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# ORGANIZERS' WELCOME LETTER

# Burrell College of Osteopathic Medicine 2<sup>nd</sup> Annual Medical Student Research Day 2019

On behalf of the Planning and Oversight Task Force, it is with great pleasure that we welcome you to the much anticipated 2<sup>nd</sup> Annual Medical Student Research Day! We thank our visitors and participants for helping make Medical Student Research Day an exciting and memorable event as we enthusiastically honor our medical students and faculty mentors to celebrate their research and scholarly activity endeavors.

The organizers are pleased to announce that a total of twenty-two abstracts were submitted for the following research areas: biomedical sciences, clinical sciences and OMT, population and public health, and medical education research. We are also pleased to announce and welcome the student researchers for the inaugural year of the Medical Student Summer Research Experience that culminates today with poster presentations at Medical Student Research Day.

Research projects will be presented and judged during the poster viewing session, and those that are exceptional will be presented with an award during the awards ceremony. The top research poster presentation in each category will be provided with a certificate and a \$250 award. Also, a grand prize will be awarded to the best overall research poster presentation, which includes a certificate and paid travel to present their research at the National Student Research Forum.

We are honored to welcome Dr. Alan Langnas, DO, from the University of Nebraska Medical Center as our Keynote Speaker. Dr. Langnas visits us today as the Director of the Nebraska Center for Transplantation and Chief of Transplantation Surgery. We would especially like to thank Dr. Langnas for agreeing to speak today.

Again, thank you for joining us today to make our Medical Student Research Day a memorable one. We hope to see you at next year's event.

Wishing you every success,

#### Steven J. Ontiveros, MBA, PhD

Assistant Professor, Anatomy & Cell Biology Director of Student Research MSRD Planning and Oversight Chair

#### Robert Goldsteen, DO, FACP

Chair of Clinical Medicine Professor, Internal Medicine

#### Norice Lee, MLIS

Associate Library Director Associate Professor, Biomedical Sciences **Matthew Steritz** 

OMS-II

Tyler Tumey *OMS-II* 

Kris Vaudrey, MAEd

Instructor, Anatomy & Cell Biology

Harald Stauss, MD, PhD

Associate Professor, Pharmacology



# MESSAGE FROM THE ASSISTANT DEAN FOR RESEARCH

Welcome to the 2019 BCOM Medical Student Research Day and congratulations to all of our students and faculty mentors. This year marks another first for BCOM in that today is the culmination of the inaugural year of the Medical Student Summer Research Experience. Abstracts in this program and the posters available for viewing represent the collaborative efforts of students and faculty. The work presented today highlights the breadth of scholarly work conducted at BCOM and affirms our commitment to providing opportunities for students beyond the classroom.

I wish to acknowledge the efforts of our Director of Student Research, Dr. Steven Ontiveros, for his efforts in leading the development and implementation of the Summer Research Program and the organization of Medical Student Research Day. In addition, I wish to acknowledge the work of our Director of Laboratories, Dr. Michael Woods, Scientific Research Associate, Kalli Martinez, and Research Officer Administrative Coordinator, Martha Enriquez for ensuring that the newly opened BCOM Research Laboratories were fully operational throughout the program. It is hard to believe that we opened these facilities just 3 months before the program began.

Today we celebrate the accomplishments of our student researchers who are presenting their research findings and thank the faculty mentors for all of their guidance which they provided to the students. I encourage you to take time to visit the posters and speak with our student researchers about their work. I could not be prouder of BCOM and what these outstanding individuals have accomplished.

Joseph N. Benoit, Ph.D.

Assistant Dean for Research Professor of Physiology & Pathology

Email: Research@bcomnm.org



# SCHEDULE OF EVENTS

# July 19, 2019

7:00 AM – 8:00 AM Poster Setup

7:30 AM – 8:15 AM Student Presenter Breakfast

Location: Room 157

8:15 AM – 8:30 AM Welcome Remarks

Dr. Don Peska, Dean & CAO, BCOM

Dr. Joseph Benoit, Assistant Dean for Research

Dr. Steven J. Ontiveros, MSRD Chair

Location: 1st Year Lecture Hall

8:30 AM – 11:00 AM Poster Session

Location: Lecture Hall Corridor

11:00 AM – 11:15 AM Coffee Break

11:15 AM – 12:15 PM **Keynote Address** 

Dr. Alan Langnas, DO

**Professor of Surgery** 

Director of the Nebraska Center for Transplantation

Chief of Transplantation Surgery

University of Nebraska Medical Center

Location: 1st Year Lecture Hall

12:15 PM – 1:30 PM Lunch

Location: Patio

1:30 PM – 2:00 PM Awards Ceremony

Location: 1st Year Lecture Hall



# **Welcome & Opening Remarks**

Dr. Don Peska, Dean & CAO, BCOM Dr. Joseph Benoit, Assistant Dean for Research Dr. Steven J. Ontiveros, MSRD Chair

1<sup>st</sup> Year Lecture Hall 8:15 AM – 8:30 AM



# **Keynote Speaker**

Dr. Alan Langnas, DO

Professor of Surgery, Director of Nebraska Center for Transplantation, and Chief of Transplantation Surgery University of Nebraska Medical Center

> 1<sup>st</sup> Year Lecture Hall 11:15 AM – 12:15 PM



### **KEYNOTE SPEAKER**

### Dr. Alan Langnas, DO

Professor of Surgery, Director of Nebraska Center for Transplantation, Chief of Transplantation Surgery University of Nebraska Medical Center

### **Biographical Sketch**

Alan Langnas, DO, is Professor of Surgery, Director of Nebraska Center for Transplantation, Chief of Transplantation Surgery. Dr. Langnas is also the clinical Director of the Liver Transplantation Program and Intestinal Program at the University of Nebraska Medical Center. In his role as the Director of Transplantation he oversees clinical programs of liver, small bowel, kidney, pancreas transplantation, hepatobiliary surgery and intestinal rehabilitation. Dr. Langnas has been a faculty member at the University of Nebraska Medical Center since 1989. He assumed the role of Chief of Transplantation in 1997. Under Dr. Langnas' direction the Transplant Program has also developed a unique clinical pathways including: Carcinoid and Neuroendocrine Tumor Clinic, Pancreatico Biliary and Auto Islet Cell Center, as well as a robust basic science research program.

Dr. Langnas earned his undergraduate degree from the University of Michigan and received his Medical Degree from the University of Health Sciences College of Osteopathic Medicine in Kansas City in 1982. He is board certified in surgery and critical care.

Dr. Langnas has been an active member of the American Society of Transplant Surgeons for over twenty years. His roles include that of Councilor, Treasurer, and President. He is now serving as Councilor to the International Pediatric Transplant Association. He is a Scientific Review Officer for the Department of Defense Congressionally Directed Medical Research Programs.



# **Poster Session**

8:30 AM – 11:00 AM



# FUNCTIONAL AND MOLECULAR CHANGES OF THE MATERNAL HEART DURING THE LATE PREGNANCY STAGE: A TWO-DIMENSIONAL SPECKLE-TRACKING ECHOCARDIOGRAPHY STUDY

Moazeni S, Umar S, Methangkool E, Sarji S, Mahajan A, Eghbali M Burrell College of Osteopathic Medicine, Las Cruces, NM; Department of Anesthesiology and Perioperative Medicine, University of California Los Angeles (UCLA), Los Angeles, CA

**Background:** During pregnancy, the heart undergoes several important changes that effects its structure and function, which are necessary for the progression of a successful pregnancy. Some of these changes include volume overload, increased cardiac output (CO), and physiological hypertrophy. During late pregnancy (LP), some investigators have identified reduced left ventricular (LV) systolic function. However, recent literature has also shown that systolic function to be highly variable when compared to non-pregnant (NP) controls. Here we investigated whether speckle tracking echocardiography (STE), a highly sensitive load independent modality, which can detect changes in the myocardium in LP female rats. Conventional 2D echocardiographic measurements such as ejection fraction (EF) and fractional shortening (FS) are limited due to the lack of sensitivity and by being dependent on loading conditions. Therefore, we believe that STE can detect subtle changes that may be attributed to hypertrophy process and/or subclinical myocardial dysfunction.

**Methods:** Adult female Sprague-Dawley rats were used in NP, LP, and post-partum (PP; day 3, 7, and 14) stages. Hearts were isolated to measure LV hypertrophy. Cardiac tissue was frozen to maintain protein and RNA integrity. Total RNA from the heart was isolated using the Trizol RNA isolation protocol and reversed transcribed with a gene specific primer. U6 was used as used as an internal reference gene. In addition, standard western blot analysis was performed using in-vivo whole heart lysates. Two-dimensional transthoracic echocardiography were acquired to monitor cardiac function by conventional parameters (LVEF, FS, and heart rate) and with STE. Myocardial global circumferential (GCS) and radial (GRS) strain were acquired from the parasternal short-axis view and were measured in triplicates.

**Results:** As expected LP rats had significantly increased hypertrophy compared to the NP group and this hypertrophy was reversed by day 14 after delivery (NP:0.48+/-0.02 g vs LP: 0.57+/-0.03 g vs PPD14: 0.49+/-0.026 g; P<0.01, normalized to NP). LP rats showed no statistically significant change in LVEF (LP: 67.65+/-1.41% vs NP: 71.35+/-1.52%; P=0.10, normalized to NP) and FS (LP: 39.07+/-0.90% vs NP: 42.643+/-1.76%; P=0.09, normalized to NP) compared to NP rats. Additionally, no difference in HR between LP and NP rats were found (LP:338.50+/-16.36 bpm vs. NP: 333.75+/-4.78 bpm vs PPD14: 331+/-6.23 bpm; P=0.414, normalized to NP). Interestingly, LP rats had significantly reduced GSC (LP: -27.50+/-1.41%; NP: -34.375+/-1.95%; PPD14: -33.725+/-1.73%; P<0.01, normalized to NP) and GRS (LP:42.77+/-3.41% vs NP: 58.3+/-4.97% vs PPD1: 52.11+/-7.54%; P<0.01, normalized to NP) strain compared to NP rats. Changes were transient as both strain values were reversed by day 14 in the circumferential plane and after 1 day in the radial plane after delivery. Western Blot analysis showed that phosphorylated Akt/Akt protein levels were decreased 7-fold at the end of pregnancy compared to NP (phospho-AKT/AKT LP: 0.13+/-0.1 vs NP: 1.0+/-0.14 in NP). Additionally, phosphorylated STAT3/STAT3 was also significantly lower (4-fold) at the end of pregnancy (phospho-STAT3/STAT3 LP:1.48+/-1 vs NP: 4.02±1.73)

**Conclusions:** The hearts of LP rats have significantly different strain changes compared to NP when using speckle-tracking echocardiography. However, whether these changes are an adaptive response or is a response to sub-clinical myocardial dysfunction has yet to be elucidated. In the future, use of STE for early detection of pregnancy associated cardiovascular complications.



# TRANSCRIPTIONAL REGULATION OF CELLULAR PROLIFERATION IN T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

Soliman M<sup>1,2</sup>, Song C<sup>1</sup>, Gowda C<sup>1</sup>, Ding Y<sup>1</sup>, Dovat S<sup>1</sup>

<sup>1</sup>Department of Pediatrics, Pennsylvania State University College of Medicine, Hershey, PA; <sup>2</sup>Burrell College of Osteopathic Medicine, Las Cruces, NM

Abstract: T-cell acute lymphoblastic leukemia (T-ALL) is an aggressive hematological malignancy that represents a therapeutic challenge. Next-generation sequencing revealed that a subset of T-ALL harbors inactivating mutations or deletion of one allele of the IKZF1 tumor suppressor. These data suggest that IKZF1 acts as a tumor suppressor in T-ALL. The IKZF1 gene encodes the Ikaros protein that functions as a regulator of transcription and a tumor suppressor in B-cell acute lymphoblastic leukemia. However, the molecular mechanism of Ikaros tumor suppressor function in T-ALL is unclear. Using quantitative chromatin immunoprecipitation (qChIP), we determined that Ikaros binds to the promoter regions of the CDC2 and CDC7 cell cycle genes in primary T-ALL cells in vivo. Gain-of-function experiments showed that Ikaros overexpression in T-ALL results in reduced expression of CDC2 and CDC7, as evidenced by quantitative RT-PCR (qRT-PCR) and Western blot. The knock-down of Ikaros with shRNA in T-ALL cells resulted in increased transcription of CDC2 and CDC7 as indicated by qRT-PCR. These data suggest that Ikaros can regulate cell cycle progression in T-ALL by repressing transcription of the CDC2 and CDC7 genes. Next, we studied the mechanisms that regulate Ikaros' ability to repress CDC2 and CDC7 in T-ALL. Ikaros' function as a transcriptional repressor is regulated by Casein Kinase II (CK2). CK2 is overexpressed in hematopoietic malignancies and increased expression of CK2 results in T-ALL in murine models. We tested the effect of CK2 inhibition on Ikaros' ability to regulate transcription of CDC2 and CDC7 in human T-ALL. Molecular inhibition of CK2 with shRNA against the CK2 catalytic subunit resulted in reduced transcription of CDC2 and CDC7, as evidenced by qRT-PCR. This was associated with increased DNA-binding of Ikaros to promoters of CDC2 and CDC7, as shown by qChIP. These data suggest that CK2 impairs Ikaros' ability to transcriptionally repress CDC2 and CDC7 and to regulate cell cycle progression in T-ALL. Inhibition of CK2 enhances transcriptional repression of CDC2 and CDC7 by Ikaros, resulting in improved control of cell cycle progression in T-ALL. In conclusion, results show that control of cell cycle progression in T-ALL occurs trough Ikaros-mediated transcriptional regulation of CDC2 and CDC7. Overexpression of CK2 impairs Ikaros' ability to repress CDC2 and CDC7 expression, which contributes to deregulation of cell cycle control in T-ALL. Results suggest a potential mechanism of therapeutic action of CK2 inhibitors for the treatment of T-ALL.



# DYNAMIC COMPUTER MODELING OF PROTEIN AND FLUID EXCHANGE IN SKELETAL MUSCLE AND ELUCIDATING THE PHYSIOLOGICAL PROPERTIES UNDERLYING THE THERAPEUTIC EFFECT OF LYMPHATIC PUMPING IN OMT

Dacquay YJ1\*, Hummel-Price BT1\*, Joseph N. Benoit2

<sup>1</sup>Burrell College of Osteopathic Medicine, Las Cruces, NM; <sup>2</sup>Department of Physiology and Pathology, Burrell College of Osteopathic Medicine, Las Cruces, NM

\*equal contributing authors

**Introduction**: The exchange of fluid and protein across skeletal muscle capillaries and lymphatics has been extensively studied in-vivo. However, less is known about these exchanges across the interstitium and into the lymphatic system, as in-vivo measurements cause disruption of the normal capillary, interstitial and lymphatic interfaces. Additionally, there is a lack of understanding of the underlying principles governing fluid removal during therapeutic lymphatic pumping interventions. For these reasons, a dynamic computer model was created that can simulate these various interfaces in edematous states and has the ability to simulate lymphatic osteopathic manipulative treatment (OMT).

**Methods:** A computer model was created using Stella Architect (ISEE Systems, Lebanon, NH) by incorporating well established mathematical fluid and protein exchange relationships in order to accurately model the transcapillary, interstitial, and lymphatic interfaces. After validation of the model, various edematous conditions were created and treated with multiple pumping pressures and oscillation frequencies for two and ten minute iterations. In total, 170 experiments were run, with data being calculated every 1/100th of a second across several variables (fluid flux, protein flux, quantity of protein, concentration of protein in the interstitium and interstitial volume). Comparative analysis was performed for the various experiments in order to determine how each variable was affected by the edematous condition and treatment selection.

**Results:** In non-edematous states, simulated lymphatic treatment of 60 mmHg, 1Hz, for 10 minutes was able to increase lymphatic fluid flux (Jv,L) by 129.21%, while capillary fluid flux (Jv,c) increased by 67.21%. The concentration of interstitial protein (Ci) decreased by 4.30%. Furthermore, interstitial volume (Vi) and quantity of protein (QP) decreased by 4.93% and 9.02%, respectively. In +2 edematous state, the same simulated lymphatic treatment was able to increase Jv,L by 6.59% and decrease Jv,c rate by 63.26%. QP decreased by 22.07%, Vi decreased by 30.29% and Ci increased by 11.79%. The percentage of contribution from Jv,c and Jv,L in reducing interstitial volume during treatment depends on the degree of edema. The Jv,c and Jv,L contributions in non-edematous state, +1, and +2 edema was (34.22%: 65.78%), (64.43%: 35.57%), and (90.57%: 9.43%) respectively. Treatment pressures of 10, 30, and 60 mmHg at 1 Hz for 10 minutes in a +2 edematous state allowed maximum decreases in Jv,c by 23.0%, 67.9%, and 135.5% respectively and all had maximum Jv,L increases of 11.0%.

Conclusion: The physiological mechanisms involved in reducing interstitial volume during OMT vary depending on treatment pressure and duration of pumping, varying degrees of edematous and non-edematous states. In non-edematous states the treatment pumps caused a greater increase in lymphatic fluid flux rate (Jv,L) and an increase in capillary filtration rate (Jv,c) than in edematous conditions. In edematous conditions treatment favored capillary absorption of fluid. The contributions of increasing Jv,L and decreasing Jv,c are dependent on the degree of edema, with more severe edema favoring a greater decrease in Jv,c and smaller increases in Jv,L. Our model findings suggest that the therapeutic efficacy of the lymphatic techniques on movement of fluid into the lymphatic system varies with the degree of edema. Our model further predicts that decreased capillary filtration and capillary absorption of interstitial fluid, not lymphatic drainage, is the primary route of fluid removal during therapeutic lymphatic pumping interventions used in the treatment of severe edema.



# DEVELOPMENT OF A MULTIPLEXED REVERSE TRANSCRIPTION-LOOP-MEDIATED ISOTHERMAL AMPLIFICATION ASSAY FOR THE DETECTION OF WEST NILE VIRUS IN THE CULEX MOSQUITO

Jaynes J, Bramblett D, Woods M

Department of Microbiology and Pathology, Burrell College of Osteopathic Medicine, Las Cruces, NM

**Introduction:** The number of cases of Arthropod-borne viruses such as West Nile Virus (WNV), Dengue Virus, and Chikungunya in North and South America have been increasing at an alarming rate. Due to its proximity to Latin America, and a changing climate, the American Southwest is especially susceptible to these illnesses. The purpose of this project is to develop a highly sensitive and specific bed-side assay for the detection of West Nile Virus that could be performed without the use of bulky and expensive laboratory equipment. Loop-Mediated Isothermal Amplification (LAMP) has been shown to be a more rapid, affordable, and sensitive alternative to Polymerase Chain Reaction (PCR). This project aims to optimize a WNV specific RT-LAMP assay for the detection of WNV RNA extracted from *Culex* mosquitoes and set-up an initial design for future field applications with urine, blood, and saliva.

**Methods:** The set of 6 primers that were used, are specific for the WNV E gene that encodes the envelope (E) protein of WNV as described by Parida et al (2003). The P $\Delta$ 430 WNV DNA plasmid, kindly provided by Kathy Henley at New Mexico State University, was used as the RT-LAMP target in order to optimize the LAMP assay. The reaction conditions were established using the RAN and RNA RT-LAMP kit from Lucigen. Hydroxynaphthol blue (HNB), a metal titration indicator, was used to create a colorimetric test for nucleic acid amplification changing from violet to blue. Magnesium sulfate concentration was titrated to establish a visibly detectable positive reaction. The samples were incubated at 70°C for 30 minutes in a thermocycler. The reaction was photographically documented prior to confirming product formation by agarose gel electrophoresis. Once the reaction was optimized with P $\Delta$ 430 plasmid template the assay was tested on RNA extracted from *Culex* mosquitos harvested by collaborators at University of St. Thomas in Houston, Texas. The RNA sample was previously analyzed by sequence confirming the presence of WNV RNA.

**Results:** The optimization of the LAMP assay for P $\Delta$ 430 WNV was successful. There was a colorimetric change in the samples from violet to blue in the positive control and reactions containing WNV nucleic acids but not in the negative controls. The positive color change was only seen at Magnesium sulfate concentrations below 0.7mM. This was followed by successful assay amplification of WNV RNA from *Culex* mosquitos at the established reaction conditions This result indicates that there was amplification WNV RNA reverse transcribed from the P $\Delta$ 430 which was confirmed through gel electrophoresis.

Conclusion/Discussion: We have found that a simple colorimetric change can be used to detect WNV RNA in mosquito samples within thirty minutes. It is important that additional experiments to confirm the specificity of the reaction be conducted. However, additional future experiments will involve establishing quick and easy sample preparation methods in which this assay can be used. HNB dye is a relatively cheap metal titration indicator as compared to other amplification indicators such as EvaGreen or SYBR green. This experiment has potential uses for patient diagnostics at the bedside or field research.



# NEUROLOGICAL RESPONSES TO STRESS ARE MODIFIED BY TIME OF EXPOSURE AND HYPERTENSION

Gilderman GS, Gosselink KL

Department of Physiology and Pathology, Burrell College of Osteopathic Medicine, Las Cruces, NM 88001

**Introduction:** Hypertension, an increasingly prevalent cardiovascular disorder, has major consequences for patients and the healthcare system worldwide. While stress does not directly cause hypertension, elevated levels of vasoconstricting hormones and repeated blood pressure elevations are mechanisms through which stress has been associated with hypertension (1). Additionally, hypertension is a risk factor for stroke, which follows circadian patterns of increased risk (6am-8am and 6pm-8pm) (2). Stress and stroke are linked in a complex relationship that involves the activation of the HPA axis and the sympathetic nervous system. Our study examined whether exposure to acute or repeated restraint stress at different times in the circadian cycle affects brain regions involved in generating stress responses and in cardiovascular control. Both spontaneously hypertensive (SHR) and normotensive control (Wistar-Kyoto; WKY) rats were included in this analysis. Our hypothesis was that SHR animals would exhibit increased neuronal activation in response to stress, specifically in brain regions known to be involved in the neuroendocrine outputs associated with stress.

**Methods:** Adult male SHR and WKY rats were acutely (30min x 1d) or repeatedly (30min x 14d) restrained during the light or dark phase of the light cycle (0900 or 1900). Control rats were not stressed. Perfused brain sections were immunohistochemically stained for period-1 (Per1) protein, a stress-sensitive regulator of circadian rhythms, which was then quantified in the paraventricular (PVN) and dorsomedial (DMH) hypothalamic nuclei and the central (CeA) and medial (MeA) amygdala. Our lab has demonstrated that SHRs fail to habituate to repeated stress exposure, as evidenced by increased Fos expression in the PVN and DMH, and that responses to acute stress differ by time of day.

**Results:** Per1 was localized to multiple regions throughout the brain, including the suprachiasmatic nucleus, cortex, hippocampus and dentate gyrus. Per1 was also found in all of our regions of interest; the number of Per1+DMH neurons was decreased by acute stress while no effect of stress was apparent in the PVN. Interestingly, repeated restraint stress reduced the number of Per1-expressing neurons in the CeA, but only in SHR rats. Low levels of Per1 expression were observed in the MeA, but a trend toward increasing expression was seen following repeated exposure to restraint stress in both WKY and SHR animals.

**Conclusions:** Our findings suggest that pre-existing hypertension can influence how the brain responds to stressful stimuli, with a trend toward enhanced stress sensitivity in terms of HPA axis function. In contrast, sympathetic influences on cardiovascular control may be diminished. The experience of stress remains significant regardless of whether an individual is hypertensive or normotensive, but the time of day in which stress is experienced may be a critical factor in the downstream consequences of stress. Gaining a better understanding of stress-hypertension interactions in the central nervous system will aid the development of treatments for these and related conditions.



# DETERMINING THE EFFECTS OF RESVERATROL ON HEXOKINASE II MITOCHONDRIAL MEMBRANE ATTACHMENT IN CANCER CELLS

Nguyen C\*, Carabajal RJ\*, Moradeyo IG\*, Ontiveros SJ

Department of Anatomy and Cell Biology, Burrell College of Osteopathic Medicine, Las Cruces, NM \*Authors contributed equally

**Introduction:** Fundamentally, cancer is a progressive disease of continuous cell proliferation where malignant cells have lost their ability to properly regulate the progression of the cell cycle. The chief concern with the use of current anti-cancer strategies is that they are also harmful to normal cells. For this reason, there is a desperate need for more target-based strategies that selectively target cancer cells.

Hexokinase (HK) proteins are glycolytic enzymes that bind mitochondrial membranes and are responsible for phosphorylating glucose within the first step of glycolysis during ATP production. Studies have shown that, unlike normal cells, cancer cells consume more glucose by shifting ATP production from a normative oxidative phosphorylation state to aerobic glycolytic mechanisms. Therefore, once cells have become malignant, glycolysis is a pivotal mechanism for the growth and maintenance of cancer cells. These differences observed between normal and malignant cells in securing ATP that serves as a potential target for therapies.

Resveratrol (2,5,4'-trihydroxy-trans-stilbene), a naturally occurring polyphenol, has been shown to have minimal toxicity to normal cells while demonstrating anticancer activity. This has been observed in a variety of cancer cell lines, including A549, HeLa, and MCF-7 cells.

In this study, we aim to determine if resveratrol is capable of inhibiting glycolysis in cancer cells by targeting HKII and its attachment to mitochondrial membranes in HeLa cells. Consequently, we hypothesize that the inhibition of glycolysis by resveratrol is achieved by HKII membrane detachment.

#### **Methods**:

<u>Cell Culture</u>: Human HeLa (cervical cancer) cells were used and cultured in this study and were seeded in 12-well or 6-well plates overnight for our studies. Cells were then incubated for 24h in the absence or presence of 25, 50, 75, 100, and 125 μM resveratrol. <u>Cell Viability Assay</u>: To determine the proliferative effects of resveratrol on cancer cells, total, live, and dead cells were counted using a NanoEnTek E1020 Hemocytometer and cell viability was calculated. <u>Immunofluorescence Assay (IFA)</u>: Hexokinase II was detected with primary antibodies, while the mitochondria and DNA were probed with MitoTracker Green and Hoeschst, respectively. <u>Enzymatic Assay</u>: Cell lysates were prepared according to manufacturers recommendations, and the activity of hexokinases was analyzed at 450nm using a Hexokinase Colorimetric Assay Kit.

**Results:** Although we observed no significant difference in the absence or presence of various concentrations of resveratrol when calculating cell viability, we did observe a significant change in the localization of the mitochondria probe, MitoTracker Green. MitoTracker Green is a green-fluorescent mitochondria stain and is well known for accumulating in healthy mitochondria. MitoTracker Green accumulated in the mitochondria of HeLa cells in the absence of resveratrol. In contrast, the mitochondria probe accumulated in the cytosol in the presence of resveratrol, which is indicative of mitochondrial stress and potential loss of mitochondria integrity.

**Conclusions**: In previous studies, resveratrol has been shown to cause the detachment of hexokinase from the mitochondria by affecting mitochondrial integrity. Herein, we show that resveratrol, after a 24 hour incubation period, does not affect cell viability, but we did observe increased cell death in the presence of drug with extended incubation periods. We also demonstrated that higher doses of resveratrol results in accumulation of MitoTracker in the cytosol, which is indicative of mitochondria stress. Currently, we are unable to assess the full extent of the mitochondria effects.



# TRANSCUTANEOUS AURICULAR VAGUS NERVE STIMULATION INCREASES CARDIAC AND GLANDULAR PARASYMPATHETIC ACTIVITY

Kurian AP, Weiler KN, Stauss HM, Whitson DDS, Kania AM, Opena M, Orellana JN Departments of Biomedical Sciences and Clinical Medicine, Burrell College of Osteopathic Medicine, Las Cruces, NM

**Introduction:** The development of new biologic drugs has revolutionized the treatment for chronic inflammatory diseases. However, a majority of patients are unable to benefit from these drugs due to the high cost and potentially severe adverse effects. Thus, there is a need for more affordable therapeutic strategies with fewer side effects. Vagal nerve stimulation (VNS) may be a potential treatment option for inflammatory diseases, because VNS may activate the cholinergic/parasympathetic anti-inflammatory reflex. Traditionally, VNS required surgical implantation of a stimulator with electrodes on the cervical vagus nerve. However, transcutaneous stimulation of the auricular branch of the vagus nerve (taVNS) may achieve similar therapeutic effects non-invasively. We hypothesized that taVNS causes an increase in parasympathetic nervous system activity that potentially activates the cholinergic anti-inflammatory reflex.

**Methods:** On each of three consecutive study days, a 30-minute baseline recording preceded 15 minutes of taVNS (10 Hz, 300 μs) or no intervention (control group), followed by 30 minutes of post-intervention monitoring. During the protocol, the ECG and non-invasive arterial blood pressure (Finapres, Ohmeda, Madison, WI) were recorded continuously. Parasympathetic tone was assessed by high frequency (HF) spectral power of heart rate variability (HRV) and indirectly by the salivary flow rate. HF HRV is a frequency-domain HRV parameter that reflects parasympathetic modulation of cardiac function. A potential activation of the cholinergic anti-inflammatory reflex will be assessed by salivary cytokine (IL-β, IL-6, IL-8, TNFα) and IgA levels determined by ELISA.

**Results:** Age tended to be higher in the control group  $(59\pm10 \text{ years})$  than in the taVNS group  $(34\pm12 \text{ years}, P=0.16)$  and body mass index was significantly higher in the taVNS groups  $(34\pm2 \text{ kg/m}^2)$  compared to the control group  $(23\pm2 \text{ kg/m}^2, P<0.05)$ . Consistent with the somewhat younger age of the subjects in the taVNS group, HF HRV tended to be higher during the initial baseline recording in the taVNS group compared to the control group  $(4.6\pm1.2 \text{ bpm}^2 \text{ vs.} 2.1\pm0.4 \text{ bpm}^2, P=0.07)$ . Following the intervention, HF HRV was not different from the initial baseline recording in the control group  $(2.3\pm0.5 \text{ bpm}^2, \text{ n.s.})$  but had increased significantly in the taVNS group  $(6.0\pm1.4 \text{ bpm}^2, P<0.05)$ . This suggests activation of the parasympathetic nervous system by the taVNS intervention. This effect of taVNS was consistent on all three study days.

Prior to the first taVNS application on the first study day, saliva flow rate was not different between the two groups  $(0.39\pm0.05 \text{ mL/min} \text{ vs. } 0.41\pm0.07 \text{ mL/min}$ , taVNS vs. control, n.s.). However, prior to the taVNS application on the third study day, saliva flow rate had doubled in the taVNS group  $(0.78\pm0.20 \text{ mL/min}, P<0.05)$  but did not change significantly in the control group  $(0.54\pm0.08 \text{ mL/min}, \text{ n.s.})$ . Saliva flow rate depends on parasympathetic innervation of the salivary glands. Thus, the increased saliva flow rate in subjects in the taVNS group on the third study day prior to the  $3^{\text{rd}}$  taVNS application suggests that repeated applications of taVNS increase parasympathetic nervous system activity into the following day.

**Conclusion:** Non-invasive taVNS increases HF HRV, a marker of parasympathetic modulation of cardiac function and increases saliva flow rate, a marker of parasympathetic innervation of the salivary glands. These data are consistent with the idea that taVNS activates the cholinergic/parasympathetic anti-inflammatory reflex and may potentially be beneficial in patients with chronic inflammatory disease.



# COMPUTER MODELLING: STABILIZING OLEOCANTHAL USING VARIOUS DOCKING MOLECULES SUCH AS LECITHIN, CYCLODEXTRIN, PEG, AND CARBON NANOTUBES

Nguyen Gonzalez C1\*, Kisule A1\*, Talipov M2, Yukl E2, Breslin P3, Selinfreund R1

<sup>1</sup>Department of Physiology and Pathology, Burrell College of Osteopathic Medicine, Las Cruces, NM; <sup>2</sup>Department of Chemistry and Biochemistry, New Mexico State University, Las Cruces, NM; <sup>3</sup>Monell Chemical Senses Center, Philadelphia, PA and Rutgers University Department of Nutritional Sciences, New Brunswick, NJ \*Equal contribution between the two authors

**Introduction:** Oleocanthal (OC), a phenolic compound found in extra virgin olive oil (EVOO), has attracted attention from researchers recently due to its anti-inflammatory, neuroprotective, and anti-carcinogenic effects. OC particularly targets cancer cells and prompts necrosis, while sparing normal healthy cells and it does so by inducing lysosomal membrane permeabilization (LMP). It is believed that the two aldehyde groups of OC are responsible for such mechanism. However, the aldehyde groups are readily reactive to water, causing OC to lose partial or all beneficial effects. Therefore, we aim to stabilize OC in the environment, especially when it is used via oral and/or transdermal administration route.

**Methods:** <u>Theoretical Method</u>: There are several intermolecular forces between molecules that determine the thermodynamic stability status of molecule combinations; including Van der Waals, dipole-dipole interaction, hydrogen bond, and ionic bond. Based on these interactions, computer models were built to maximize the interactions between OC and the docking molecules. <u>Computer Modelling Method</u>: Avogadro, version 1.2.0, was used to build structures of OC, lecithin, cyclodextrins (alpha, beta, and gamma), PEG (diethylene glycol and triethylene glycol), and carbon nanotubes (CNT). OC was then placed next to each molecule of interest in different arrangements and different ratios. For each combination, auto optimizing tool was used to generate optimized molecular geometry and measure stabilization energy. Force field was UFF (Universal Force Field), with four steps per update and steepest descent algorithm. VMD 1.9.3 software was then used to enhance and visualize the optimized structures.

**Results:** The hypothesis for the computer modeling experiment was that the sum of stabilization energy of the individual molecules (oleocanthal and the docking molecule of choice) would be higher than that of the docked combination. This was true for certain docking combinations and not others. In addition, special interest was given to docking molecules that efficiently wrapped around the highly reactive aldehyde groups on OC conferring protection from other reactants like water. Two of the docking molecules were utilized to sandwich OC and offer protection to the aldehyde groups. Cyclodextrin as a docking molecule offered the most stability. Particularly, two beta cyclodextrins wrapped around one molecule of OC (2:1) generated the most thermodynamic stability by 268.5 kJ/mol, and the aldehyde groups were most protected. Followed were two alpha cyclodextrins wrapped around one molecule of OC with stabilization energy difference of 246.5 kJ/mol, however, the alpha cyclodextrins were arranged in such a way that aldehyde groups were exposed to the environment. The least stable cyclodextrin-OC combination was observed when a single alpha cyclodextrin was used to protect the aldehyde group of OC (77.6 kJ/mol). Favorable results were obtained from a combination of OC surrounded by four triethylene glycol molecules, and by four diethylene glycol molecules with stabilization energies of 159.8 kJ/mol and 123 kJ/mol respectively. Furthermore, two lecithin molecules intercalated by OC was fairly stable by 81.8 kJ/mol. The combination of OC with polyethylene glycols or lecithin did not provide enough protection for the aldehyde groups. Lastly, carbon nanotubes and OC combinations offered the least stability compared to the aforementioned docking molecules used. Of note is the docking provided by the 6x2 carbon nanotube that yielded a destabilization energy of 4.2x10<sup>4</sup> kJ/mol.

**Conclusion:** The data shows that beta cyclodextrins offers the best stabilization energy among lecithin, cyclodextrins, diethylene glycol, triethylene glycol, and carbon nanotubes. This was achieved by using two beta cyclodextrins wrapping around one molecule of oleocanthal. Whether this arrangement could be used therapeutically remains to be evaluated. The next phase will be a cellular assay to determine the actual physical properties of this combination and calculate the stability *in vitro*.



# ANALYSIS OF KEY CELL CYCLE REGULATORS DURING G2/M PHASE CELL CYCLE ARREST IN HUMAN NEURAL PROGENITOR CELLS AFTER ZIKA VIRUS INFECTION

Cady Z, Khalique U, Blaine J, Long, J, Woods ME

Department of Physiology and Pathology, Burrell College of Osteopathic Medicine, Las Cruces, NM

Introduction: Zika Virus (ZIKV) is a mosquito-borne flavivirus known to be a teratogenic agent. ZIKV can cross the placenta, leading to depletion of Neural Progenitor Cells (NPCs), restriction of brain growth, and microcephaly (Gharbaran, 2018). Studies have shown that ZIKV induces G2/M phase cell cycle arrest and inhibits proliferation of neural cells (Liu, 2018). Several key cell cycle regulators such as cyclin B1 are also downregulated after ZIKV infection, contributing to abnormal nervous system development (Liu, 2018). The mechanisms of how RNA viruses such as ZIKV take advantage of the G2/M phase cell cycle arrest to replicate in host and cause pathophysiological effects are not completely understood. In this study, we aim to further elucidate the mechanisms of Zika-induced cell cycle arrest by observing the expression levels of key cell cycle regulators including Cyclin-Dependent Kinase 1 (CDK1), Cell Division Cycle 25C (CDC25C), and Proliferating Cell Nuclear Antigen (PCNA), which are important regulators of G2/M phase. We hypothesized that the previously mentioned cell cycle regulators are downregulated and/or have undergone further post-translational modifications which prevent their key functions in cell cycle regulation, making the cell vulnerable to virus-mediated damage.

**Methods:** NPCs were infected with ZIKV (strain MEX1-7) at an MOI 10 for 6, 12, 24, 48, and 72 hours. While investigating the G2/M phase cell cycle arrest after ZIKV infection we also treated NPCs with nocodazole at the aforementioned time points as a positive control of G2/M phase arrest. Nocodazole destabilizes microtubules, a key component of cellular division, and induces a G2/M arrest. We compared ZIKV- and nocodazole-treated NPCs with mock NPCs and monitored the protein expression of cell cycle regulators, including CDK1, PCNA, and CDC25C.

**Results:** Our preliminary data showed no significant change in expression levels of the cell cycle regulators in NPCs infected with Zika virus or treated with nocodazole, which is consistent with these proteins being post-translationally regulated via phosphorylation or ubiquitination. We are currently investigating changes in activation status of these proteins.

**Conclusion:** We have developed a model system for further investigations into the mechanisms of cell cycle arrest following Zika virus infection in human neural progenitor cells.

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# NEUROANATOMICAL CHARACTERIZATION OF GHSR1A EXPRESSION LEVELS IN STRESS AND HYPERTENSION

Besong T, Gosselink K

Department of Physiology and Pathology, Burrell College of Osteopathic Medicine, Las Cruces, NM

Introduction: Stress is associated with an increased incidence of hypertension, which is mediated in part through HPA axis activation. The result is enhanced cortisol secretion and its downstream effects on arterioles and aldosterone activity. Sympathetic nervous system activation and epinephrine/norepinephrine release are also characteristic of the stress response; more recently, it has been shown that the "hunger hormone" ghrelin is also secreted in response to stress. Produced primarily by gastric endocrine cells, ghrelin acts on the hypothalamus and other brain regions through the type 1a growth hormone secretagogue receptor (GHSR1a). This orexigenic peptide functions in energy balance and homeostasis by stimulating food intake, but also impacts anterior pituitary function and plays a role in circadian regulation, reward system, and cardiovascular control. With regards to the effects on the cardiovascular system, reduced circulating ghrelin levels have been observed in hypertensive individuals; identifying an interesting stress-ghrelin-hypertension interrelationship that is not fully understood. The goal of our study, therefore, is to compare and quantify GHSR1a expression in the brains of stressed and non-stressed hypertensive and normotensive rats. We hypothesized that acute or repeated stress exposure would increase the production of ghrelin, resulting in increased GHSR1a expression, with its effect being reduced in the hypertensive animals.

**Methods:** Adult male spontaneously hypertensive rats (SHR) and normotensive Wistar-Kyoto (WKY) rats were acutely (30min x 1d) or repeatedly (30min x 14d) restrained or were not stressed (control). Perfused brain sections were immunohistochemically stained for GHSR1a, which was quantified in multiple brain regions including the paraventricular (PVN), dorsomedial (DMH), and arcuate (ARH) hypothalamic nuclei as well as the central (CeA) and medial (MeA) amygdala. Our laboratory has demonstrated stress-induced changes in neuronal activation, via Fos expression, in the PVN and DMH of both SHR and WKY rats. Those data highlighted the fact that repeated restraint stress exposure leads to a habituation of the stress response in WKYs, but not SHRs; suggesting that pre-existing hypertension alters the way the brain responds to stress.

**Results:** We confirm and extend existing information regarding the broad distribution of GHSR1a expression in the brain. As expected, GHSR1a+ cell bodies were seen in the ARH, with stained fibers also observed in the ARH and the median eminence. The CeA also contained positively-stained cells and fibers, and GHSR1a expressing cells were seen in the DMH and in the parvocellular PVH (with some in the magnocellular and periventricular subregions). In SHR animals, repeated but not acute restraint stress reduced the number of neurons expressing GHSR1a in the ARH, MeA and DMH. Suggestive decreases were also seen in the PVH and CeA of repeatedly-stressed SHRs.

**Conclusions:** Somewhat contrary to our hypothesis, repeated stress exposure in SHRs reduced ghrelin sensitivity in multiple brain regions that are critical in cardiovascular control and neuroendocrine mediated responses to stress. This may be a protective mechanism against long-term elevations in ghrelin that would occur with repeated stress, which could lead to further alterations in cardiovascular function and energy balance.



### A RARE INSTANCE OF A BENIGN OVARIAN CYSTIC TERATOMA WITH MULTIPLE TEETH

Albrechtsen CL<sup>1</sup>, Todd D<sup>2</sup>, Wellington B<sup>2</sup>

<sup>1</sup>Burrell College of Osteopathic Medicine, Las Cruces, NM; <sup>2</sup>Memorial Medical Center, Las Cruces, NM

**Abstract:** Benign ovarian cystic teratomas, or dermoid cysts, are common ovarian tumors with elements of ectoderm, mesoderm and endoderm. The majority of these are asymptomatic and discovered incidentally on imaging or during workup of abdominal pain as 16% present as ovarian torsion. This case reviews the findings of a woman who presented to the ED with lower abdominal pain which revealed a benign cystic teratoma. Surgical excision revealed an enlarged right ovary with a large mass of hair, sebaceous fluid, cartilage, bone, marrow, muscle and 9 teeth. All elements were carefully resected and excised while minimizing spillage of contents. The incidence of dermoid cysts with multiple teeth is not well documented, but agreed to be rare.



#### EXTRA-OSSEOUS CHORDOMA OF SPINE IMITATING NEUROGENIC TUMOR

Fadah K<sup>1</sup>, Velimirovic B<sup>2</sup>

<sup>1</sup>Burrell College of Osteopathic Medicine, Las Cruces, NM; <sup>2</sup>Neurosurgery Department, Del Sol Medical Center, El Paso, TX

**Introduction:** Chordoma is a rare primary malignant tumor of the spine and skull base. It has been categorized as an osseous tumor, which is mainly found at the clivus and sacrococcygeal region. Spine extra-osseous chordoma (SEC) has a better prognosis, and is usually ignored and presumed to be benign neurologic tumor.

Results and Discussion: Currently, there are only 20 case reports in scholarly literature that discuss SEC. Therefore, the purpose of this article is two-fold. Firstly, to increase awareness by reviewing the limited cases available in previous literature on SEC. Secondly, to analyze one case of SEC, on a 19 year-old female with this type of chordoma. Initially, it was thought to be a neurologic tumor and only after reviewing the pathology report was our attention directed toward SEC. In the mobile spine and sacrum, the primary surgical treatment of chordoma is an en-bloc resection. However, in this case the posterior and anterior approach was executed, this is a novel approach commonly used for dumbbell cervical tumors. Due to the critical location and size of the tumor, some of the tumor was not resected on the anterior side, and chemotherapy was a supplementary treatment used in this case to eradicate remaining tissues. Spine extra-osseous chordoma of Notochordal origin was found mostly in the base of the skull and sacrum reign is malignant with low rate of metastasis. Resection of the entire tumor is the main treatment approach reported in the majority of the literature. The ultimate intention of the paper is to promote accurate diagnoses and appropriate treatment of SEC tumors in the future.

**Conclusion:** Spine extra-osseous chordoma is very rare and usually can be found in the cervical and epidural area. SEC has good prognosis because of its lower recurrence rate and it's not as aggressive as other chordoma tumor types. Frequently, it's ignored and presumed to be benign neurologic tumor. The en-bloc resection approach of the chordoma tumor is still the golden treatment approach and accomplishing a wide excision is necessary to shrink risk of recurrence rate.



# PARAMETERS OF UCL REPAIR COMPARED WITH RECONSTRUCTION IN THE TREATMENT OF ULNAR COLLATERAL LIGAMENT TEAR

Hunsaker BD, Richards KD, An YW

Burrell College of Osteopathic Medicine, Las Cruces, NM; New Mexico State University, Las Cruces, NM

**Introduction:** Overhead throwing athletes are experiencing increasing rates of ulnar collateral ligament (UCL) tears.¹ Torn UCL's lead to pain, loss of performance in athletes, and functional deficits.8 In general, two options to fix UCL tears are utilized: reconstruction or repair. Early reports on UCL repair demonstrated a high level of post-operative failure in high-level baseball pitchers.⁴ Moreover, repair is contraindicated in ligamentous tissue that is of poor quality due to long throwing careers and repetitive microtrauma.⁴ On the other hand, UCL reconstruction using autografts has resulted in return to sport rates as high as 97% for professional baseball pitchers in some studies. Therefore, UCL reconstruction remains the gold standard for treating patient populations such as overhead throwing athletes.⁵ However, although surgical reconstruction has shown benefits in high demand athletes in terms of prolonging careers and replacing poor quality tissue, UCL repair may be a valuable option in terms of gap formation, valgus load tolerance, and time to return to sport activity.²

**Results:** We analyzed several articles in response to the question, "Does an internal bracing UCL repair have less gap formation, better valgus load tolerance, and faster return to sport rates when compared to UCL reconstruction using grafts?" Two systematic reviews and one biomechanical study were analyzed. Cadaveric models were used to recreate UCL tears with subsequent reconstruction or repair. Decreased gap formation and increased valgus load tolerance after stressing events was found in the UCL repair group. <sup>4,5</sup> Both systematic reviews found that UCL repair resulted in less gap formation and quicker return to sport rates than the reconstruction groups. <sup>3,5</sup>

**Conclusion:** Based off the strength-of-recommendation taxonomy<sup>7</sup>, consistent findings suggest level A evidence in support of UCL repair techniques as a treatment option for athletes with partial UCL tears and shorter career expectations.



#### CASE REPORT: DORSAL PENILE FOREIGN BODY

Hunsaker B, Nelsen A

Burrell College of Osteopathic Medicine, Las Cruces, NM

**Introduction:** Insertion of foreign bodies in the penis has been practiced throughout the world.<sup>1</sup> As with some provinces of Papa New Guinea, people perform penile manipulation as rituals to show manliness, maintain sociocultural tradition, increase pleasure, or even with the thought of improving genital hygiene.<sup>2</sup> Reports of incarcerated men in the Southwest region of the United States have been published of using various techniques to insert foreign bodies into their penis', specifically domino game pieces.<sup>3</sup>

Case: We report a case of a 33 year old, male patient who was brought to the emergency room from a state jail with the chief complaint of penile infection. The patient was accompanied by two jail guards and was found to have inserted a plastic deodorant roller ball in the mid-shaft dorsum of his penis. There was a poorly healed 2 cm incision in this location, which had been sutured using the wire from a pair of headphones. Urology was consulted and surgery was performed on the penis. General anesthesia was given to the patient and a dorsal penile block was administered intraoperatively. The headphone wire holding the incision closed, was removed. The existing incision was used to extract the deodorant roller ball and purulent drainage was expelled from the wound. For anti-bacterial therapy, 2 grams of Levofloxacin were used as an intravenous drip during the procedure. After debridement, the wound was left open to heal by secondary intent and wrapped with an anti-septic gauze. The patient was taken back to the jail and care was handed over to the nursing staff there. Further follow-up was lost due to incarcerated status of the patient.

**Conclusion:** The findings from this case report demonstrate the incidence of a novel penile foreign body as compared to those found in studies mentioned. As penile foreign bodies continue to be reported in incarcerated individuals, it is important to be aware of such practices while working in healthcare. While means of prevention of this issue remains uncertain and individualized, awareness of the possibility of such cases is important in order to care for such patients and ultimately patient safety.

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# SUBOCCIPITAL DECOMPRESSION LOWERS BLOOD PRESSURE THROUGH REDUCTION OF SYMPATHETIC TONE

Weiler KN, Kurian AP, Orellana JN, Stauss HM, Whitson DDS, Kania AM, Opena M Burrell College of Osteopathic Medicine, Las Cruces, NM

**Introduction:** Blood pressure is not well controlled in many patients with hypertension, even with aggressive pharmacologic treatment. There is a need for additional approaches to control arterial blood pressure. Some osteopathic manipulative treatment (OMT) techniques have been demonstrated to alter autonomic tone and thereby may reduce arterial blood pressure. With OA decompression, pressure is applied to the investing and prevertebral layers of the deep cervical fascia that overlies the vagus nerve as it exits the skull and extends to the site of the sympathetic superior cervical ganglion. Thus, there is a possibility that OA decompression affects both, parasympathetic and sympathetic nervous system activity. We hypothesized that repeated applications of the OMT technique, suboccipital (OA) decompression, reduces arterial blood pressure potentially through alterations in autonomic tone.

**Methods:** On each of three consecutive study days, a 30-min baseline recording preceded 5 min of suboccipital (OA) decompression or no intervention (control group), followed by 10 min of rest and 30 min of post-intervention monitoring. During the protocol, the ECG and non-invasive arterial blood pressure (Finapres, Ohmeda, Madison, WI) were recorded continuously. Autonomic modulation of sinus node function was assessed by time-domain heart rate variability (HRV) analysis which measures the spontaneous fluctuations in heart rate over time. Sympathetic modulation of vascular tone was assessed by low frequency (LF) spectral power of systolic blood pressure.

Results: Subject characteristics were not significantly different in the two groups. In the OMT group, systolic blood pressure decreased during application of OA decompression (-8.4±4.4 mmHg, P=0.08) but then exceeded baseline levels during the post-intervention monitoring (+13.7±5.2 mmHg, P<0.01). In contrast, no significant changes in systolic blood pressure were observed over the experimental protocol in the control group. Consistent with the somewhat younger age of the subjects in the OMT group (44±13 years vs. 59±10 years in the control group), overall heart rate variability determined by SDNN (standard deviation of RR intervals) was higher in the OMT (60.9±8.5 bpm) compared to the control group (36.7±2.7, P<0.05). SDNN, significantly decreased during OA decompression (-10.3±3.2 bpm, P<0.01) and then returned to baseline levels during the post-intervention monitoring (59.7±8.7 bpm). In contrast, SDNN exceeded baseline levels at the end of the experimental protocol in the control group (+9.3±4.5 bpm, P<0.05). Throughout the experimental protocol, RMSSD (another HRV parameter) remained constant in both groups, suggesting no change in parasympathetic tone. Specifically, there was no change in RMSSD during OA decompression (49.7±12.9 bpm during baseline vs. 48.2±12.0 bpm during OA decompression, n.s.). SDNN is modulated by both sympathetic and parasympathetic tone, whereas RMSSD is only modulated by the parasympathetic nervous system. Thus, the decrease in SDNN during OA decompression together with the lack of a change in RMSSD, suggests that OA decompression reduces cardiac sympathetic tone. To assess sympathetic modulation of vascular tone, we also determined low frequency (LF) systolic blood pressure variability (BPV<sub>SYS</sub>). During OA decompression there was a significant decrease in LF BPV<sub>SYS</sub> (15.6±2.5 mmHg<sup>2</sup> vs. 30.8±5.8 mmHg<sup>2</sup> at baseline, P<0.05) that lasted into the post-intervention monitoring (19.6 $\pm$ 3.4 mmHg<sup>2</sup>, P<0.05).

**Conclusion:** The hypotensive effect of OA decompression was associated with reduced SDNN without changes in RMSSD and a reduction in LF  $BPV_{SYS}$ , suggesting reduced cardiac and vascular sympathetic tone. These data suggest that the hypotensive effect of OA decompression is mediated through a reduction in overall sympathetic tone.



# NON-FRUCTOSE BASED BEVERAGES: ASSESSMENT OF PROGRESSION OF METABOLIC SYNDROME

Sridhar S, Melgarejo K, Selinfreund R, Breslin P

Burrell College of Osteopathic Medicine, Las Cruces NM; Department of Nutritional Sciences at Rutgers University, New Brunswick NJ; Monell Chemical Senses Center, Philadelphia PA

Introduction: The importance of an evidence-based approach to developing beverages is a controversial topic that is perhaps hampered in part by the lack of clinical data. High fructose sugar-based beverages are consumed daily by millions of people around the world and have been indicated as the largest source of dietary fructose in the United States. Increased consumption of dietary fructose has also been implicated in the progression of metabolic syndrome and the development of non-alcoholic fatty liver disease (NAFLD); both risk factors for the development of Type 2 Diabetes Mellitus (T2DM). While the observation that there is a lack of metabolic balance in consumer products has been well studied in animal models, there is much less data on human subjects. Here we have started the process to undertake a human clinical trial to monitor the progression of metabolic parameters and liver health in adults with obesity and metabolic syndrome by replacing fructose sweetened beverages with a proposed metabolically balanced beverage made with isocaloric fructose-free sweetener. If the isocaloric fructose-free sweetener contained within the study beverage demonstrates an improvement of metabolic parameters, we will have an opportunity to improve patient compliance with recommended diet and lifestyle and reduce the risk of developing T2DM.

**Methods:** In our project we have developed an Institutional Review Board (IRB) protocol where participants will be randomized into one of three groups: experimental (non-fructose based beverage), negative control (fructose based beverage), or positive control (water). They will consume 3 – 4 beverages daily while eliminating all other sugar sweetened beverages for 60 days and otherwise maintaining their carbohydrate and caloric intake, and exercise regimen. Participants will undergo weight, blood pressure, and blood testing (fasting triglycerides, fasting HDL, AST, ALT) on Day 0 and Day 60, and blood pressure and finger stick glucose testing on Day 31.

This study protocol has been presented to Pearl IRB along with other regulatory requirements needed for a clinical study and we expect that our work will result in an approved protocol that allows for this study to move forward at the Burrell College of Osteopathic Medicine.



#### TESTICULAR CANCER ALONG THE UNITED STATES-MEXICAN BORDER

Taylor ZD<sup>1</sup>, McLeod EM<sup>1</sup>, Wright MT<sup>1</sup>, Gard C<sup>2</sup>, Woods ME<sup>1,3</sup>

<sup>1</sup>Burrell College of Osteopathic Medicine, Las Cruces, NM; <sup>2</sup>Department of Economics, Applied Statistics and International Business, New Mexico State University, Las Cruces, NM; <sup>3</sup>Department of Physiology and Pathology, Burrell College of Osteopathic Medicine, Las Cruces, NM

**Introduction:** Testicular cancer is the most common cancer affecting young males between the ages of 15 and 35 in the United States. The 5-year survival rate for all-stage testicular cancer is 95% and upwards of 99% if the cancer is detected when disease is localized to the testis. While incidence and survival data is readily available for the United States as a whole, there is a lack of literature examining trends in testicular cancer in New Mexico or in the United States-Mexico border region. This study examines the incidence and survival data of testicular cancer in New Mexico and further categorizes this data for border counties, non-border counties, Hispanic populations and non-Hispanic populations.

**Methods:** This study used data from the SEER 18 database. Incidence rates and 5-year survival rates for testicular cancer were obtained using the SEER\*Stat program following established NCI protocols. Data was filtered for New Mexico and then subdivided for border and non-border counties using the La Paz classification. Log rank analysis was used to examine differences in survival between groups.

**Results:** From 2000-2015, New Mexico had an incidence rate of testicular cancer of 6.3 per 100,000 people, significantly higher than the remaining SEER18 aggregate at 5.5 per 100,000 (P<0.001). New Mexico demonstrated a lower 5-year survival rate than the remaining SEER18 aggregate; however, this relationship was not statistically significant (P=0.3). New Mexico non-border counties demonstrated a lower 5-year survival than New Mexico border counties, though not significant (P=0.07). Hispanic populations living in border counties demonstrated significantly lower survival rates as compared to non-Hispanics living in the border region (P=0.03). Survival did not significantly differ between Hispanic populations in border counties and Hispanic populations in non-border counties (P=0.9). There was not a significant difference between stage at diagnosis between border and non-border communities in New Mexico.

Conclusion: Hispanic populations in the border region have higher rates of mortality from testicular cancer when compared to their non-Hispanic counterparts. This may be due in part to lower rates of insurance coverage and decreased access to doctors experienced by Hispanic border populations. Barriers to care for Hispanic populations living in the border region may lead to delays in diagnosis, but analysis of stage at diagnosis in this study was limited due to the small amount of cases that were staged. The higher incidence of testicular cancer in New Mexico does not appear to have a clear explanation and requires further investigation.



# PERCENTAGE OF STAPHYLOCOCCUS AUREUS AND MRSA COLONIZATION IN FIRST-YEAR OSTEOPATHIC MEDICAL STUDENTS

Meza-Rodriguez SM<sup>1</sup>, Bonilla J<sup>1</sup>, Johnson E<sup>1</sup>, Lay W<sup>1</sup>, Ayala S<sup>1</sup>, Ponce de Leon M<sup>1</sup>, Ortega A<sup>1</sup>, Hooshmand C<sup>1</sup>, Gutierrez S<sup>2</sup>, Woods M<sup>1</sup>, Domínguez DC<sup>2</sup>, Bramblett D<sup>1</sup>

Burrell College of Osteopathic Medicine<sup>1</sup> Las Cruces, NM; The University of Texas at El Paso<sup>2</sup>, El Paso, TX

**Introduction:** Growing antibiotic resistance to the most widely used antibiotics in the United States by common bacterial organisms is becoming a growing public health threat. The CDC has listed Methicillin-Resistant *Staphylococcus aureus* (MRSA) as a serious antibiotic-resistant threat in the United States, responsible for over 80,000 infections per year and over 11,000 deaths per year. MRSA infections can be acquired by coming in contact with a contaminated object or an infected wound. Furthermore, exposure to healthy individuals colonized with the pathogen is a risk factor for nosocomial acquisition of MRSA. MRSA colonization commonly occurs on several sites of the body including the hands and anterior nares, and the risk of colonization increases with increased exposure to the pathogen, as seen in healthcare workers. This project is a longitudinal study that aims to monitor the colonization rates of medical students throughout their four years of medical school. Screening will begin during their first year of medical school and continuing every year thereafter as they transition from their pre-clinical studies to their clinical rotations. This project aims to evaluate how experience and exposure in the medical field plays a role in participating as a risk factor for *S. aureus* and MRSA colonization.

**Methods:** Nasal swabs were obtained in the Fall of 2018, from first-year medical students attending Burrell College of Osteopathic Medicine. Students from Dona Ana Community College and New Mexico State University were recruited as controls. To obtain demographic information and previous healthcare exposure among students, they completed a survey after providing nasal swab samples. The samples were transported to The University of Texas at El Paso to be cultured for *S. aureus* and further genetic analysis for MRSA. To determine if the samples were *S. aureus*, they were plated on Mannitol Salt Agar (MSA) and a coagulase test was performed on positive MSA samples to confirm the presence of *S. aureus*. DNA was extracted from *S. aureus* samples and PCR was performed to asses for the presence of the mecA gene to confirm if the samples was positive for MRSA.

**Results:** A total of 74 samples were obtained, 52 participants were medical students and 22 participants were controls. 19% were positive for *S. aureus* and 1.4% were positive for MRSA. Among medical students only, 15.4% were positive for *S. aureus* and 1.9% were positive for MRSA. Among controls, 27.3% were positive for *S. aureus* and 0% were positive for MRSA.

**Conclusion:** The CDC estimates an average of 30% *S. aureus* colonization among the population and 1% colonization with MRSA. The results of this collection demonstrate a *S. aureus* colonization percentage below the national average, and a MRSA colonization percentage slightly above the national average. However, colonization can occur at multiple sites of the body and this project only evaluated colonization in the anterior nares, which can result in variable colonization percentages. Nasal swabs will continue to be obtained for the next three years to assess for a change in colonization rates among the medical students.



# FOUNDER EFFECT AND MUTATIONS IN BRCA1 GENES IN NEW MEXICO: A HISTORICAL LITERATURE REVIEW

Aburto J<sup>1</sup>, Nguyen-Espino BX<sup>2</sup>, Nguyen-Espino JT<sup>2</sup>

<sup>1</sup>Department of Clinical Specialties, Surgery, Burrell College of Osteopathic Medicine, Las Cruces, NM;

**Background:** The ancestors of Spanish crypto-Jewish populations in the Southwestern United States fled the Spanish Inquisition, and came to present-day New Mexico and the surrounding areas. The term Spanish crypto-Jews refers to the Jewish population who were forcedly baptized despite their resistance towards Catholicism. Though some families converted to Christianity, others escaped persecution and continued their Jewish traditions while settling in Colorado, New Mexico, Texas, Arizona and California. The notion of founder effects in the Spanish crypto-Jewish population could potentially explain the 185delAG mutations in the BRCA1 genes and the increased risk for developing breast cancer in the Southwest region.

**Objective:** To understand the historical background of Jewish descendants in New Mexico that would shed light on the susceptibility of the 185 delAG mutations in the BRCA1 genes.

**Methods:** A literature search was performed in the electronic database of PUBMED using the terms 185delAG, Spanish, and Jewish. The search was performed in English. A total of ten papers were identified, and six were selected for the literature review.

**Results:** The results show that individuals with BRCA1 mutations of Spanish crypto-Jewish ancestry carried the 185delAG mutation and shared a common ancestry in both Sephardic and Ashkenazi populations. These findings are consistent with the historical accounts of Jewish migration and the possibility of the founder effect occurring in the following states: New Mexico and Colorado.

**Conclusion:** In the Southwestern United States, there is great heterogeneity of Spanish and Jewish populations with increased risk of BRCA1 mutations. Therefore, New Mexico's population with Spanish crypto-Jewish ancestry should be screened for mutations in BRCA1.



<sup>&</sup>lt;sup>2</sup>Burrell College of Osteopathic Medicine, Las Cruces, NM

#### **REVISITING MICROTIA IN NEW MEXICO**

Christensen T¹, Diaz S¹, Vaudrey K², Velazquez M¹, Minugh-Purvis N² ¹Burrell College of Osteopathic Medicine, Las Cruces, NM; ²Department of Anatomy and Cell Biology, Burrell College of Osteopathic Medicine, Las Cruces, NM

**Introduction:** Microtia is a developmental anomaly of the external ear, characterized by phenotypes ranging from scarcely noticeable, minor deformities (microforms) to complete absence of the auricle and external canal. Associated conductive hearing deficits, if undetected, negatively impact quality of life and are detrimental to developing children. Microtia is relatively rare in global terms, occurring, on average, in 0.8 - 4.2 cases per 10,000 live births world-wide (Alasti and van Camp, 2009). Notably, prevalence is higher among many Native American groups and Latin American populations with indigenous admixture. We hypothesize: With a population approximately 9.4% American Indian and 46.3% Hispanic, an above average number of New Mexicans are at risk for microtia and its co-morbidities than is typical elsewhere in the US.

**Methods:** Literature review and explorations of online public health databases were undertaken in an attempt to address the following questions: 1. What is the etiology of microtia? 2. What is the incidence and distribution of microtia world-wide? 3. What is known of the distribution and incidence of microtia among the diverse ethnic groups of New Mexico? 4. What programs are in place in New Mexico to a) detect and b) remediate hearing loss? Simultaneous with this, we began to develop tools for assessing levels of microtia in the state. New Mexico does not participate in the *National Birth Defects Prevention Network (NBDPN)* nor does the *New Mexico Birth Defects Prevention and Surveillance System (BDPASS)* publish numbers of babies born annually with microtia. Given that the state is large and predominately rural with significant sociocultural heterogeneity, we surmised that multiple instruments would best assure the collection of data permitting accurate estimates of microtia in all resident sociocultural groups. We have thus designed a pilot study to determine the incidence of microtia in Doña Ana County and test the effectiveness of study instruments for future, expanded assessments.

Results: Our literature search has revealed that the etiology of microtia is currently poorly understood. The condition is clearly multifactorial, but none of several candidate gene(s) have yet been clearly isolated as specifically responsible. Nor are the majority of cases accounted for by implicated teratogens. Studies by Jaffee (1968), Tegtmeier and Aase (1973) and Nelson and Berry (1984) reporting above average rates of microtia among Navajo support our hypothesis but rigorous, updated studies are needed to confirm their accuracy and currency. The incidence in more southern portions of the state has, apparently, never been documented. However, far southern New Mexico, including much of Doña Ana County, is part of the Borderlands and the Mexican population of this region may be characterized as largely continuous with that of the northern Mexican state of Chihuahua. Mexico's *Registro y Vigilancia Epidemiologica de Malformaciones Congenitas Externas (RVEMCE)* reports a high incidence of microtia nationally. This implies a high frequency of microtia among US Mexicans immigrants from south of the border – a finding confirmed by Ramadhani et al., 2009 and which also adds credence to our hypothesis. Finally, we have learned that a staggering >50% of New Mexico's newborns failing government-mandated neonatal hearing screenings are subsequently lost to follow-up. We wonder, how many have unidentified microform microtias and are lacking appropriate treatment, resources, and accommodations to remediate their disability?

**Conclusions:** New Mexicans of American Indian and Mexican descent are likely at high risk of microtia and associated hearing impairments and psychological burdens. Enabling the successful development of affected individuals through childhood needs to begin with an accurate determination of the incidence of microtia in New Mexico. Our model assessment system aims to assist with obtaining these data, county by county, for the entire state.



# TRADITIONAL TEXTBOOK USE COMPARED TO EXTERNAL RESOURCE USE IN A FIRST AND SECOND YEAR U.S. OSTEOPATHIC MEDICAL SCHOOL CURRICULUM

Ivey KM<sup>1</sup>, Nguyen TN<sup>1</sup>, Fleckman EM<sup>1</sup>, McLeod EA<sup>1</sup>, Funk CK<sup>2</sup>

<sup>1</sup>Burrell College of Osteopathic Medicine, Las Cruces, NM; <sup>2</sup>Office of Academic Affairs, Burrell College of Osteopathic Medicine, Las Cruces, NM

**Introduction:** There has been a significant shift in medical education from textbooks as a primary study tool to the use of technology and medical applications. For years the variety of medical educational tools available has increased and medical students are finding themselves using more electronic sources of information throughout their clinical years (Peterson et. al., 2004). However, much information is lacking regarding the preclinical years. Textbooks are assigned as primary sources of information in medical schools across the country, with numerous companies that have a stake in preclinical medical education, providing new and innovative ways to learn the same material traditional textbooks provide. With a plethora of options available today, there is a clear need to identify what resources students are using to supplement their medical education during their preclinical years. The purpose of this study is twofold. First, we sought to determine what resources students at Burrell College of Osteopathic Medicine use as their primary study tools for various disciplines. Second, we determined if there were differences in confidence levels and/or academic performance in each designated subject area based on the primary resource utilized.

**Methods:** Data was collected through an anonymous Google survey consisting of questions for each of the following subjects: anatomy, physiology, pathology, microbiology, and pharmacology. Respondents were first and second year osteopathic medical students. There were a approximately of 160 first year medical students and 150 second year medical students at the time of this survey. After presentations to each class about the research project and scope of work, 22% of the student body agreed to participate with, a total of 69 voluntary responses were collected, 65 of which were used. 48% of respondents were OMS 1 and 52% of respondents were OMS 2. Four respondents were excluded due to user error inputting their identification number used or an incomplete survey. Each participant was given a pre-designated identification number, which was used to ensure that the study remained blind. Data was then analyzed with correlation statistics using the program Excel.

**Results:** There was no significant correlation between textbook use and confidence levels in all surveyed subjects. However, the primary resources used in every subject were all external resources. Textbooks were among the least used resources by the subjects of this study. Every subject surveyed indicated that course lectures were the main study material used.

Conclusions: With medical education changing and students not using textbooks as their primary resource material there is a need for further discussion and examination of the utility of textbooks in medical education, as well as the implications of students not using textbooks for medical education. Educators are facing more challenges than before with technology and external resources, but this is an opportunity for advancement in education. The rigor of medical school is driving students to find a variety of resources to adapt their studies to ensure their success. It is promising to see the breadth of resources available to students, but it is understood that certain concerns can come with using resources that have not been vetted by faculty. Therefore, we suggest in addition to further research, a balanced approach with a few selected resources that faculty can incorporate, or at least be familiar with, in conjunction with textbooks in the future.



# ENHANCING PALPATORY SKILL DEVELOPMENT IN ENTERING OSTEOPATHIC MEDICAL STUDENTS

Balogun A<sup>1</sup>, Chajec N<sup>1</sup>, Vaudrey K<sup>2</sup>, Minugh-Purvis N<sup>2</sup>

<sup>1</sup>Burrell College of Osteopathic Medicine, Las Cruces, NM; <sup>2</sup>Department of Anatomy and Cell Biology, Burrell College of Osteopathic Medicine, Las Cruces, NM

**Introduction:** Palpatory skill is a vital part of the tool-kit in most medical specialties, but especially for the osteopathic physician practicing osteopathic manipulative medicine (OMM). However, such skills can be difficult to master, with the result that entering first year osteopathic medical students' enthusiasm for OMM often quickly diminishes as they struggle to learn with fingertips rather than through visual information-gathering. We hypothesize: A brief course of Braille training, involving content recognition coupled with analysis of manually obtained information, enhances palpatory discrimination in entering first year osteopathic medical students.

**Methods:** We reviewed the published literature to examine 1. previous investigations attempting to provide preparatory or supplementary training in palpatory skills to medical students and/or professionals and 2. current knowledge regarding peripheral and central neurological substrates involved in the manual acquisition and processing of information during learning. We then designed a study comprised of a pilot training program and accompanying assessments, to test our hypothesis. Because this study involves working with human subjects, it must have IRB approval prior to administration. We will proceed to conduct this research at the earliest available opportunity, following IRB approval.

**Results:** To date we have no results, as our training program has not yet been administered. However, in designing the program, 4 of the 6 co-investigators themselves learned Braille to the extent expected of future training program participants. This provided valuable information regarding the feasibility of mastering the Braille content sufficiently to apply it to problem solving within a short timeframe that would be respectful of students' demanding schedules at the outset of their first year. We found this experience invaluable in organizing a schedule for this prospective study in that it yielded information regarding length of time required for content mastery; the modalities involved with content retention; and insight into some of the difficulties and interindividual variability training subjects may be expected to encounter during the experience.

**Conclusions:** Learning limited Braille is quickly accomplished and likely represents a time-efficient, feasible medium for providing systematic, tactile-based learning to busy, first-year osteopathic medical students. We anticipate that, if our hypothesis is confirmed, such training could potentially ease students' introduction to OMM and thus positively reinforce their initial enthusiasm for the field rather than discouraging them early in their medical education due simply to unfamiliarity with tactile modes of learning.



# POSTER COMPETITION AWARDS

Recipients of the BCOM Medical Student Research Day Poster Awards will be determined on the judging criteria listed below. The BCOM Medical Student Research Day Awards include:

- MSRD Best Research Poster Award
  - o One overall winner will receive paid travel to present their research at the National Student Research Forum in Galveston, TX
- Biomedical Research
  - o 1st Place will receive a \$250 award
- Clinical/OMT Research
  - o 1st Place will receive a \$250 award
- Population and Public Health Research
  - o 1st Place will receive a \$250 award
- Medical Education Research
  - o 1st Place will receive a \$250 award

# POSTER JUDGING CRITERIA

The purpose of a poster exhibit is to clearly communicate and convey the significance and major points of the research project to a wide variety of audience members. Posters will be scored out of 50 possible points, and will be judged according to the following criteria:

- Novelty of content
- Significance of work
- Scientific approach
- Depth of knowledge
- Overall organization
- Clarity of presentation



# POSTER COMPETITION JUDGES

#### **Biomedical Sciences Research:**

#### Pedro Del Corral, MD, PhD

Assistant Professor, Pathology Burrell College of Osteopathic Medicine

#### Miriam Donohue, PhD

Chair of Anatomy and Cell Biology Associate Professor, Anatomy and Cell Biology Burrell College of Osteopathic Medicine

#### **Clinical Sciences and OMT Research:**

#### Robert Goldsteen, DO, FACP

Chair of Clinical Medicine Professor, Internal Medicine Burrell College of Osteopathic Medicine

#### Leah Swift, DO, FAAP

Assistant Professor, Pediatrics Burrell College of Osteopathic Medicine

#### **Population & Public Health Research:**

#### Harald Stauss, MD, PhD

Associate Professor, Pharmacology Burrell College of Osteopathic Medicine

#### Joanne Ray, DO, FAAP

Assistant Professor, Pediatrics Burrell College of Osteopathic Medicine

#### **Medical Education:**

#### Scott Ochs, PhD

Associate Professor, Pharmacology Burrell College of Osteopathic Medicine

#### Kristin Gosselink, PhD

Associate Professor, Physiology Burrell College of Osteopathic Medicine



# POSTER JUDGING RUBRIC

Judge's Name:	
Student Name(s): Poster Number:	
Presentation Title:	
1. Introduction Significance and Background of W	ork (0-10 points)
A) An explanation of the topic that demonstrate	tes a certain depth of knowledge.
B) Rationalizes practical and scholarly signific	cance of project.
C) Synthesizes across studies, including semin	nal and quality studies.
2. Methods / Scientific Approach (0-5 points)	<u> </u>
A) Research question is clear, precise, and pro	vides needed detail about the study.
B) Description of tools used to collect data and	d how and why they were used.
C) Indication of what is unique or novel about	the experimental design.
D) Statistical calculations used to analyze resu	ilts as appropriate.
3. Results (0-5)	_
A) Data clearly presented in appropriate tables	s with titles, figures with legends and labels.
4. Conclusion and/or Recommendations (0-5 points	s)
A) Summarizes key points and findings.	
B) Notes ambiguities or limitations in the curr	ent study.
C) Project points to potential areas for further	study.
5. Student Presentation (0-5 points)	
A) Student presents in an organized way refere	ring to figures/poster as appropriate.
B) Student <u>clearly</u> describes the purpose, meth	ods and outcomes of project.
C) Student answers questions with ease and po	pise.
6. Poster Quality (0-5 points)	
A)Poster is organized, readable, aesthetically 1	pleasing, and novel.
B) Poster flows well from start to finish.	
7. Appropriate Citations and References Listed (	)-5 points)
9 . D	(0.10 )
8. Presenter(s) Handled Questions Appropriately	(0-10 points)
	TOTAL POINTS (50 Max):



Thank you for attending BCOM's 2nd Annual Medical Student Research Day!



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