestinians as compared to Israelis. The functional genotype distribution, demonstrated by plotting paraoxonase vs lactonase activities, showed a modest between-group difference (p=0.024), with 12.1% RR in Palestinian Arabs vs 8.4% in Israeli Jews, but no overall difference in allele frequencies. Lactonase correlated inversely with age (Spearman’s rho = -.156), weakly with BMI (-.059), positively with HDL-C (.173) and non-HDL-C (.103), but was not associated with triglycerides or fasting glucose. Palestinians showed consistently lower lactonase activity in logistic regression models adjusted for multiple covariates and for functional genotype (odds ratios of 1.81 and 1.98, respectively, for the lower fifth vs the upper 4 fifths of lactonase activity P<0.0001).

**Conclusions:** We showed a lower physiologically-significant lactonase PON1 activity in an Arab population, a finding consistent with the high cardiovascular and diabetes risk of Palestinians.
Postprandial Paraoxonase 1 Lactonase Activity Excursions in Healthy Men: Association with Triglycerides and HDL-C
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Background: Postprandial hypertriglyceridemia is regarded as an independent risk factor for atherosclerosis. The oxidative stress caused by increased postprandial triglyceride (TG) creates an atherogenic environment. Paraoxonase 1 (PON1) is considered to be responsible for most of the antioxidant properties of high density lipoprotein, and lactonase activity is considered to be physiologically relevant to the activity of PON1. However, postprandial PON1 activity changes after consuming an ordinary meal have yet to be clarified.

Aims: To evaluate the postprandial responses of lipid and PON1 lactonase and arylesterase activities after consumption of recommended amounts of mixed meals in healthy men.

Methods: Nine healthy male volunteers consumed three different meals in random order on separate days. The test meals were as follows: S) white rice; SMF) addition of fat-containing protein-rich main dishes to the S meal; SMFV) addition of vegetables to the SMF meal. Serum concentrations of lipid parameters and PON1 lactonase and arylesterase activities were determined at several time points during a 3 h period after consumption of these meals.

Results: PON1 lactonase activity decreased after consumption of each of the test meals as compared with the fasted state (p < 0.05). In contrast, arylesterase activity increased after each of the test meals as compared with the fasted state (p < 0.05) No significant differences in postprandial responses were observed for PON1 lactonase and arylesterase activities among the 3 test meals. Lactonase/HDL-C decreased but arylesterase/HDL-C increased after consumption of each of the test meals. On the other hand, the lactonase/TG and arylesterase/TG ratios did not change after the S meal. Both lactonase/TG and arylesterase/TG decreased after the SMFV meal (p < 0.05) and tended to decrease after the SMF meal (p = 0.063) as compared with those after the S meal at 120 and 180 min.

Conclusions: This is the first study, to our knowledge, to measure postprandial PON1 lactonase activity after the consumption of routine mixed meals in amounts corresponding to ordinary dietary intakes. Postprandial PON1 lactonase activity decreased while PON1 arylesterase activity increased. These inverse changes were also observed in the ratios of PON1 lactonase

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and PON1 arylesterase activities to HDL-C. Although the postprandial changes in PON1 lactonase and arylesterase activities did not differ among test meals, lactonase/TG and arylesterase/TG ratios decreased after consumption of the mixed meal containing fat as compared with those after the meal consisting only of white rice. These findings are potentially useful for clarifying postprandial PON1 responses after consumption of an ordinary meal.
Optimized zymogram to study PON1 in HDL subclasses shows functional changes in HDL in acute inflammation: a pilot study.
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Background: Solving the HDL paradox will necessitate the development of techniques to explore HDL function that are practical and well adapted to clinical studies and eventually become useful in patient monitoring. PON1 is a key player in HDL function and its activity is modified by inflammation/acute phase. To make some inroads into studying active PON1 distribution across HDL subclasses we had previously developed a zymogram method that we validated and employed in several studies [1-5].

Aims: To modify and optimize our method and employ it in a pilot study to explore HDL PON1 function changes in acute inflammation, as a model we employed post cerebrovascular accident (CVA) patients.

Methods: Native lipoproteins from serum are separated in a 4-12% gradient gel and activity is detected in situ using para-nitro-phenylacetate, scanning and densitometry. A total of 10 patients (men/women = 6/4, mean age 66.0 ± 12.0 years), diagnosed with ischemic CVA were studied. The study was approved by the Ethics Committee of Showa University. Blood examinations were performed at 3 sequential points (i.e., admission, 1 day, 7 days).

Results: The new method allows for a 1 step, shorter zymogram process as compared to our previous procedure that needed a coupled reaction. When we applied it to acute post-CVA patients the method shows that the significant drops in PON1 1 day after the event (25 +/- 7 %, p 0.03) correspond to changes in PON1 distribution in HDL subclasses or to specific loss of activity in very large and very small HDL. The changes are more apparent for HDL3, with recovery after one week paralleled by changes in CRP.

Conclusions: We have developed a practical, 1 step zymogram method to measure PON1 activity in HDL subclasses. With this tool the effects of inflammation on HDL antioxidant function can be followed up. Our pilot data show quick deleterious effects of acute phase and inflammation on PON1 distribution in HDL particles


Effect of hemodialysis on oxidative stress in end-stage renal disease: preliminary report.
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Background: The major cause of mortality in patients with end-stage renal disease (ESRD) receiving renal replacement therapy is cardiovascular disease associated with oxidative stress. Uric acid is an important plasma antioxidant that is not present in hemodialysis (HD) fluids, so the procedure leads to wide excursions of urate. These may then change the delicate balance pro-oxidant/antioxidant of urate in a cyclic, pro-oxidant fashion. Another player in the antioxidant system in plasma is HDL, which is not only important in reverse cholesterol transport but has the ability to protect low-density lipoprotein (LDL) against oxidation, is an anti-inflammatory mediator, protects the endothelium, and modulates coagulation. There is mounting evidence that paraoxonase 1 (PON1) could be implicated in several of these processes.

Hypothesis and Aims: We hypothesize that HD-induced cyclical, fast and large excursions in urate are associated with changes in plasma total antioxidant capacity which may explain part of the increased oxidative stress in these patients while PON1 may display a protective effect. We set out to explore these excursions as well as PON1 activity in these patients.

Methods: For this preliminary study 47 ESRD patients on HD were selected from the patient population at KSOSN (Kidney Specialists of Southern Nevada). Blood was drawn at initiation of HD and upon completion of HD. Measurements were repeated once either 1 or 2 months after the first sample. Total antioxidant capacity of plasma or serum (TAOC) was measured with an assay that relies on the ability of antioxidants in the sample to inhibit the oxidation of ABTS⁺ (2,2'-azino-di-[3-ethylbenzthiazoline sulphonate]) to ABTS⁺ · + by metmyoglobin. Serum PON1 arylesterase activity was kinetically measured using phenylacetate as a substrate at 37°C, and the absorbance changes are recorded at 270 nm. The PON1 lactonase activity was kinetically measured using dihydroxycoumarin (DHC) as a substrate at 37°C, and recorded at 270 nm. We employ a Versamax Microplate Reader (Molecular Diagnostics, CA, USA). Other covariates assayed locally to monitor treatment (electrolytes, BUN, creatinine).

Results: We have analyzed 18 subjects so far. Uric acid decreased significantly with a delta of 5.35 +/-1.97 mg/dL, p= 9 x 10⁻⁹. TAOC decreased by 10% from 2.34 +/- 0.32 mmol/L to 2.13 +/- 0.21 mmol/L (P+ 0.03). Arylesterase and lactonase activities were lower than those found in our lab for healthy subjects. Both activities displayed a trend to increase after dialysis. Notably some subjects show up to 20% increase while others show no improvement.
Conclusions: Our preliminary data support our hypothesis: TAOC decreases after dialysis as uric acid is depleted, showing the increase in oxidative stress generated by the procedure. The magnitude of the change in TAOC is less than expected from the uric acid changes, suggesting other antioxidant systems may be compensating. The likely changes in PON1 activity point to one mechanism for this compensation. Ongoing analysis of the whole cohort as well as correlations (deltas and dialysis efficiency parameters) will shed more light on this complex equilibrium.
Evaluation of Bispectral Index as an Adjunctive Measure of Sedation in Therapeutically Paralyzed Patients in the ICU
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Background: The risk of awareness throughout therapeutic paralysis is principally due to limitations of concurrent sedation assessment by behavioral methods. Bispectral index (BIS™) provides an objective measure of sedation; however, the role of BIS is not well defined for ICU patients on neuromuscular blocking agents (NMBA).

Hypothesis and Aims: The purpose of this study was to delineate the relationship between BIS™ and level of sedation for critically ill patients during therapeutic paralysis. The study hypothesis is that BIS less than 60 is predictive of deep sedation.

Methods: This was a retrospective observational study conducted in ICU patients receiving continuous infusion NMBA and BIS™ monitoring. The primary endpoint was sensitivity of BIS™ less than 60—signaling general anesthesia—while on NMBA therapy in predicting a deep to un-arousable level of sedation (RASS -4 to -5) upon emergence from paralysis.

Results: Thirty-one patients were included in this study. The sensitivity and positive predictive value of BIS™ less than 60 in predicting deep sedation (RASS -4 to -5) was 100% (95%CI 0 to 100%) with positive predictive value of 55.6%. The sensitivity and positive predictive value of BIS™ less than 60 in predicting light sedation or deeper (RASS -2 to -5) was 92.9% (95%CI 83.3 to 100%). The specificity of BIS™ greater than or equal to 60 in predicting inadequate sedation (RASS -1 to +4) was 33.3% (95%CI 0 to 86.7%).

Conclusions: Approximately 8 in 10 patients with BIS™ consistent with general anesthesia during therapeutic paralysis were lightly sedated to un-arousable upon emergence from paralysis.
Patient Preferences for Diabetes Education
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**Background:** Despite clear benefits of diabetes education only 6% of people with diabetes ever receive diabetes education. There are a myriad of reasons for the gap in this training. The setting and mode of education may be one of the barriers to getting education.

**Hypothesis and Aims:** Patients would prefer to get a mixture of methods to receive diabetes education. This exploratory study will examine patient preferences in order to develop a more patient centered diabetes education experience.

**Methods:** Using a convenience the investigators surveyed people presenting to a diabetes specialty center. The survey included population demographics and specifics about patient preferences to the setting and location of diabetes education. Participants were invited to join a focus group at a later time after completing the survey. Focus groups were held by a researcher and CDE but without the provider. Transcripts form the focus groups were used to advise further patient preferences.

**Results:** Thus far, 85 surveys have been completed. Almost half, 44% of participants, prefer a combination of education (the combination can include in person private or in person group, or web based on either a home computer or tablet) with 50% preferring a web-based education being incorporated into the education. Focus groups results found that participants prefer online education but they would also like some way to follow up with questions or concerns they may have. Further, participants believe the educational should be no longer than 15 minutes and in its simplest form. Lastly, participants want to know why the information is important and why they need to take the information into consideration for the care of their diabetes.

**Conclusions:** In this population patients want a variety of modes and settings for diabetes education. These patient centric type studies can improve the ability to reach more people who need diabetes education.
Medically supervised fasting followed by low carb diet for extreme insulin resistance
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**Background:** People with type 2 diabetes (T2DM) are maximally insulin resistant at diagnosis. Often insulin is needed for hyperglycemia treatment but may feed the insulin resistance.

**Objective:** To evaluate the effectiveness of an outpatient supervised dietary fast protocol followed by a low carbohydrate diet in improving glucose control in extremely insulin resistant patients with T2DM.

**Methods:** Obese, extremely insulin resistant T2DM patients at a single center were fasted for 48 to 72 hours, then transferred to a high protein/low carbohydrate diet for one month, then attempted to maintain a modified ADA diet for a year. Total daily dose of insulin, weight and hemoglobin A1c (A1c) were measured at baseline, 3, 6, and 12 months post-fast.

**Results:** Thirty six patients completed the 72-h fast. Mean HbA1c for the entire group decreased from 9.5% at onset to 8.5% at 3 months, 6 months, and 12 months post-fast. The average daily insulin dose decreased from 160 units initially to 127 units at 3 months and 6 months and increase to 156 units’ average per day at 12 months. Mean weight decreased initially from 249 lbs. to 236 lbs. at 3 months (-5%), 245 lbs. at 6 months but returned to pre-fasting weigh (249 lbs.) at 12 months. Ten of the 36 were considered “responders” and exhibited significant, fairly sustained improvement while the others returned to near base-line in all parameters at one year.

**Conclusion:** A short-term fast followed by high protein/low carb diet improves glycemic control and reduces insulin requirements short-term. However, most of the parameters measured reverted to baseline at one year. Additional interventions need to be added to maintain these short-term improvements or to find the best way to identify prospectively the “responders”.

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Effect of Pre-Exercise Osteopathic Manipulative Treatment on Blood Lactate Accumulation and Clearance After High Intensity Exercise: PILOT STUDY

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**Background:** Metabolic conditions resulting in elevated tissue and blood lactate/H\textsuperscript{+} levels are associated with muscle fatigue (e.g. intense exercise) and metabolic lactic acidosis (e.g. hypoxemia). Thus, examining factors influencing lactate accumulation and identifying interventions that delay lactate accumulation or facilitate clearance through the Cori cycle and uptake by certain tissues as respiratory fuels (heart, brain, oxidative skeletal muscle fibers) is physiologically and clinically important areas of investigation. However, identifying these mechanisms is complex. For instance, maintaining muscle blood flow and contractile activity through continuation of low intensity physical activity after high intensity exercise (active recovery) significantly accelerates lactate clearance compared to sedentary rest (passive recovery). However, massage treatment targeting similar mechanisms does not. Interestingly, data from our studies examining the impact of post-exercise Osteopathic Manipulative Treatment (OMT) on lactate clearance showed distinct patterns of lactate clearance compared to control and active recovery groups following a bout of high intensity cycling exercise. Furthermore, results from our most recent study suggest different patterns of lactate clearance between subjects who undergo pre-exercise versus to post-exercise OMT.

**Hypothesis and Aims:** The aims of the present pilot study are (1) to examine whether addition of pelvic and lower extremity manipulation to the pre-exercise OMT regimen will further distinguish this pattern of lactate accumulation and clearance from other interventions and (2) to assay plasma glucose levels in parallel with blood lactate throughout the time course to compare and contrast the dynamics of these respiratory fuels in response to OMT. Our hypotheses are that (1) pre-exercise OMT including lower limb treatments results in lower peak post-exercise lactate levels and faster overall clearance compared to non-OMT treated subjects and (2) plasma glucose fluctuation over the time course will be less in pre-exercise OMT versus non-OMT subjects.

**Methods:** After determining resting blood lactate (Lactate Plus-Nova Biomedical) and blood glucose (Abbott Freestyle Freedom Blood Glucose Metering System), subjects will either (1) rest in a supine position on an OMT table for 20 min. or (2) receive a 15-20 min OMT regimen prescribed to optimize tissue lymphatic flow and vascular and autonomic tone such that oxidative metabolic conditions in muscle are prolonged during the exercise period. Following rest or OMT, each subject will perform three sets of progressive resistance recumbent cycling to maximum effort with 2-min rests in between sets. Immediately after the last set, blood lactate and glucose will be measured and subjects will rest quietly in a supine position. Thereafter, lactate and glucose will be assayed at 10-15 min intervals for 60 min. Peak lactate level and clearance time course will be determined during the recovery period and statistically analyzed for group differences.
Results: Results in progress.

Conclusions: Data from this proposed study may lead to a better understanding of mechanisms underlying lactate clearance, exercise recovery, and the benefits of OMT. (TUC IRB approval M-0412)
Effect of sodium and fluid exposure on serum sodium and creatinine levels in patients with intracranial hypertension

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Background: Cerebral edema and intracranial hypertension (ICH) are common complications of traumatic brain injuries (TBI), subarachnoid (SAH), intracranial hemorrhage (ICH), and intracranial malignancy. Hypertonic saline (HTS) is used to mitigate cerebral ischemia by reducing intracranial pressure (ICP) and improving cerebral blood flow. The effects of continuous infusion HTS on ICP appear to be limited and contradictory. There are safety concerns with chloride-rich fluids and possible association with kidney damage.

Hypothesis and Aims: The purpose of the study was to determine the effect of sodium exposure on the serum sodium and creatinine levels in patients with ICH.

Methods: This was a retrospective observational study of adult ICU patients study (01/12 – 11/13) that received 3% NaCl continuous infusion for intracranial hypertension. Patients were excluded that had stage 5 chronic kidney disease (CKD-5), SIADH, cerebral salt wasting syndrome or diabetes insipidus. A sample size of 95 subjects was identified to detect a correlation of 0.3 or greater (alpha 0.05) using 80% power.

Results: Serum sodium concentration increased by 0.51 mEq/liter for every liter of 3% NaCl that was infused, assuming 0.9% NaCl was held constant (p-value=0.0139). For every liter of 0.9% HS, there was a 0.1898 mEq/liter increase in plasma sodium concentration, assuming 3% NaCl was held constant (p-value=0.0047). There was no observed correlation between net fluid exposure and plasma sodium concentration (p= 0.8834) or the cumulative fluid exposure and plasma sodium concentration (p=0.2329). The prevalence of AKI was 12% (6/50) for patients that received 3% NaCl via continuous infusion.

Conclusions: The total volume of 3% HTS and 0.9% NaCl appear to have an incremental effect on serum sodium levels. There was a substantial rate of AKI; chloride exposure did NOT appear to affect the overall risk.
HbA1c Non-Use in the Inpatient Hospital Setting: A Missed Opportunity for Hyperglycemia Detection
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Background: Nearly 90% of those with pre-diabetes and 1/3 of those with type 2 diabetes do not know that they have it. Often people will present with elevated glucose in the emergency room but will not have this evaluated as it is assumed it is stress hyperglycemia. The HbA1c test obtained in the inpatient-setting offers an opportunity for early diabetes detection, which in turn can lead to earlier intervention thereby reducing the likelihood of end-organ damage.

Objective and Aims: This retrospective study evaluated the follow up of people who presented to the emergency room and hospital and who had hyperglycemia.

Methods: This chart review was obtained after obtaining hospital and pharmacy records that included a diagnosis of diabetes, elevated glucose lab value or use of a hyperglycemic medication. Outpatient ER visits, same day surgery, obstetrics and newborn nursery admissions were excluded.

Results: A total of 348 independent patients’ records were reviewed. Fifty patients had hospital hyperglycemia (and an HbA1c) with no known history of diabetes. Of these, 6 (12%) had an HbA1c diagnosis of pre-diabetes, and 18 (36%) had an HbA1c value diagnostic of diabetes. The mean HbA1c in the group with hyperglycemia but no known diabetes was 8.4% compared to an HbA1c of 8.1% for the entire group and 8.0% for those with known diabetes.

Conclusions: In this small study, the use of an HbA1c testing was useful to distinguish spontaneous and transient hospital hyperglycemia from occult pre-diabetes and diabetes. The results of this study urge more careful identification of the etiology of inpatient hyperglycemia.
INSPIRE Diabetes: A pulse of basal bolus analog insulin as the first treatment of type 2 diabetes
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Background: Most people with type 2 diabetes (T2DM) require increasing medication over time to maintain glucose control due to progressive beta cell failure. However, with this therapy only about half attain target glucose control.

Hypothesis and Aims: INSPIRE Diabetes is a multicenter randomized open label clinical trial that evaluated the treatment of adults with newly diagnosed T2DM. Primary outcome was time to rescue therapy and need for rescue therapy. Secondary outcomes included HbA1c reduction, hypoglycemia rates, beta cell function and insulin resistance based on OGTT.

Methods: Participants (23) were randomized to: (1) a pulse of basal bolus analog insulin (glargine, glulisine) that was used for a total of 12 weeks with weight based initiation and twice weekly titration with forced down titration (EIT) versus; (2) intensive oral therapy (IOT) as recommended by the 2009 ADA treatment recommendations-metformin, glimepiride, pioglitazone with monthly titration for 15 months or oral therapy.

Results: There was no difference in time to rescue (16.4 weeks RC vs 24.0 weeks EIT) or need for rescue therapy (2/10 RC vs 6/13 EIT). The A1c at baseline was 10.1% +/- 1.2% RC vs 9.9% +/- 1.2% EIT. This improved to 7.01% +/- 0.8 IOT vs. 6.7% +/- 0.8 EIT. At 15 months A1c for IOT was 6.7% +/-0.8 and EIT 6.8% +/-0.4%. The EIT group lost weight (2.4 kg) vs weight gain of 2.1 kg for IOT (NS). When excluding participants with a BMI >50 the EIT arm lost significantly more weight than IOT (p<0.05). The EIT group also had significantly higher fasting and stimulated c-peptide levels (p<0.001). There were only 10 hypoglycemic episodes in the study (7 EIT, 3 IOT) and zero severe hypoglycemic episodes.

Conclusions: Twelve weeks of EIT was as effective as IOT for people with newly diagnosed T2DM and is not associated with the weight gain and hypoglycemia seen later in the disease. Further, there is some evidence that EIT improves beta cell function over 15 months. This study is limited by its size and the dramatic response in the IOT. EIT produced not only rapid control of glucose but may have a legacy effect on beta cell function.
Effects of Emtricitabine/Tenofovir on Bone Mineral Density in HIV-Negative Persons in a Randomized, Double-Blind, Placebo-Controlled International Trial

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Background: Pre-exposure prophylaxis (PrEP) with once-daily oral emtricitabine and tenofovir disoproxil fumarate (FTC/TDF) decreases the risk of HIV acquisition. In HIV-infected people, initiation of TDF as part of combination antiretroviral therapy decreases bone mineral density (BMD). However, HIV infection itself, immune activation, and other antiretroviral drugs can also decrease BMD.

Aim: To determine the effect FTC/TDF on BMD in the absence of HIV infection and assess the potential risk of bone loss associated with use of FTC/TDF for HIV prevention.

Methods: BMD was measured by dual-energy X-ray absorptiometry at baseline and 24-week intervals in a randomized, double-blind, placebo-controlled trial of FTC/TDF PrEP in high-risk men who have sex with men. Plasma and intracellular tenofovir concentrations were measured in those randomized to FTC/TDF as a measure of adherence.

Results: A total of 498 participants (247 FTC/TDF, 251 placebo) enrolled in five cities on four continents. More than half were age 25 years or less, and more than half were Hispanic. By intent-to-treat analysis, BMD in those randomized to FTC/TDF decreased modestly but statistically significantly by 24 weeks in the spine (net difference -0.91 [-1.44 to -0.38]%, P=0.001) and hip (-0.61 [-0.96 to -0.27]%, P=0.001). Changes within each subsequent 24-week interval were not statistically significant. Changes in BMD by week 24 correlated inversely with intracellular tenofovir diphosphate (TFV-DP), which was detected in only 53% of those randomized to FTC/TDF. Net BMD loss by week 24 in participants with TFV-DP levels indicative of consistent dosing averaged -1.42±29% and -0.85±19% in the spine and hip, respectively (P<0.001 vs. placebo). Spine BMD tended to rebound following discontinuation of FTC/TDF. There were no differences in fractures (P=0.62) or incidence of low BMD.

Conclusions: In HIV-uninfected persons, use of FTC/TDF for PrEP was associated with small but statistically significant decreases in BMD by week 24 that inversely correlated with intracellular drug levels. These results demonstrate an effect of FTC/TDF on BMD that is independent of HIV infection and other antiretroviral therapy. The relatively small bone loss associated with FTC/TDF PrEP is offset by the prevention of HIV infection.

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Background: Prediabetes is estimated to affect 37% of American adults over the age of 20, yet fewer than 10% have been diagnosed.¹ Progression from prediabetes to diabetes can take as little as 5 years.² There is strong evidence that a robust lifestyle intervention can effectively delay or prevent the conversion to diabetes (Diabetes Prevention Program). The CDC has charged healthcare professionals to focus on prediabetes detection, which may prove burdensome to the average primary care practice. Community pharmacists have both the training and opportunity to improve prediabetes detection.

Hypothesis and Aims: Hypothesis: Prediabetic patients can be distinguished from the non-diabetic population through non-invasive biometric measures with a certain level of accuracy.

Aims: 1) Develop a prediction algorithm for prediabetes based on those measures (age, gender, ethnicity, height, weight, waist circumference, blood pressure, personal and family health history, and inspection for acanthosis nigricans of the posterior neck) and validate the algorithm with point-of-care hemoglobin A1C testing. 2) Provide guidance for policy makers to develop replicable and reimbursable pharmacist-delivered prediabetes screening and lifestyle intervention services in the community pharmacy setting.

Methods: The study was conducted in several Albertson Safeway pharmacies in Northern California. After obtaining consent from volunteers who were over age 18 and reported no prior prediabetes or diabetes diagnosis, pharmacists collected information including age, gender, race/ethnicity, height, weight, waist circumference, blood pressure, personal and family health history, and evidence of acanthosis nigricans of the posterior neck. A1C was measured using a finger stick (point-of-care) A1C test.

Results: Among the total of 127 patients recruited in different pharmacies, the majority (67.7%) were found to have a normal A1C <5.7%, 26.8% were identified as prediabetic with an A1C between 5.7% and 6.4, and 4 patients (3.1%) were identified as diabetic with an A1c>6.5%; an A1C was not recorded for 3 patients. Compared to the non-diabetic group, the prediabetic group is significantly older (47.38 (16.02) vs 40.6(15.57), p=0.04166), has a larger proportion of males (47% vs. 33.3%), and has a larger percentage of whites (38.2% vs 31.5%). Those with prediabetes also have higher systolic blood pressure (126.21(16.83) vs. 121.71(19.6)) and diastolic blood pressure (79.56 (10.8 ) vs. 75.71(13.36) ), as well as a larger proportion of overweight patients with BMI>25 (64.7% VS 32.6%), although the difference is not statistically significant. The female prediabetic patients have a higher proportion of abdominal obesity than their normal counterparts (55.6% vs. 39.6%); similarly the male prediabetic patients have a higher percentage of abdominal obesity than their normal counterpart (26.7% vs. 20.%). The prediabetic group also shows higher risk for diabetes in terms of lifestyle factors such as hours of sitting per day and hours of exercise per week. However, none of those factors shows a
statistical difference. The self-reported family history of diabetes is 29.4% for the prediabetic group and 27.8% for the non-diabetic one. Similarly, inspection for acanthosis nigricans did not yield a statistically different result.

**Conclusions:** The prevalence of prediabetes identified in the study is lower than the CDC’s estimate of 37%. This is partly due to the small sample size of the study as a result of difficulty in recruiting volunteer patients in already busy pharmacy settings. Although there are no statistically significant differences identified between the two groups based on commonly used risk factors, the data suggest those at greatest risk for prediabetes share one or more of the following characteristics: older age, male gender, white, overweight, positive family history of diabetes, more hours sitting, fewer hours exercising. From a clinical aspect, assessment of blood pressure and inspection for acanthosis nigricans were not useful. Overall, the study tends to support the feasibility of implementing a similar non-invasive screening program in community pharmacies, and its capacity to identify prediabetic patients. However, it might involve additional training for pharmacists and resetting logistic around workflow in pharmacy to scale up the screening intervention.

**Sources:**


The Relationship between Emotional Distress Levels Relating to Diabetes and Risk of Developing Cardiovascular Complications in a Type-2 Diabetic Population with a Lower Socioeconomic Status
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Background: Diabetes induces stress in those who live every day with this diagnosis. This induced stress may be especially acute in the socioeconomically disadvantaged patients, since the low socioeconomic status (SES) itself creates distress for patients. Patients with low SES have limited access to resources to support their diabetes management, which in turn might lead to less-than-optimal clinical outcomes. Our study, therefore, was performed in patients at a safety-net clinic, aiming to decipher the relationship between the diabetes-induced emotional distress and the risks of cardiovascular complications relating to diabetes. Results of the Diabetes Attitudes Wishes and Needs (DAWN) 2™ study – obtained from administering the Problem Areas in Diabetes (PAID) questionnaire – identified that many aspects of the quality of life for individuals with diabetes are negatively impacted by the diabetes diagnosis. The results also revealed that at least 50% of diabetic patients expressed that their diabetes diagnosis generated negative impacts on their physical health and on their emotional well-being. Patients’ emotional distress levels may play an important role in determining individuals’ abilities to assume the rigorous behavioral demands required in managing Type-2 diabetes. The PAID questionnaire helps identify emotional distress in diabetic patients, so we asked whether results from this survey are associated with the estimated 10-year cardiovascular complication risks relating to diabetes and whether these survey results are also related to patients’ socioeconomic statuses. Any such associations would further demonstrate the clinical utility of the PAID questionnaire, since it would now be employed in a non-specialist setting with patients from a variety of socioeconomic and ethnic backgrounds. Identifying psychological challenges may enhance health care providers’ ability to help patients successfully navigate through the stressors associated with diabetes management, which may ultimately help minimize complications resulting from uncontrolled diabetes.

Hypothesis and Aims: The purposes of this study are (1) to discover the relationship between the PAID emotional distress levels in managing Type-2 diabetes and the risks of developing cardiovascular complications (e.g., coronary heart disease and stroke; fatal and non-fatal) relating to diabetes; (2) to predict the relationship between emotional distress levels in managing Type-2 diabetes and diabetes management outcomes parameters (e.g., HbA1c, blood pressure, and total cholesterol); (3) to discover how occupational status (as a proxy to indicate socioeconomic status) impacts diabetes management outcomes parameters and risks of developing cardiovascular complications. We thus hypothesize that diabetic patients’ emotional distress levels and their socioeconomic statuses exhibit an association with their risks of developing cardiovascular complications; in addition, we also hypothesize that a patient’s A1c highly associates with their diabetes-induced emotional distress.

Methods: This is a cross-sectional, survey-base study, utilizing the PAID questionnaire to identify diabetic patients’ emotional well-being at LifeLong Medical Center in East Oakland. Patients were asked to complete the PAID questionnaire, and the UK Prospective Diabetes
Study (UKPDS) Risk Engine 2.0 calculator, which required patients’ laboratory parameters, was also employed for estimating the 10-year cardiovascular complication risks. Additionally, the Nam-Power-Boyd Occupational Status Scale was used to identify patients’ socioeconomic status. To determine if the data from the latter two data sets were associated with the PAID questionnaire items, regressional analyses (e.g., linear regression and multiple linear regression) were performed.

**Results:** During the preliminary phase, thirty-six participants were enrolled into the study. Results from the four separate simple linear regression performed on the total PAID Scale score with each of the cardiovascular complication risks predicted by the UKPDS Risk Engine 2.0 calculator showed that non-fatal and fatal coronary heart disease might be associated positively with the PAID Scale score (cannot be confirmed having a statistical significance at this point). The regressional coefficient between the risks of non-fatal coronary heart disease (CHD) and the PAID Scale score was 0.136 (p = 0.066), meaning for each one-point increase in the PAID Scale score, non-fatal CHD risk increased by 0.136%. In addition, the regressional coefficient between the risks of fatal CHD and the PAID Scale score was 0.119 (p = 0.066), suggesting that for each one-point increase in the PAID Scale score, fatal CHD risk increased by 0.119%. No such pattern was observed between the risks of stroke and the total PAID Scale score. An association might also exist between the total PAID Scale score and participants’ laboratory parameters related to diabetes (again, cannot be confirmed having a statistical significance at this point). A multiple linear regressional test was performed on the total PAID Scale score with participants’ diabetes management outcomes parameters (e.g., total cholesterol, HDL, LDL, triglyceride, A1c, systolic blood pressure). Among these parameters, the regressional coefficient – without taking into account the Nam-Power-Boyd Occupational Status Scale score – between the PAID Scale score and A1c was 3.80 (p = 0.063), showing for each one-percent increase in A1c (controlling for all other parameters), the total PAID Scale score increased by 3.80 points. After including the Occupational Status Scale score, the regressional coefficient was similar at 3.74 (p = 0.068).

**Conclusions:** Although at this point, all the aforementioned associations identified by the regressional analyses are not proven to be statistically significant; however, all the p-values are trending towards showing statistically significant results. The less-than-significant p-values might have been contributed by the inadequate sample size, so the next step would be to continue enrolling participants into the study and monitoring regressional coefficients and their corresponding p-values. In addition, a more thorough chart review is needed for collecting the following data: BMI, exact age, insulin status, number of insulin used, number of active medications, number of diabetes medications, number of active medical problems, and residential locations. With a larger sample size and more parameters being included for each participant, stronger degrees of association between the 10-year cardiovascular complication risks and the total PAID Scale scores will be identified.
Exploration of Patient and Care Characteristics that Heighten Risk for Readmission among Congestive Heart Failure Patients
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Background: Unplanned re-hospitalizations result in Medicare costs in excess of $17 billion annually. Among the disease states that are associated with heightened readmission risk, those with heart failure are commonly associated with the most frequent re-hospitalizations. Due to the high rate of unplanned re-hospitalizations in patients with heart failure, predictive models are needed to identify patients who are at high risk for readmission.

Objective: To evaluate the diagnosis and timing of 45 days readmissions and to identify patient and care characteristics associated with readmissions among patients with an index visit for heart failure.

Methods: We utilized electronic health records to study 2,420 index admissions for heart failure at a single acute care institution from October 2008 to October 2014. Among those included were patients with a coded primary discharge diagnosis consistent with heart failure. Descriptive statistics were used to compare the readmitted and non-readmitted cohorts. Logistic regression was used to develop a predictive model to assess which patient and care variables were associated with 45 day readmission.

Results: The mean age of the study cohort was 77 years and 55% were males. The majority of the population was white (55%), married (42%), and currently not employed (91%) with 68% utilizing a Medicare payer. Over the study time period we identified 500 (20.7%) 45-day readmissions after 2,420 hospitalizations for heart failure. The three most common causes for readmission were heart failure (36.4%), renal disorders (8.2%), and other cardiac diseases (6%). Consecutive analysis showed that 9.4% of patients readmitted during days 0-3, 12% during days 4-7, 24.8% during days 8-15, 32.6% during days 16-30, and 21.2% during days 31-45.

Conclusion: This study will provide a deeper understanding of patient and care characteristics that are associated with 45 day readmissions after index hospitalization. Evaluation of these characteristics will provide additional information to guide clinical strategies meant to reduce readmission rates among heart failure patients.
A Study on the Effects of Corticosteroids on the Blood Glucose of Inpatients and the Effects of Insulin Protocol for Steroid-Induced Hyperglycemia in the Hospital Setting
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AIMS: To compare a NPH based hyperglycemic treatment regimen to routine insulin management for inpatients with glucocorticoid induced hyperglycemia. To compare these regimens in those with known diabetes versus those with no history of diabetes.

METHODS: Randomized nonblinded pilot study. Patients were randomized either to the experimental NPH insulin group or the routine care group (physicians choice insulin regimen-basal-bolus or correction scale). The initial dose of NPH for steroid-induced hyperglycemia was 0.1 unit/kg/dose regardless of the patient’s diabetes history. This dose is given concomitantly with each corticosteroid dose. The data was analyzed with Linear Mixed-Effects Regression (LMER) modeling. Data were presented in the text below as mean±SD unless stated otherwise. In all analyses, the treatment (NPH vs. Control) was the independent variable. Gender, weight, diabetic or non-diabetic status, and baseline glucose levels were included as covariates to control their potential effects on the dependent variables.

RESULTS: There were twenty-four (24) patients who participated in the study. The mean age of the participants was 57.2 years and mean weight was 87.8 kg (Table 1). The 22 patients provided 157 observations of finger-stick glucose (~7 observations/participant). Patients with diabetes had 92 mg/dl (27.85 SEM, p<0.01) higher blood glucose levels than patients without diabetes. One hypoglycemic event was recorded at 65 mg/dl.

CONCLUSION: The starting dose of NPH insulin at 0.1 unit/kg/dose was not effective in controlling the blood glucose levels of patients who received corticosteroid medications, more particularly in patients with diabetes.
Factors Motivating PGY2 Residency Pursuit and Program Growth Trends

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Background: The American College of Clinical Pharmacy recommends that postgraduate training be a prerequisite to clinical pharmacy practice positions. Pharmacy residencies are critical in providing additional education and training to new graduates. Completing a PGY2 residency allow pharmacists to specialize in a particular field. There is a lack of literature comparing trends in PGY2 residency programs’ growth and examining factors involved in PGY1 residents’ decision to pursue PGY2 residencies.

Hypotheses and Aims: We hypothesized that the main motivational factors for these PGY1 residents in pursuing PGY2 residency were to gain knowledge and experience, as well as the desire for specialized training. We predicted the future demand for PGY2 residencies will exceed the growth rate of PGY2 residencies. Finally, the study aimed to compare the trends in PGY2 residency programs’ growth and examine the factors involved in PGY1 residents’ decision to pursue PGY2 residencies.

Methods: Using an online Qualtrics system (Provo, UT), a cross-sectional study evaluating motivating factors and barriers to pursuing a PGY2 residency was distributed to residents at the Western States Conference, via residency program directors’ emails. Data between 2008-2014 from the National Matching Service and American Society of Health-System Pharmacist (ASHP) were used to identify trends in PGY2 residency growth nationally and within California.

Results: The final response rate of the survey was 27.8%. Of the completed surveys, 52% of respondents were interested in or were currently pursuing PGY2 residencies. Based on a 3-point Likert type scale, the top motivational factor was to “gain knowledge and training in specialized area” (98%) and the top barrier was “financial obligations (42%).” The top programs of interest in California were critical care, infectious disease, ambulatory care and emergency medicine. Per NMS and ASHP data, from 2008 and on, the programs that generated the most interest from the survey shared a similar increase in total positions per program nationally. When comparing California and national programs, California lags in opening up new programs that are currently popular, specifically emergency medicine.

Conclusions: Based on the survey, many residents are interested in pursuing a PGY2 residency, specifically in California, but there are not enough positions to support the anticipated demand. Further studies are needed to evaluate resident interest and long-term growth of PGY2 residencies.
Clinical Experience with Human Regular Insulin U500
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Background: Insulin resistance is a core pathophysiologic feature of type 2 diabetes. Obesity complicates the treatment of type 2 diabetes (T2D) and related insulin resistance. As more people live chronically with T2D the need for concentrated insulins will increase. Most physicians have little to no knowledge or experience with concentrated insulin.

Hypothesis and Aims: This descriptive retrospective study describes the experience of patients when they were changes from U100 insulin to Human insulin U500, Variables included glucose control as measured by A1c, body weight, total daily insulin requirements, and hypoglycemia before using U500, on their first follow up within 3-11 months, and after 12 months of U500 insulin use.

Methods: Chart review of patients who were started on Humulin R U500 insulin in 2013. To be included the person had to an established patient who was switched over during the study time period and continued on U500 for a minimum of 3 months.

Results: Seventeen patients on U500 were included in this review. Three had Type 1 DM and 14 had Type 2 DM. Six patients are using U500 in an insulin pump and 11 are on multiple daily injections. The mean A1c prior to U500 was 9.6%, 8.6% at the 3-11 months follow up and 7.9% one 1 year after. Nine of the 14 were high responders who had a mean 2.6% A1c reduction by the 3-11 months follow up visit. The mean body weight in prior to U500 use was 273.3 lbs., within 3-11 months of U500 use was 271.2 lbs. and after 1 year was 283.2 lbs. Three of the 17 patients prior to U500 use reported significant hypoglycemia. Six U500 patients had early hypoglycemic episodes (within 3-11 months) while only 1 patient reported hypoglycemia after 1 year of U500 use.

Conclusions: Uncontrolled diabetes patients with severe insulin resistance who require large doses of insulin can improve by switching to Humulin R U500 insulin. However, there was associated with increase in weight and hypoglycemia.
Diabetes Patients’ Perceptions of Preparedness for Self-Management Post Hospitalization
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Objective: Despite the key role diabetes education plays in self-management and adherence to diabetes treatment prescriptions, little is known about inpatient diabetes education, particularly patients’ readiness to manage diabetes post hospital discharge. This study design explored patients’ perceptions of preparedness for diabetes self-management via a 44-item survey.

Methods: Descriptive cross-sectional study that recruited patients from medical/surgical units of a community hospital October 2013 - December 2014. Eligible subjects included English-speaking adults admitted with a diagnosis of type 1 or type 2 diabetes mellitus. 103 diabetes patients (mean age=59±14 years, 51% female women, 92% Non-Hispanic White, 5% college education or higher, A1C=9.7± 2.8%, 50% on insulin, 27% smokers) completed the survey.

Results: Prior to the hospital admission, 71% of the patients had received prior diabetes education. When asked about preparedness to perform diabetes self-care behaviors, 57% felt extremely prepared to check blood glucose levels, 31% felt extremely prepared to manage medications, 32% felt extremely prepared to manage hyperglycemia, 32% felt extremely prepared to manage hypoglycemia, 12% felt extremely prepared to manage their diet, and 14% felt extremely prepared to manage physical activity. Only 50% of these patients had an appointment scheduled with their primary care physician post-hospitalization and 94% planned to keep that appointment.

Conclusions: Most patients did not feel well prepared to complete recommended diabetes self-care behaviors. Hospitalization is an opportunity to address self-management educational deficiencies, and in turn, improve patients’ behavioral and clinical outcomes. Future trials are needed to explore the relationship between diabetes self-management preparedness and readmission rates.
EDUCATION
Missing the Easiest Test Items is a Predictor for Multiple Venues of Poor Student Performance

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Background: Item analysis of standardized exams stratifies performance of the easiest to most difficult items. Ideally, test items should separate high from low performing students. On any given exam, there are always some students who incorrectly answer items that >90% of their classmates answered correctly. This led us to hypothesize that students who routinely do this might be at-risk academically.

Hypothesis and Aims: We sought to determine if first year osteopathic medical students (OMSIs) who miss test items that were most readily answered correctly did so repeatedly. If so, could such students be impaired in performance in their classes or on COMLEX, or in the ability to progress through our program in a timely manner? Such analysis might provide another tool that can predict for lack of student success, allowing for early and targeted intervention.

Methods: Test results. The study sample consisted of the four most recent matriculated cohorts [Classes of 2015 through 2018] from Touro University College of Osteopathic Medicine-CA (n=540). Exam taker and item results from the two first year Integrated Systems courses (Fundamentals of Osteopathic Medicine (FOM) and Cardiovascular/Respiratory/Renal (CVRR) were stratified for responses of 90-99% or 95-99% correct, with or without a biserial of >0.15. Results were compared to final course grades, whether or not students progressed to 2nd year with their entering Class, COMLEX performance and COMLEX failure.

Statistical analysis. Results were analyzed with Prism (GraphPad Software) using a non-parametric Mann-Whitney or nonparametric Spearman’s correlation analyses.

Results and Conclusions:

• Students who consistently miss multiple easy test items are at risk for finishing in the bottom 15% of the FOM and CVRR courses.
• On average, the bottom 15% of students in FOM miss easy exam items greater than would be expected by chance alone, as compared to the top 15% of students.
• Missing multiple easy items in the FOM course predicts that students will delay in progressing to the second year, and thus fail to finish medical school in four years.
• Missing multiple easy items in both CVRR and FOM is not only a predictor for finishing in the bottom 15% of COMLEX, it is also a risk factor for COMLEX failure, with the CVRR course being a better predictor.
Exploring the Perceptions of Australian and US Medical Students and their Teachers about Clinical Professional Attire
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ABSTRACT

Purpose: Doctors’ attire plays an important role in how they are perceived by society. This multi-institutional project explored the perceptions of medical students and their teachers about “appropriate” clinical attire.

Method: An anonymous, voluntary 55-question survey was electronically distributed to medical students and their teachers at two US and two Australian medical schools. The survey incorporated 30 images of sample attire, 9 demographical questions, and 16 questions regarding culture and context of clothing and accessories.

Results: 411 students and 73 teachers participated in this study. The data revealed that white coats and neckties are nearly absent in Australian clinical attire. Students (as a group) were significantly more supportive of full facial coverage due to religious/cultural values as compared to teachers (P=0.0004), and US students were significantly more supportive than Australian students (P=0.0003). All cohorts preferred dress code policies to direct students to avoid perfume/cologne, rather than to prohibit their use. Nose rings were controversial with significantly more support for use from students than teachers (pooled cohorts, P=0.002). There was an overwhelming trend for US students to be more accepting of casual footwear such as running shoes and various boots in clinical settings, as compared to Australian students. Students in both USA and AU indicated they were most influenced by modelling doctors at work (N=155, 38%), as compared to courses in medical ethics (N=19, 5%), school policy (N=16, 4%), and hospital policy (N=9, 2%).

Conclusion: These data break new ground in the social and cultural understandings of clinical professional attire.
Comprehensive Contraception Workshop and Evaluation: Pre-and Post-Intervention Evaluation of a Contraception Workshop for Osteopathic Medical Students and Allied Health Professional Students

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BACKGROUND: Unintended pregnancy is a major public health issue in the United States. Physicians and allied health professionals play a principal role in providing current, accurate, and unbiased reproductive health information. The Medical Students for Choice chapter leadership at Touro University-California identified the public health implications of accessible contraception, the discussion of all-current contraceptive methods, and effective contraception options counseling as gaps in the current curriculum.

HYPOTHESIS AND AIMS: This study describes the process of creating, implementing, and evaluating a collaborative, hands-on contraception workshop conducted in order to address these deficits.

METHODS: Forty-two students from the osteopathic medicine, physician assistant, and public health programs attended the workshop. All attendees agreed to participate in pre- and post-intervention evaluation, which assessed changes in knowledge and attitude as well as collected acceptability information.

RESULTS: This workshop achieved its goal of increasing knowledge about contraception and contraception options counseling. While attitudes about the importance of contraception information in curriculum and the likelihood of using contraception options counseling skills in the future did not significantly change, they were high to start with and they trended in a positive direction.

CONCLUSIONS: This workshop has the potential to inform the development of similar contraception workshops in medical or allied health profession programs with similar curricular deficits. Improved training preclinical contraception training has the potential to optimize women’s contraception counseling experiences and help reduce the high number of unintended pregnancies in the United States.
A Comparison of Basic Science Knowledge Between TUCOM Students and MD Students

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Background: The ACGME/AOA merger produced a single GME accreditation process for DO and MD residencies. The merger would not have been plausible without similar expectations for basic-science knowledge in both professions. The National Board of Medical Examiners (NBME) designs and administers the MD board exams, and builds expectations of the MD profession for basic science learning into its shelf exam the Comprehensive Basic Science Exam (NBME-CBSE). NBME-CBSE has been shown to be effective in predicting MD board exam outcomes. Results of the Medical College Admission Test (MCAT) and grade point average in pre-clinical courses (Pre-Clinical GPA) have been shown to significantly predict outcomes on Comprehensive Osteopathic Medical Licensing Exam USA Level 1 (COMLEX1).

Hypothesis and Aims: Our hypothesis is that if TUCOM students perform the same as the national cohort on NBME-CBSE, and if NBME-CBSE predicts TUCOM student outcomes on COMLEX1 as well as MCAT and Pre-Clinical GPA, then expectations for learning basic science are the same for TUCOM students and MD students.

Methods: Linear and logistic regressions were used to investigate COMLEX1 results from 643 Touro University College of Osteopathic Medicine (TUCOM) students from classes of 2009 to 2014. Independent variables included MCAT components, Pre-Clinical GPA, and NBME-CBSE. Variance Inflation Factor was calculated to investigate multi-collinearity. Results of graphical Receiver Operating Characteristic (ROC) analysis and regression coefficients were studied to compare models that included or excluded NBME-CBSE results. T-tests were used to compare NBME-CBSE performance of TUCOM students to the national cohort.

Results: More variance in COMLEX1 scores is explained, with less error, and no evidence of multi-collinearity, by models that include NBME-CBSE. COMLEX1 pass/fail outcome is also better predicted by including the NBME-CBSE. Graphical ROC analysis illustrates that NBME-CBSE alone predicts COMLEX1 pass/fail outcome with a ratio of true positives to false positives similar to Pre-Clinical GPA, and greater than the Biology component of MCAT. T-tests show average performance of TUCOM students on NBME-CBSE is the same as the national cohort.

Conclusions: These findings demonstrate the utility of a widely utilized MD measure, the NBME-CBSE, in predicting an important milestone of Osteopathic medical education, the COMLEX1 outcome, among TUCOM students. The data suggest that using the NBME-CBSE exam at TUCOM could enhance student advising about preparation for both USMLE and COMLEX board examinations. We interpret the diagnostic accuracy of the NBME-CBSE for COMLEX1 outcome, and the equivalence of TUCOM and national cohort average scores, to imply that expectations for basic science learning are the same for TUCOM students and MD students.
Lessons Learned from a Pilot Nutrition Elective at an Osteopathic Medical School
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Background: Physicians occupy a front line position in the promotion of good nutrition and lifestyle practices, but medical school education continues to inadequately prepare physicians to counsel patients about nutrition-related health conditions such as obesity, diabetes, cardiovascular disease, cerebrovascular disease and cancer. Our strategy to address this was to offer advanced nutrition training to an interprofessional group of preclinical students in a course designed to overcome faculty time constraints and leverage the principles of adult learning theory.

Methods: The course was offered to all students from programs in Osteopathic Medicine, Pharmacology, Physician Assistant and Public Health on the Touro University California campus. The course was a peer-taught, seminar-style elective, designed to appeal to “adult learners” who would prefer active and independent learning on a topic of their own choosing.

The course student learning objectives (CSLOs) were:

- Acquire knowledge about specific nutrition topics
- Interact professionally with a faculty mentor
- Access and evaluate the medical literature on a topic of interest in the field of clinical nutrition
- Develop teaching skills including articulating learning objectives, multimedia presentation, test question writing

CSLOs were assessed using standardized questions with narrative feedback responses interpreted on a scale ranging from “Exceeds Expectations”, “Meets Expectations” or “Below Expectations”.

Results:

- CSLOs were all met or exceeded by all participating students.
- Although students from all schools expressed interest, only 8 students enrolled in and completed the course; all were from the College of Osteopathic Medicine.
- Inconsistent quality of performance was noted in research and teaching skills.
- Participating students rated course high overall.
- Non-participating students cited preference for conventional directed learning format and difficulty with scheduling as predominant reasons in informal convenience sample interviews.

Conclusions:

- Course was successful with all students achieving at least “Meets Expectations” for all CSLOs.
- The highest percentage of “Exceeds Expectations” was in Teaching Skills. This may be the domain where most learning occurred, or perhaps peer grading is inflated.
• Overall enrollment was low, especially compared to expressed student interest. Contributing factors likely include a lack of ‘marketing’, scheduling conflicts especially for non-COM programs, and significantly, the self-directed learning format, an observation which points out the over-simplified view of medical students as “adult learners”.

• Variability of student presentation content and quality may have been improved with closer faculty supervision, more clearly articulated expectations, and increased attention to EBM skills in the core curriculum.

• Participating students and faculty both expressed enthusiasm for the course especially citing the one on one interactions as meaningful.

• Faculty time spent was not measured so comparison to conventional course delivery could not be made.

Future Directions:

• 2015 course adopted Nutrition In Medicine (NIM), a directed learning, online curriculum focusing exclusively on CSLO Knowledge. Enrollment has more than doubled, notably with involvement from other programs.

• Ultimately we hope to mainstream a Nutrition content into our core curriculum, while offering an advanced elective to motivated students.
PUBLIC HEALTH
The prevalence rate of poor glycemic control and its associated factors among diabetic patients in Jimma Zone: a cross-sectional multi-step study in Jimma Zone, Southwest Ethiopia
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Background: The incidence and prevalence of diabetes mellitus is increasing quickly in Sub-Saharan Africa. Between the years 2000 and 2030, it is estimated that the number of diabetic cases will increase from 7 million to 18.6 million. Diabetes mellitus is a major cause of morbidity and mortality and is associated with a variety of microvascular complications. Controlling glucose levels has been shown to reduce these complications. However, glycemic control is both difficult and limited in low-resourced settings. There are currently no studies using national data on the epidemiology of diabetes in Ethiopia where hospitals and health centers are the major sources of health care. These health facilities are reported to have inadequate diabetes care with deficiencies in glycemic control.

Hypothesis and aims: This cross-sectional, quantitative study attempts to determine the prevalence of poor glycemic control and identify the factors associated with inadequate glycemic control among diabetic patients in the Jimma Zone. We hypothesize that poor glycemic control is multifactorial and is related to both external and patient-related factors.

Methods: n659 patients with either type 1 or type 2 diabetes attending follow-up care in government health facilities in the Jimma Zone (1 referral hospital and 3 health centers) were enrolled in the study and given a questionnaire on sociodemographic factors, disease factors, and factors related to treatment processes. Clinical parameters were measured and HbA1c levels were determined for each patient.

Conclusions: The relation between glycemic control and the sociodemographic variables, type of diabetes, duration, and site of health care is discussed.
Background: Anal high-grade squamous-cell intraepithelial lesions (HSIL) can progress to anal cancer, similar to the progression of cervical HSIL to cervical cancer. Both cancers are causally associated with human papillomavirus (HPV). However, the natural history of low-grade squamous-cell intraepithelial lesions (LSIL) remains unclear. Anal LSIL may regress to normal epithelial tissue, may progress to HSIL or remain unchanged. Treatment guidelines do not currently recommend treating anal LSIL. HIV-infected men who have sex with men (MSM) are at high risk for HPV infection, anal LSIL and HSIL, as well as anal cancer.

Hypothesis and Aims: Our aim was to determine the incidence of progression to anal HSIL in a cohort HIV-infected MSM diagnosed at baseline with anal LSIL. We also aimed to identify risk factors for progression and regression. We hypothesized that most HIV-infected MSM with baseline anal LSIL would progress to anal HSIL.

Methods: 508 HIV-infected MSM who were enrolled in a prospective cohort study received a sexual behavior questionnaire, anal cytology, high resolution anoscopy-guided biopsy, and anal HPV testing of anal swabs using L1 MY09/MY11 PCR. Men were followed every 6 months for 2+ years. We used Cox-proportional hazards models to determine risk factors for progression to anal HSIL.

Results: The mean age of participants was 44 years, 90% were non-Hispanic white, and 60% had completed college. 17% had CD4+ levels <200 cells/µL and 45% had a detectable HIV viral load. 91% of men had anal HPV infection and 80% had at least one oncogenic HPV type. 127 MSM (25%) were diagnosed at baseline with anal LSIL. Of those, 74% progressed to HSIL, 20% remained LSIL, and only 6% regressed to normal. Oncogenic HPV infection (hazard ratio (HR): 2.0), smoking 100+ lifetime cigarettes (HR: 1.6) and CD4+ level <200 (HR: 2.4) all were associated with progression to anal HSIL (p-value ≤0.05) after adjustment for education, injection drug use, alcohol use, and wasting syndrome.

Conclusions: A large proportion of HIV-infected MSM diagnosed with anal LSIL progress to HSIL. HIV-infected MSM with anal LSIL should be followed closely for potential early diagnosis and management of HSIL.
Human papillomavirus (HPV) infection in India: A Systematic Review of the Literature

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Background: HPV infection is the most common sexually transmitted infection and is the established necessary cause of cervical cancer. The prevalence of HPV infection among women in the US is approximately 30%, and the incidence of cervical cancer has been declining since standardized screening programs were put in place. Cervical cancer is the most common type of cancer in Indian women. Consistent with studies of women in other populations, HPV types 16 and 18 are the most common types found in Indian cervical cancers. There have been several studies of cervical HPV infection in Indian women and prevalence estimates range from a low of 7% to a high of 63%. Several studies have identified high prevalences of oncogenic HPV types that are not common in Western populations. However, published studies vary greatly in size, methodology, HPV types detected, and quality. HPV infection and HPV-associated diseases are preventable through several licensed HPV vaccinations. Although the Indian Academy of Pediatrics Committee on Immunization recommends that all females should receive this vaccine, there is very low uptake of this vaccine. Before vaccine uptake interventions are planned and implemented in India, it is important to determine the type-specific prevalence of HPV infection so that we can match the appropriate vaccine to the circulating HPV types, and discover if the recently approved Gardisil 9 vaccine includes prevalent oncogenic HPV types in India. In order to provide researchers and policy makers with the most current information available on the type-specific prevalence of HPV infection among Indian women, we have initiated a systematic review of the literature.

Hypothesis and Aims: Our specific aim is to systematically review the published literature on type-specific HPV infection among Indian women and risk factors for infection. We hypothesize that although overall HPV prevalence in India may be similar to that of Western populations, the HPV-type distribution and risk factors for infection will be different.

Methods: We have searched the databases Proquest and PubMed using the following search terms: India, India/Epidemiology, HPV, Cervical Cancer, Prevalence, Incidence, PCR, HPV DNA, and HIV. Further records will be identified through bibliographic searches of screened articles and author contact. All unique publications identified have been entered into a database. Two reviewers are independently screening title and abstracts of all identified articles for inclusion. Articles that pass the primary screen are retrieved and secondarily screened at the full-text level. Articles will be included in the study if they present primary data, test for cervical HPV DNA using PCR based methods, and include women from India. We will collect the following data from each published study: Date of publication, sample size, HPV DNA types tested, method of detection, prevalence/incidence of each HPV type, city and state, age, and risk factors reported. We will use a standard risk/bias assessment tool to rate the quality of studies.

Results: 1732 records were identified and have been entered into the database. Primary and secondary screening and data abstraction are currently on-going.
Conclusions: Type-specific HPV results will be analyzed and presented overall, by region, by age, and by important risk factors. If sufficient quality data is available, summary prevalence or incidence measures will be calculated using meta-analysis methodologies.
Epidemiology of HPV 6, 11, 16, 18 Antibodies Among Adults in the United States Across Six Years: NHANES 2005-2010

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Objective: To assess the prevalence, distribution and trends of human papillomavirus (HPV) antibodies (Ab) contained in the quadrivalent HPV vaccine (HPV 6, 11, 16 and 18) among US adults.

Methods: The sample population consisted of 11,186 men and women ages 18-59 years with HPV antibody available data included in the National Health and Nutrition Examination Surveys (NHANES) 2005-2006 (pre-HPV vaccine), 2007-2008 and 2009-2010 (post-vaccine). HPV type-specific Ab serostatus was established using the competitive Luminex Immunoassay of Antibodies to Neutralizing Epitopes on HPV 6, 11, 16 and 18 L1 VLPs. Both cervical and oral HPV types were assessed using the Roche Linear Array Assay. Data analyses consisted of weighted prevalence with 95% confidence intervals, accounting for complex sampling with the SVY module of Stata V13. A p value <0.05 was set for statistical significance.

Results: Prevalences of HPV Ab 6, 11, 16 and 18 were 16.4%, 5.9%, 12.4% and 4.8%, respectively. Among women, Ab prevalence increased from 15.7% in 2005 to 23.4% in 2010 (HPV16) and from 5.6% to 9.5% (HPV18) (p<0.05) with a dose response by number of vaccine shots.

Conclusions: Significant Ab prevalence increases were seen across survey years among women but not among men, likely attributable to the effect of HPV vaccination.
Is knowledge enough to change the attitude and practice of a community?
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Background: Schistosomiasis is one of the top neglected tropical diseases, producing over 200,000 deaths per year. The helminth exists in the freshwater of Lake Victoria used by the population for daily needs. Many intervention programs target education and prevention to shift behaviors. This study examines the knowledge of Lake Victoria residents about schistosomiasis and the residents’ habits in regards to disease prevention.

Hypothesis and Aims: We hypothesized that although the education about schistosomiasis prevention is adequate, attitude and practice remain unchanged among Burere and Masonga residents. The purpose of this study is to demonstrate whether knowledge is sufficient to change attitude and practice towards decreasing schistosomiasis incidence.

Methods: An analytic observational case-control study was carried out at health dispensaries among the population of Burere and Masonga, Tanzania. The study population consisted of anyone 4 years and older who gave verbal informed consent to participate in a survey, screening, treatment and education. 313 persons responded to the radio advertisements announcing the screening and treatment of schistosomiasis. Medical students carried out a multiple-choice survey in Swahili with translator assistance. Subjects testing positive for schistosomiasis were given praziquantel under direct observation of district hospital doctors. The study was IRB-approved by Touro University and Shirati hospital board.

Results: 72.8% of the survey population is aware that drinking contaminated water can expose one to schistosomiasis, but 64.2% drink un-boiled water from the lake. 67% of subjects said boiling water will prevent infection by schistosomiasis, but only 39.3% of subjects boil water before use. 75.4% is aware of schistosomiasis infection through contact with contaminated water while swimming, bathing, or fishing, yet 78% swim and 87.5% bathe in the lake. 63% of patients said urinating or defecating in the water spreads schistosomiasis. However, when we asked patients where they defecate, 54.6% of patients defecate in the lake and 79.2% of patients use latrines. 91.8% of subjects know that the schistosomiasis parasite survives in snails.

Conclusions: From this data it was concluded the studied population is knowledgeable about schistosomiasis prevention and spread, yet the risky behavior is not changed accordingly, as the majority of the population continues to bath in lakes and use unclean drinking water. If the patient population is engaging in behaviors that risk their health, it may be out of necessity and seemingly insurmountable obstacles to change. The barriers to changing risk behaviors must be addressed if an effective intervention is to be instituted to decrease incidence of schistosomiasis. A limitation was that health dispensaries may not have been the optimal site to reach a majority of populations, producing a small sample size. This project was funded by Global Physicians Corps.
Factors Associated with Sex Work among At-risk Female Youths in Cambodia: A Cross-Sectional Study
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Background: Globally, almost 60% of all new HIV infections among young people occur among adolescent girls and young women. In the Asia-Pacific region today, 38 percent of new HIV cases are among women compared to 21 percent in 1990. The growing feminization of the HIV epidemic in Asia continues to cause alarm among health officials. National and international governing bodies are making efforts to understand the pathways of risk for this group in order to develop and implement tailored prevention strategies. In Cambodia, despite great achievements in reducing the prevalence of HIV in the general population, reducing new HIV infections among young at-risk women remains a challenge.

Aims: To describe the prevalence of risky sexual behaviors of sexually-active female youths in Cambodia and to explore risk factors associated with engagement in transactional sex.

Methods: Sexually-active female youths aged 10-24 were enrolled at risk “hotspots” in eight provinces in Cambodia. We collected data on demographic factors, sexual behavior, and factors hypothesized to be associated with transactional sex. Multivariable logistic regression was used to identify associations between demographic and sexual behavior and transactional sex.

Results: Of the 280 respondents, the mean age was 21.2 and 48.1% had been paid for sex in the past year. After adjustment, at-risk females who engaged in transactional sex remained significantly more likely to never have been married (AOR 4.36, 95% CI=2.20-8.65), to have completed less than 6 years of school (AOR 4.54, 95% CI=2.32-8.88), to have one or more parents who have died (AOR 4.13, 95% CI=2.03-8.39), to be a heavy alcohol drinker (AOR 3.58, 95% CI=1.78-7.18), to have used a condom with their boyfriend during last sexual encounter (AOR 3.62, 95% CI=1.57-8.30) and to have ever had an HIV test (AOR 4.25, 95% CI=2.12-8.52).

Conclusion: The identification of risk factors for sex work, such as orphan status, can be used to tailor interventions to female youths at hotspots and also to younger vulnerable females. Other interventions that focus on reducing alcohol use, promoting condom use with boyfriends, and promoting HIV testing should be developed for at-risk youth.
Research Ethics Training of Trainers: Developing Capacity of Bolivian Health Science and Civil Society Leaders
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Program/Project Purpose: The University of San Andres, Faculty of Medicine in La Paz, Bolivia in collaboration with Touro University California, Public Health Program was awarded a National Institute of Health Research Ethics Planning Grant in June, 2013 to develop strategies and processes for implementation of a comprehensive national research ethics program for Bolivia. Although the importance of scientific research based on ethical principles is highlighted in the Bolivian constitution and national health legislation, few Bolivian academics, researchers and health professionals have received formal training in the principles and practices of research ethics. A principle aim of the Planning Grant is to develop and implement a Research Ethics Train the Trainers (TOT) course with the goal of training faculty for future implementation of a national research ethics program.

Structure/Method/Design: A Project Directors Committee representing public health science universities from four participating Bolivian Departments/States (La Paz; Santa Cruz, Cochabamba & Chuquisaca) was formed to oversee all project activities including implementation of a three day in-person TOT followed by a 10 week online virtual training. Training modules utilized materials developed by Bolivian academics and scientists and international research ethics programs at PAHO (Pan American Health Organization) and CITI (Collaborative Institutional Training Initiative), University of Miami. TOT University and civil society representatives were selected from each participating Department/State for a total of 19 participants. Upon completion of the training, participants were asked to implement educational research ethics activities in their local communities and institutions.

Outcomes/Evaluation: A pre-test/post-test study design was used to assess change in participant knowledge related to research ethics principles and practices. The mean score improved from 73% correct at baseline and 84% at course completion. Participants completed a course evaluation after the in-person and virtual components of the course. Participants highlighted the most useful topics in the course as respect for persons and human rights, principles of bioethics, informed consent and the function of research ethics committees. The most positive aspects of the in-person component of the course were the high level of participation, group work, communication and debate among participants representing different academic disciplines and social sectors. Eighty percent of participants completed the course with two dropping out during the virtual component. Most students reported that the instructions for using the virtual platform were clear and they received sufficient support from the Course Coordinator, however, most stated that some of the teachers provided insufficient academic support.

Going Forward: Integrating the group interaction strengths of the in-person TOT component...
with the flexibility of the virtual component recommends using a mixed methods approach while providing additional training to teachers related to virtual teaching methodologies.

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Cardiovascular Disease and Access to Healthful Food: A Link Between Patients and their Neighborhoods
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Background: Cardiovascular disease (CVD) is the leading cause of death in Alameda County, California, and socioeconomic factors, including food insecurity, have been identified as contributors. This study assessed the association between the modified retail food environment index (mRFEI) and CVD diagnosis in Alameda County. Exploring patient-specific and neighborhood contextual characteristics provides a more complete picture of the link between patient health and the environment.

Hypothesis: We hypothesized that patients residing in neighborhoods with a lower mRFEI would have higher odds of CVD diagnosis.

Methods: We analyzed data from all patients seen at Highland Hospital between July 1, 2013 and June 30, 2014, who could be matched with a geographically coded address (n=39,533). Neighborhoods were defined as census tracts. Patient addresses were linked to neighborhood-level data (e.g. education level, median household income) and mRFEI, which represents the percentage of retailers within a 0.5 mile buffer of a given census tract that are more likely to sell healthful food. CVD diagnosis was determined based on the patients’ ICD-9 principal diagnosis codes given on their initial hospital visit. Bivariate analyses examined the crude association between patients with and without a CVD diagnosis and the mRFEI, as well as patient- and neighborhood-level sociodemographics. Logistic regressions modeled the CVD-mRFEI association, considering all covariates.

Results: Patients with CVD were more likely to be older, male, and black and to reside in neighborhoods with a lower median household income and lower proportion of residents with more than a high school degree or equivalent. CVD-diagnosed patients were also more likely to reside in neighborhoods with a lower ratio of healthy to unhealthy food options (mean=8.1; SD=6.1 vs. mean=8.3; SD=6.1, p<0.001). The association persisted after accounting for all covariates (OR=0.97; 95% CI: 0.96 - 0.99).

Conclusions: Patients with a CVD diagnosis were more likely to reside in neighborhoods with poorer food options, independent of patient or neighborhood characteristics. Our findings suggest the availability of healthful food options may play a role in the distribution of CVD. With the recognition that diet-related illnesses are increasing, community-based strategies involving multiple stakeholders, including hospitals, are critical to solving the food desert problem.
Level of Knowledge, Attitudes and Practices on Community-Based Health Insurance, and Associated Factors among the Community of Dembecha Town, West Gojjam Zone, Amhara, Ethiopia, 2014

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Background: This study investigates associations between the utilization of a community-based health insurance (CBHI) program in Ethiopia and community member’s knowledge of, and attitudes towards the program. Such information, which is largely lacking, is crucial for the planned nation-wide scale-up of this program.

Hypothesis and Aims: The main aim of this study is to assess the level of knowledge, attitude, and practice with regard to CBHI, and to determine the factors associated with uptake or non-participation of CBHI in Dembecha town, West Gojjam zone, Amhara region, Ethiopia.

Methods: This cross-sectional study uses a survey of 328 randomly selected households in Dembecha, a peri-urban town in the Amhara region. Data were analyzed using multivariate linear and logistic regression models.

Results: Although the majority of residents (67%) had information about CBHI, mostly from health institutions (48%) most (62%) did not know that there was a CBHI program in Dembecha. Moreover, over half of respondents had incorrect knowledge about policies on monthly premiums and fees. Higher education, income, negative health status of family members, and being an adult aged 26 to 45 years old were positively associated with program knowledge (p<0.01). Attitudes about CBHI were generally positive. Low-income individuals, high health spenders, civil servants, and those knowledgeable about the program were all more likely to view CBHI favorably (p<0.01). The vast majority (84%) of respondents had not enrolled in CBHI; mainly because they lacked information about it (70% of non-enrollees). Health service utilization was modest for CBHI enrollees. The main reason for non-utilization was lack of coverage or availability of the needed health service. High CBHI knowledge and gender as female were positively related to overall utilization (p<0.01). However, attitude towards CBHI does not significantly predict enrollment.

Conclusions: This study underlines the low utilization of CBHI in Dembecha town despite the near universal, basic knowledge and favorable attitude towards CBHI. The current enrollment uptake (16%) in Dembecha town is much lower than the national enrollment rate at 46% (Derseh et al., 2013), which was mainly due to the lack of information on CBHI, the lack of money, and the poor understanding of the more complicated concepts of health insurance. This study confirmed the important role of knowledge in its influence of behavior (enrollment), and attitude is a not strong predictor in behavior. After all, improving knowledge of potential health risks and providing more information regarding CBHI’s benefits would be the first step to change people’s perception of health insurance and eventually encourage people to participate in CBHI. Future research should address the patterns of utilization among members, the efficiency of the referral system, the impact of community health education, and quality of care services.
that CBHI provided, and focus more on qualitative research on CBHI performance and households’ perception on CBHI.
Characteristics Abortion Care Service Provision in Debre Markos, Ethiopia.
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Background: Unsafe abortion is one of the top three causes of maternal deaths in Ethiopia. In 2005, the Ethiopian government liberalized laws on abortion to address this problem. There is much to learn about how patients and providers have responded to this new access. To that end, this study examines the characteristics of patients seeking abortion services and the types of care offered to them at a tertiary public facility in Ethiopia.

Hypothesis and Aims:

The project’s research aims are to:

- Identify the reasons why women request safe abortion services in Ethiopia
- Examine the types of care offered to women seeking safe abortion services in Ethiopia.

Methods: This retrospective study uses secondary data extracted from medical records for women requesting safe abortion services at the Debre Markos Referral Hospital, in the Amhara region for the year 2013.

Results: On average the women (N=415) were 27 years old. The majority sought care because of incomplete abortion (43%) or to terminate a pregnancy due to rape (34.7%). Younger women were more likely than others to cite rape as the reason for seeking care (paired t-test p<0.001). Most women presented in their first trimester. The most common abortion procedures were manual vacuum aspiration (56.57%) and medical abortion (MA) (20%). Unexpectedly, MA was more common in women presenting later rather than earlier in pregnancy (OR=1.23 p<0.001). There were no fatalities and very few (<5%) complications among patients. Use of MA was associated with reduced likelihood of complications after controlling for risk factors. Most women (80%) received both contraception and HIV counseling and the majority (63.83%) said they wanted contraception.

Conclusions: More intensive contraceptive counseling might be needed to increase uptake and further investigation into the reasons for the relatively low use of MA for the termination of early pregnancies is warranted.
The Spatial Distribution of Health-Related Community-Based Organizations in Malawi
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Background: Community-based organizations (CBOs) implement a growing share of global health initiatives in low-income countries yet we have little comprehensive knowledge about where these organizations are placed sub-nationally, their longevity, and whether they are organic structures that address felt community needs or opportunistic organizations that develop in reaction to the availability of foreign aid resources. To fill this gap, this project maps the geographic distribution of CBOs involved in health and HIV/AIDS in Malawi over a 15-year period.

Research Aims: These maps will serve as the data source for studies of the effectiveness of aid resources in facilitating the formation of community organizations and the impact of CBO involvement in health service provision on service quality and health outcomes.

Methodology: The study team recorded, categorized, and geo-coded over 3000 organization-locations for a 15 year period using data collected through interviews with district-level health officials and reviews of reports from sources such as NGO boards, the National Aids Commission, and previous mapping exercises conducted by the US State Department and the Malawi Longitudinal Study of Families and Health.

Results: Analysis is still in progress. CBOs are clustered in urban areas and the Southern region where HIV prevalence is relatively high. There is little other association between CBO placement and health needs. The majority of organizations are involved in either “impact mitigation” of HIV/AIDS or “capacity building”. While the number of CBOs has been stable over the past 10 years, the turnover of organizations appears to be quite high.

Conclusion: These preliminary findings suggest that with the exception of HIV/AIDS organizations, the formation of health CBOs may be donor- rather than need-driven.
The Practice and Perceptions of Women-Centered Care among Midwives and Midwifery Students in Debre Markos, Ethiopia
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Background: Ethiopia’s maternal mortality rate remains persistently high; 676 women die for every 100,000 live births in the country. Midwives are at the center of Ethiopia’s initiative to decrease maternal mortality by drastically scaling up population coverage of mid-level health care providers at public facilities in underserved areas. A poorly studied challenge of this scale-up is ensuring the quality and responsiveness of new services. Such study is crucial because poor service quality and fears of provider mistreatment are significant reasons for women’s low rates of maternal health service utilization, which, in turn contributes to high maternal mortality.

Hypothesis and Aims:
- Assess provider attitudes towards and awareness of patient-centered care in reproductive health services in Ethiopia
- Discuss the extent to which patient’s rights is integrated into the training of Ethiopian midwives
- Explore how midwifery providers and students define patient abuse and disrespect and review the extent to which they consider this mistreatment to be a problem

Methodology: The study conducts structured in-depth interviews with 16 third-year bachelor’s degree midwifery students from Debre Markos University and four midwives from health centers in the town. Interviews involve questions on the coverage of patient rights in midwifery training, respondent knowledge of patient’s rights, their experiences of provider-patient interactions, and their observations of patient mistreatment. Data are triangulated with information from interviews with local women who have recently given birth.

Results: Data analysis is ongoing. Preliminary analysis suggests that the subject of patients’ rights is only partially covered in the midwifery curriculum and that such training focuses on protecting patient confidentiality and privacy not providing sensitive care. However, all study participants described respecting clients’ rights as a fundamental factor in developing a positive relationship between clients and providers. Most respondents report having witnessed disrespect and abuse of patients. The most common type of abuse was slapping patients to get their attention or to get them to move into the required position. Other reported types of mistreatment included verbal abuse, stitching episiotomies without anesthesia, performing procedures without informing the patient and refusing follow up care to patients who had refused other care. Such abuse was described as unintentional, resulting from overwork due to very high patient loads, and patients who are unresponsive or uncooperative because of the
pain and stress of labor.

**Conclusions:** These preliminary results suggest that the abuse of patients during labor and delivery is relatively common, that training in patients’ rights could be strengthened in midwifery curriculum development, and that students would be responsive to such training. However addressing structural issues around provider workload should complement these initiatives if Ethiopia is to increase provision of respectful patient-centered care.