The University of North Carolina at Chapel Hill Department of Anesthesiology Annual Research Report 2014-2015





Dear Reader:

Welcome to our 2014-2015 UNC Department of Anesthesiology Annual Research Report. I hope that this summary gives you a better understanding of the exciting research work being done in the department. Our goal is to serve our patients through discovery, and we have had a very productive year.

The research success summarized in this report is achieved by three main factors. First, we are fortunate to have gathered together an incredible group of faculty and staff in the department. Second, these individuals excel at working together in collaborative, multidisciplinary teams. Research is truly a team sport. The effective collaboration of individuals in each of the projects described in this report accounts for our success, and we are fortunate that our numbers continue to grow. Finally, we have a Chair who fully embraces the mission of the university to reduce suffering and improve outcomes through advances which lead to improved patient health. Dr. Zvara has provided the infrastructure and leadership necessary for transformative research, even during very challenging economic times.

I encourage you to check back often and keep up with our department research activities via <u>http://www.med.unc.edu/anesthesiology/research.</u> Also, if you have any questions regarding our research or work, don't hesitate to email me any time at <u>smclean@aims.unc.edu.</u>

Sincerely,

Samuel McLean, MD, MPH Vice Chair, Research, Department of Anesthesiology The University of North Carolina at Chapel Hill Chapel Hill, NC

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# **Areas of Departmental Research Focus**

### **1. TRYUMPH Program:**

Trauma RecoverY: Understanding Mechanism and Promoting Healing

# A. African American CRASH: Applying the Biopsychosocial Model to Post-MVC Pain Development in African Americans (R01AR060852, Pl McLean)

The goal of this study is to examine genotypic and phenotypic characteristics associated with the development of pain and related outcomes in African Americans experiencing motor vehicle collision. Patients involved in motor vehicle collision are enrolled via a network of study sites including sites in Michigan, Massachusetts, Pennsylvania, New Jersey, Washington D.C., North Carolina, Alabama, and Florida. This study is supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health (R01AR060852), and is enrolling 900 African Americans experiencing motor vehicle collision. Study participants complete

a baseline assessment in the ED as well as a follow-up interview 6 weeks, 6 months, and 1 year following the motor vehicle collision.

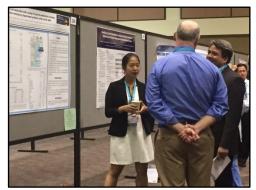


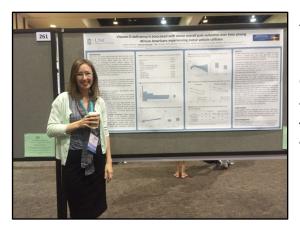
This study completed its 4<sup>th</sup> year of funding in 2014-2015. An updated listing of abstracts and manuscripts from R01AR060852 is available at:

http://www.med.unc.edu/anesthesiology/research/tryumph-research-group-1/tryumph-studies/african-american-project-crash

#### 2014-2015 abstracts and publications related to R01 AR060852 (African American CRASH)

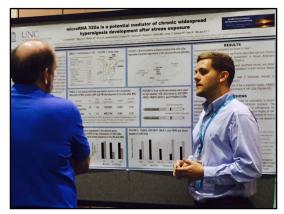
A. Liu, J. Hu, T. Platts-Mills, B. Lateef, Y. Qadri, H. Wang, M. Velilla, C. Pearson, E. Zimny, C. Lewandowski, P. Hendry, K. Damiron, R. Domeier, S. Kaushik, J. Feldman, J. Jones, M. Villard, S. McLean, (224) Education status is not associated with opioid medication receipt among African American emergency department patients with acute pain, The Journal of Pain, Volume 16, Issue 4, Supplement, April 2015, Page S32, ISSN 1526-5900.





A. Bortsov, S. Linnstaedt, M. Velilla, K. Damiron, C. Pearson, J. Jones, P. Hendry, M. Kurz, S. McLean, (260) Vitamin D deficiency is associated with worse overall pain outcomes over time among African Americans experiencing motor vehicle collision, The Journal of Pain, Volume 16, Issue 4, Supplement, April 2015, Page S41, ISSN 1526-5900, http://dx.doi.org/10.1016/j.jpain.2015.01.177.

S. Linnstaedt, K. Riker, J. Nyland, E. Zimny, C. Lewandowski, P. Hendry, K. Damiron, C. Pearson, M. Velilla, J. Jones, R. Swor, R. Domeier, S. McLean, (257) microRNA 320a is a potential mediator of chronic widespread hyperalgesia development after stress exposure, The Journal of Pain, Volume 16, Issue 4, Supplement, April 2015, Page S40, ISSN 1526-5900, http://dx.doi.org/10.1016/j.jpain.2015.01.174.



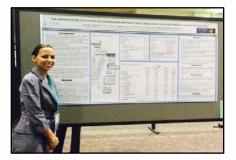
B. European American CRASH: Genetic Predictors of Acute and Chronic Musculoskeletal Pain After Minor MVC (R01AR056328, PI McLean) Project CRASH is a prospective cohort study examining genotypic and phenotypic characteristics associated with the development of acute and persistent pain and related outcomes after motor vehicle collision. This study is funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases. Over 900 patients involved in motor vehicle collision were enrolled in the study at one of nine emergency department study sites in Michigan, Massachusetts, New York, and Florida. Study participants completed a baseline assessment in the ED as well as a follow-up interview 6 weeks, 6 months, and 1 year following the motor vehicle collision. Recruitment and follow-up for this study have been completed. Data analyses and manuscript preparation from this project are ongoing. An updated listing of



abstracts and manuscripts from R01AR056328 is available at: http://www.med.unc.edu/anesthesiology/research/tryumph-research-group-1/tryumph-

studies/european-american-project-crash

#### 2014-2015 abstracts and publications related to above R01 AR056328

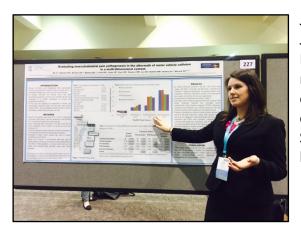


M. Villard, F. Beaudoin, J. Hu, D. Orrey, D. Peak, J. Jones, R. Swor, R. Domeier, D. Lee, N. Rathlev, P. Hendry, S. McLean, (230) Few individuals at high risk of persistent musculoskeletal pain after motor vehicle collision receive early psychological or physiotherapy intervention, The Journal of Pain, Volume 16, Issue 4, Supplement, April 2015, Page S33, ISSN 1526-5900,

http://dx.doi.org/10.1016/j.jpain.2015.01.145.

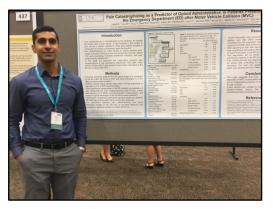
J. Hu, K. Bollen, S. Lane, A. Bortsov, D. Peak, J. Jones, R. Swor, R. Domeier, D. Lee, N. Rathlev, P. Hendry, S. McLean, (100) Evaluation of the influence of stress-induced pain vulnerability and sociodemographic characteristics on acute pain after a motor vehicle collision using structural equation modeling, The Journal of Pain, Volume 16, Issue 4, Supplement, April 2015, Page S1, ISSN 1526-5900, http://dx.doi.org/10.1016/j.jpain.2015.01.014.





J. Hu, R. Kessler, A. Bortsov, S. Battles, D. Peak, J. Jones, R. Swor, R. Domeier, D. Lee, N. Rathlev, P. Hendry, S. McLean, (227) Evaluating musculoskeletal pain pathogenesis in the aftermath of motor vehicle collision in a multi-dimensional context, The Journal of Pain, Volume 16, Issue 4, Supplement, April 2015, Page S32, ISSN 1526-5900, http://dx.doi.org/10.1016/j.jpain.2015.01.142.

B. Lateef, A. Liu, J. Hu, R. Swor, D. Peak, J. Jones, N. Rathlev, D. Lee, R. Domeier, P. Hendry, M. Martel, S. McLean, (436) Pain catastrophizing as a predictor of opioid administration in patients presenting to the emergency department (ED) after motor vehicle collision (MVC), The Journal of Pain, Volume 16, Issue 4, Supplement, April 2015, Page S85, ISSN 1526-5900, http://dx.doi.org/10.1016/j.jpain.2015.01.355.



#### 2014-2015 Publications Related to Above Studies

Linnstaedt SD, Hu J, Bortsov AV, Soward AC, Swor RA, Jones JS, Lee DC, Peak DA, Domeier RM, Rathlev NK, Hendry PL, McLean SA. μ-Opioid Receptor Gene A118G Variants and Persistent Pain Symptoms among Men and Women Experiencing Motor Vehicle Collision. Accepted *J of Pain* 

Musey PI, Linnstaedt SD, Platts-Mills TF, Miner JR, Bortsov AV, Safdar B, Bijur P, Rosenau A, Tsze DS, Chang AK, Dorai S, Engel K, Feldman JA, Fusaro AM, Lee DC, Rosenberg M, Keefe FJ, Peak DA, Nam CS, Patel R, Fillingim RB, McLean SA. Gender Differences in Acute and Chronic Pain in the Emergency Department: Results of the 2014 Society for Academic Emergency Medicine Consensus Conference Pain Section. *Acad Emerg Med*. 2014 Nov 24.

Qadri YJ, Bortsov AV, Orrey DC, Swor RA, Peak DA, Jones JS, Rathlev NK, Lee DC, Domeier RM, Hendry PL, McLean SA. Genetic Polymorphisms in the Dopamine Receptor 2 Predict Acute Pain Severity after Motor Vehicle Collision. *Clin J Pain*. 2014 Nov 3.

Shin G, McLean SA, Hu J, Gotz D. Visualizing Temporal Patterns by Clustering Patients. Accepted *Workshop on Visual Analytics in Healthcare*. 2014 Nov 15.



TRYUMPH Research Group, August 2015

Back Row (L to R): Dr. Andrey Bortsov, Johanna Wicker, Joey Duronio, Sean Flannigan, Dr. Sam McLean, Dr. Tim Platts-Mills, Dr. Sarah Linnstaedt

Front Row (L to R): Ben McLean, Natalie Richmond, Sherie Royster, Adeola Keku, Andrea Liu, June Hu, April Soward, Felisha Westbrook

Not Pictured: Sara Battles, Jackie Kostyla, Dr. Matthew Mauck, Bobby Nicholson, Kyle Riker, Ashley Villard, Jackie Kostyla

C. Older Adult CRASH: Persistent Pain in Older Adults after Motor Vehicle Collision (K23 AG038548, PI Platts-Mills)



The Older Adult CRASH study is the first prospective study to examine the incidence, predictors, and etiology of persistent pain among independently living older adults who come to the emergency department for care after motor vehicle collision and are discharged to home. The study enrolls patients 65 and older at eight study sites, and it has enrolled over 100 patients from these eight sites. This project was supported by Dr. Platts-Mills' KL2 career development award funded by the National Center for Research Resources through UNC's Translational and Clinical Sciences Institute. In May of 2013, Dr. Platts-Mills received a K23 career development award

from the National Institute on Aging to continue this study and to examine the contributions of fear of movement and PTSD symptoms to the development of persistent pain and functional decline after MVC. An updated listing of abstracts and manuscripts from this project is available at:

http://www.med.unc.edu/anesthesiology/research/tryumph-research-group-1/tryumph-studies/older-adult-project-crash

### Related Abstracts 2014-2015

Sean A. Flannigan , Andrey V. Bortsov , Robert A. Swor , Jeffrey S. Jones , David C. Lee , David A. Peak, Robert M. Domeier , Niels K. Rathlev , Phyllis L. Hendry , Samuel A. McLean , and Timothy F. Platts-Mills. Derivation of a Simple Clinical Prediction Tool to Identify Older Adults at Increased Risk of Persistent Pain after Motor Vehicle Collision. Academic Emergency Medicine, Volume 22, Issue Supplement S1, May 2015, Page S108, ISSN 1069-6563

(Presented as an oral presentation at the Society for Academic Emergency Medicine meeting)

Robert J. Nicholson, Katherine M. Hunold, Mark A. Weaver, Leslie A. Lytle, Francis J. Keefe, Samuel A. McLean, and Timothy F. Platts-Mills. Effect of Reduced Physical Activity on the Development of Persistent Pain After Motor Vehicle Collision in Older Adults: a Propensity Score-Matched Analysis. Academic Emergency Medicine, Volume 22, Issue Supplement S1, May 2015, Page S17, ISSN 1069-6563 (Presented at the Society for Academic Emergency Medicine meeting and at the American Geriatric Society meeting)



Bo C. Nebolisa, Erin E. Isenberg, Robert M. Domeier, Robert A. Swor, Phyllis L. Hendry, David A. Peak, Niels K. Rathlev, Jeffrey S. Jones, David C. Lee, Samuel A. McLean, and Timothy F. Platts-Mills. Post-Traumatic Stress Disorder among Elderly Motor Vehicle Collision Victims Receiving Care in the Emergency Department: a Prospective Study. Academic Emergency Medicine, Volume 22, Issue Supplement S1, May 2015, Page S119, ISSN 1069-6563

(Presented as an oral presentation at the Society for Academic Emergency Medicine meeting and as a poster at the American Geriatric Society meeting)



Society for Academic Emergency Medicine Research Breakfast, May 2015 (L to R): Dr. Chris Jones, Sean Flannigan, Bobby Nicholson, Dr. Tim Platts-Mills, Katie Hunold

### 2014-2015 Related Publications

Pereira GF, McLean SA, Tkacik TJ, Robert A. Swor, Jeffrey S. Jones, David C. Lee, David A. Peak, Robert M. Domeier, Niels K. Rathlev, Phyllis L. Hendry. Pain, distress, and anticipated recovery for older versus younger emergency department patients after motor vehicle collision. *BMC Emergency Medicine*. 2014;14:25. doi:10.1186/s12873-014-0025-y.

Platts-Mills, Timothy F., Sean A. Flannigan, Andrey V. Bortsov, Samantha Smith, Robert M. Domeier, Robert A. Swor, Phyllis L. Hendry, David A. Peak, Niels K. Rathlev, Jeffrey S. Jones, David C. Lee, Francis J. Keefe, Philip D. Sloane, and Samuel A. Mclean. "Persistent Pain Among Older Adults Discharged Home From the Emergency Department After Motor Vehicle Crash: A Prospective Cohort Study." *Annals of Emergency Medicine* (2015)

Richmond, Natalie L., Sean A. Flannigan, Lukas G. Keil, Marian E. Betz, and Timothy F. Platts-Mills. "Cessation of Driving Is Rare in Older Drivers Seen in the Emergency Department After a Motor Vehicle Collision: A Prospective Cohort Study." *J Am Geriatr Soc* 63.1 (2015): 183-85.



Poise Research Group Spring Dinner, April 2015.

Back (L to R): Sean Flannigan, Wesley Holland, Bobby Nicholson, Dr. Tim Platts-Mills, John Butler Front (L to R): Meredith Hoover, Natalie Yosipovitch, Erin Isenberg, Sowmya Mangipudi, Tiffany Ho, Collin Burks.

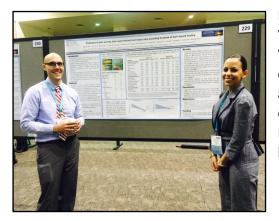
### D. The BURN Experiences Study (Jaycee Burn Center Foundation, PI McLean)

The BURN Experiences Study is a prospective longitudinal pilot study examining the recovery process after major thermal burn injury. Participants requiring tissue autograft surgery after major thermal burn injury are enrolled at the time of initial admission and followed prospectively for one year. The study is being conducted at a network of burn centers including the Jaycee Burn Center at The University of North Carolina at Chapel Hill, the Nathan Speare Regional Burn Treatment Center at Crozer-Chester Medical Center, and the Burn Center at MedStar Washington Hospital Center. Data collected are being used to demonstrate study feasibility and to collect pilot data for a largescale trial. An up-to-date listing of abstracts and manuscripts from this project is available at:



http://www.med.unc.edu/anesthesiology/research/tryumph-research-group-1/tryumph-studies/burn-experiences

#### Related Abstracts 2013-2014



M. Mauck, A. Liu, A. Bortsov, S. Jones, J. Hwang, F. Williams, J. Shupp, R. Karlnoski, D. Smith, A. Krishnan, B. Wesp, M. Gellatly, B. Cairns, S. McLean, (229) Predictors of pain severity after major thermal burn injury vary according to phase of burn wound healing, The Journal of Pain, Volume 16, Issue 4, Supplement, April 2015, Page S33, ISSN 1526-5900, http://dx.doi.org/10.1016/j.jpain.2015.01.144.

#### E. The HELP PAIN Trial (Mayday Fund, PI McLean)

The HELP PAIN Trial is an Emergency Department-based randomized controlled trial. The purpose of this first-in-kind study is to assess the potential efficacy of venlafaxine in reducing acute pain and the transition to persistent pain in high-risk patients that present to the Emergency Department following a motor vehicle collision. Patients presenting to the Emergency Department post-MVC with



# The HELP PAIN Trial

severe musculoskeletal neck pain will be randomized to receive either venlafaxine or placebo. Data from this pilot study is being used to assess study feasibility and to design a large-scale randomized controlled trial.

# F. The Women's Health Study: Influence of PTSD Symptoms on Chronic Pain Development after Sexual Assault (1R01AR064700-01A1, PI McLean)



Women's Health Study

The Women's Health Study is a large-scale prospective study of sexual assault survivors. The fiveyear study will enroll 900 women who present for emergency care after sexual assault and will follow them prospectively for one year. This study will yield important new insights into sexual assault survivor experiences. In addition, the study will evaluate genetic, psychosocial, and environmental factors influencing adverse outcomes after sexual assault including chronic pain and posttraumatic stress disorder. This past year was spent identifying and developing study sites, and beginning our nationwide study launch.

# G. OSPREY II: Observational Studies of Pain Medication Response in the Elderly (KL2 RR025746-03, PI Platts-Mills)

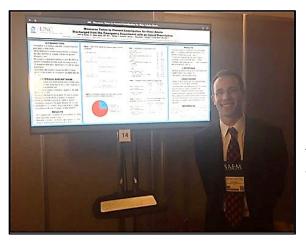
OSPREY II is an observational study of the relationship between shared decision making and pain and pain recovery among adults age 65 or older with acute musculoskeletal pain. Results from the first OSPREY study were recently published in the Journal of the American Geriatrics Society. OSPREY II addresses the major limitations of the first study by assessing shared decision making in the first 24 hours after motor vehicle collision using a validated measure. This study has enrolled 30 patients and is now expanding to a second site. An updated listing of abstracts and manuscripts from this project is available at:



http://www.med.unc.edu/anesthesiology/research/tryumph-research-group-1/tryumph-studies/osprey

#### **Related Abstracts 2014-2015**

John M. Butler, Kevin Biese, Wesley C. Holland, Natalie L. Richmond, and Timothy F. Platts-Mills.



Measures Taken to Prevent Constipation for Older Adults Discharged from the Emergency Department with an Opioid Prescription. Academic Emergency Medicine, Volume 22, Issue Supplement S1, May 2015, Page S192, ISSN 1069-6563

(Presented as an ePoster at the Society for Academic Emergency Medicine meeting and as a poster at the American Geriatric Society meeting)

#### H. Linnstaedt Lab

Research in the Linnstaedt Lab defines molecular mediators that drive the transition between



trauma exposure and chronic pain or PTSD development. Initial studies have focused on the role of blood microRNA to predict chronic pain development following motor vehicle collision in African American individuals (as a part of AA CRASH). The results of this work have been recognized two consecutive years in a row by Genetics and Basic Science Special Interest Groups organized by the American Pain Society (APS). Current and future studies aim to expand microRNA studies related to AA CRASH, begin microRNA studies in a cohort of women

sexual assault survivors, and to perform mRNA expression studies in

both cohorts. Human sample studies are complimented in the lab with the use of cell culture, molecular assay, and animal model sample analyses. In late 2014, Dr. Linnstaedt was named a "Future Leader in Pain Research" by APS, and received a prestigious grant to support some of these studies. She was also awarded a grant through the Mayday Fund (Co-PI with Dr. Samuel McLean). A long-term goal of the lab is to one day develop clinically useful biomarker assays or to identify novel targets for therapeutic intervention.



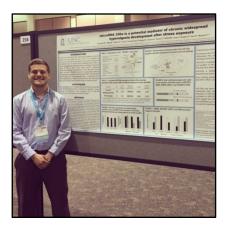
#### 2014-2015 Related Abstracts:

Linnstaedt SD, Walker MG, Bortsov AV, Sons RL, Swor RA, Jones JS, Lee DC, Peak DA, Domeier RM, Rathlev NK, Hammond SM, McLean SA. A genetic variant in ADRA2A is associated with acute

pain severity and is a determinant of miR-34a binding efficiency. *Poster presentation* at the 2014 RNA silencing Keystone Meeting, January 31 – Feb 5, Seattle, WA

Linnstaedt SD, Walker MG, Bortsov AV, Swor RA, Jones JS, Lee DC, Peak DA, Domeier RM, Rathlev NK, McLean SA. The ADRA2A genetic variant rs3750635 influences extent and severity of acute pain after motor vehicle collision and may do so by regulating microRNA function. *Poster presentation* at the 2014 Annual Meeting of the American Pain Society, Tampa FL, May 2014





Linnstaedt SD, Walker MG, Parker JS, Sons RL, Velilla MA, Pearson C, O'Neil BJ, Zinny E, Lewandowski CL, Damiron K, Hendry PL, Barnes S, Rosenber M, Hammond SM, McLean SA. Circulating microRNA evaluated in the early aftermath of motor vehicle collision predict widespread pain development in African Americans and provide potential pathogenic insights: results of a preliminary analysis. *Poster presentation* and *Selected for Oral presentation* at the 2014 Annual Meeting of the American Pain Society, Tampa FL, May 2014

Linnstaedt SD, McCarthy KR, Riker KD, Kutchko KM, Laederach A, McLean SA. A genetic variant in the glucocorticoid receptor co-chaperone FKBP5, associated with chronic pain vulnerability, changes RNA structure and alters binding by miR-320a. *Poster presentation* at the 2014 Bi-Annual Meeting of the International Association for the Study of Pain, Buenos Aires, Argentina, October 2014

Linnstaedt SD, Riker KD, Nyland JE, Zimny E, Lewandowski C, Hendry PL, Damiron K, Pearson C, Velilla MA, Jones J, Swor R, Domeier R, McLean SA. microRNA 320a is a potential mediator of chronic widespread hyperalgesia development after stress exposure. *Poster presentation* at the 2015 Annual Meeting of the American Pain Society, Palm Springs CA, May 2015

Bortsov AV, Linnstaedt SD, Velilla MA, Damiron K, Pearson C, Jones JS, Hendry PL, Kurz MC, McLean SA. Vitamin D deficiency is associated with worse overall pain outcomes over time among African Americans experiencing motor vehicle collision. *Poster presentation* at the 2015 Annual Meeting of the American Pain Society, Palm Springs CA, May 2015

Linnstaedt SD. MicroRNA mechanisms mediating persistent pain development after motor vehicle trauma. *Invited oral presentation* at the Basic Science SIG Meeting at the 2015 Annual Meeting of the American Pain Society, Palm Springs CA, May 2015

### 2014-2015 Related Publications:

Musey PI, **Linnstaedt SD**, Platts-Mills TF, Miner JR, Bortsov AV, Safdar B, Bijur P, Rosenau A, Tsze DS, Chang AK, Dorai S, Engel K, Feldman JA, Fusaro AM, Lee DC, Rosenberg M, Keefe FJ, Peak DA, Nam CS, Patel R, Fillingim RB, McLean SA. Gender Differences in Acute and Chronic Pain in the Emergency Department: Results of the 2014 Society for Academic Emergency Medicine Consensus Conference Pain Section. Acad Emerg Med 2014 Dec; 21(12):1421-30.

**Linnstaedt SD**, Hu JunMei, Bortsov AV, Soward AC, Swor R, Jones J, Lee D, Peak D, Domeier R, Rathlev N, Hendry P, McLean SA.  $\mu$ -Opioid Receptor Gene A118 G Variants and Persistent Pain Symptoms Among Men and Women Experiencing Motor Vehicle Collision. The Journal of Pain 2015 Jul;16(7):637-44.

## Linnstaedt Lab Research Assistants



Matt Carson, Freshman undergraduate student, UNC



**Gonzalez,** student, UNC

**Evan Harmon,** 2<sup>nd</sup> year medical student, UNC

**Lindsey Jung,** Junior undergraduate student, UNC



Linnstaedt Lab, July 2015

From left: Lindsey Jung (Junior), Karan Koyani (3<sup>rd</sup> year medical student), Sarah Linnstaedt, Michael Gonzalez (2<sup>nd</sup> year medical student), Evan Harmon (2<sup>nd</sup> year medical student), Kyle Riker (Junior), Matt Carson (Freshman), Alan Wu (Senior)

#### I. Bortsov Epidemiology Research

Dr. Andrey Bortsov is currently involved in several projects evaluating the predictors of chronic pain after trauma.

# Clinical prediction tool to identify individuals at increased risk of chronic axial pain development after motor vehicle collision



Millions of Americans present to the emergency department (ED) each year after motor vehicle collision (MVC). Acute musculoskeletal pain is the norm in these individuals and 20-40% transition to chronic musculoskeletal pain, most commonly in the axial region (neck/shoulders, back). ED-based risk stratification tools have been developed for a variety of clinical conditions, and are a necessary foundation for the development of effective preventive interventions for high-risk individuals. However, no risk stratification tools are available for chronic post-MVC axial pain. We are developing a risk stratification tool for pain, using data from a prospective multisite longitudinal study of individuals evaluated 6 weeks, 6 months, and 1 year after MVC (n=860). Chronic post-MVC axial musculoskeletal pain was present in

37% of participants. Initial modeling identified substantial differences in predictors (interactions) by sex, thus separate models were developed for men and women. The reduced models (separate for males and females) demonstrated good discrimination and calibration. We then developed a web-based version of the tool which can be accessed via the Department website. This tool may be used for validation testing or other research purposes and allows the user to set the desired probability threshold. We are currently working on further refinement and validation of the tool.

# Vitamin D deficiency and chronic pain among African Americans experiencing motor vehicle collision

Evidence suggests that rates of chronic pain development after trauma (such as minor MVC) are increased in African Americans. Biological mechanisms responsible for elevated risk in this population remain poorly understood. Vitamin D deficiency is known to be more prevalent among African Americans. It has previously been suggested that vitamin D deficiency increases the risk of chronic pain via augmenting neuroinflammatory processes. We evaluated the hypothesis that vitamin D deficiency is associated with worse overall pain and axial pain outcomes among a cohort of AAs (n=133) seen in the ED after MVC and discharged to home. We found that study participants with vitamin D deficiency experienced more severe overall pain than participants with normal vitamin D levels. The influence of vitamin D deficiency on worse pain outcomes was somewhat attenuated after adjustment for measures of socioeconomic status (education and income) that have also been linked to vitamin D deficiency. These data warrant further studies evaluating the potential association between vitamin D deficiency and post-MVC pain and psychological outcomes.

## 2. Anesthesiology Clinical Trials Research Unit

The UNC Anesthesiology Clinical Trials Research Unit specializes in pain management interventional studies involving medications or devices. Their facilities at the hospital of UNC Health Care and the Pain Management Center at Southern Village allow them to attract a diverse patient population.

They work with Department of Anesthesiology faculty to manage and conduct both industrysponsored clinical trials and investigator-initiated studies. Their track record is a testament to this outstanding team: UNC is currently a national and international leader in the recruitment and retention of individuals for several clinical trials. Their team of professionals includes a fulltime research coordinator and nursing staff, as well as regulatory and other support staff. Individual faculty studies performed in collaboration with the clinical trials team are described below.

A. A Phase IV Study to Evaluate the Pharmacokinetics and Safety of Oxycodone Oral Solution in Pediatric and Adolescent Subjects (VistaPharm, Inc. and Lehigh Valley Technologies, Inc., Site PI Valley)



The objective of this study is to characterize the pharmacokinetics and to evaluate the safety of single and multiple doses of Oxycodone Oral Solution in pediatric and adolescent subjects following a surgical procedure. It is an open-label, multicenter study. Subjects are enrolled preoperatively or postoperatively with the expectation that they will require IV access after surgery and postoperative analgesia with an opiate-level medication. After dosing, subjects are carefully monitored for safety and pharmacokinetic samples are obtained for a 24-hour period.

## 3. Faculty Research Studies

# A. Teaching CA-1 Anesthesia Residents by "Flipping the Classroom" Improves Knowledge Acquisition and Resident Satisfaction, Dr. Susan Martinelli



This study compares two instructional methods to determine which is most effective and which is most preferred by residents. Residents will be taught material through a traditional lecture-based style and then the same teachers that delivered the traditional lecture will prepare a video of their lecture that will be used for the flipped classroom style teaching. Data will be collected regarding residents' opinion on the different teaching methods, the amount of preparation time outside of the classroom, prior ITE and USMLE test scores, and any prior graduate medical training. As the "flipped classroom" sessions will provide more active learning, we anticipate the residents to perform better on

multiple-choice tests corresponding to their flipped classroom curriculum and the residents will have higher satisfaction with the flipped classroom model.

# B. Enhanced Recovery after Surgery (ERAS): A multidisciplinary perioperative protocol to improve outcomes for patients undergoing pancreatic surgery, PI Kolarczyk



The primary objective of Dr. Lavinia Kolarcyzk and her team is to determine if the Enhanced Recovery After Surgery (ERAS) pathway can improve the quality of care of pancreatic surgery patients at UNC. ERAS is a set of well-established best practice guidelines for patients undergoing a variety of intra-abdominal surgeries. The goals of the ERAS guidelines are to maintain normal physiologic function and to facilitate early postoperative recovery. These goals are met through a variety of interventions throughout the perioperative period, including: decreased use of preoperative bowel preps, carbohydrate drinks on the day of

surgery, thoracic epidural analgesia, intraoperative goal directed fluid therapy, standardized anesthetic protocols, thromboembolic prophylaxis, early mobilization and oral intake in the postoperative period, and the limited use of urinary catheters and nasogastric tubes. ERAS protocols allow for standardization of best practice perioperative care, which ultimately improves the quality of care delivered, accelerates recovery and safety, and optimizes utilization of health care resources.

ERAS protocols for colorectal and pancreatic surgeries have shown to decrease 30 day morbidity by over 50% and reduce length of stay by 2.5 days. What has not yet been well studied is the application of an ERAS protocol for upper gastrointestinal surgery. Our plan is to introduce a perioperative ERAS protocol for major gastrointestinal surgeries at UNC Hospitals. Through a multidisciplinary, team-based approach, we will create, implement, and study our own ERAS protocol. The goals of our project are to: 1) improve patient outcomes and satisfaction through standardization of perioperative care, 2) accelerate patient recovery, and 3) establish a vehicle for future projects.

### 4. Resident Team-Based QI/Research Projects

The Anesthesiology Research Department at UNC Chapel Hill is committed to engaging our residents in a variety of ways. During the 2014-2015 academic year, all of our clinical anesthesia residents participated in Team-based Quality Improvement (QI) project. Each team was comprised of one resident from each residency class and a faculty mentor. The CA-2 resident served as the team leader and was responsible for developing the project and carrying it through to completion. The department implemented these team-based projects because we recognize that continuous quality improvement must be a core component of any contemporary academic training program and health care organization. These projects also have increased resident participation at regional and national conferences, and led to academic publications and improved patient care. All of the team-based projects from the 2014-2015 academic year were presented at the Resident Symposium.



1<sup>st</sup> Place Pediatric Intraoperative Emergencies: Educating Our Perioperative Team Chelsea Willie, MD, Jennifer Jutson, MD, Eva Waller, MD, Peggy McNaull, MD, Kimberly Blasius, MD

2<sup>nd</sup> Place Enhanced Pathway Decreases Hayden



Recovery after Surgery (ERAS): Clinical for Patients Undergoing Pancreatic Surgery Hospital Length of Stay Kirby, MD, Timothy Rohman, MD (presenter), Ryan Bialas, MD, Lavinia MD

Kolarczyk,



3<sup>rd</sup> Place Intraoperative Fluid Administration Practices in Pediatric Anesthesia: the Good, the Bad, and the Ugly Kevin Powell, MD, Christoforos Frangopoulos, MD, Gabe Rice, MD, Ann Bailey, MD, Kimberly Blasius, MD "Where in world have they been?": Resident presentations at national and international conferences in 2014-2015

| Presenter | Title   | Conference   | Place            |
|-----------|---|--|------------------|
| Ganesh    | Medically challenging case: Dilemma of the Echodensity: Reexplore or Anticoagulate?   | American Society of<br>Anesthesiologists Annual<br>Meeting 2014        | New Orleans, LA  |
| Helgren   | Case Report and Poster Presentation, Medically<br>Challenging Cases: Successful Crisis Resource<br>Management, Cognitive Aid, and "Reader"<br>Utilization in Malignant Hyperthermia.  | American Society of<br>Anesthesiologists Annual<br>Meeting 2014        | New Orleans, LA  |
| Helgren   | Case Report and Poster Presentation, Medically<br>Challenging Cases: AV Fistula Ligation in a Patient<br>with Orthopnea, Pulmonary Hypertension and<br>Concurrent Antiplatelet Therapy.   | American Society of<br>Anesthesiologists Annual<br>Meeting 2014        | New Orleans, LA  |
| Helgren   | Case Report and Poster Presentation: Tumefactive<br>Multiple Sclerosis Presenting as Acute Neurologic<br>Deficits in Pregnancy  | Society of Obstetric<br>Anesthesia and<br>Perinatology Meeting<br>2014 | Toronto, Canada  |
| Potisek   | Perioperative arrest: Is our Team Ready?  | SOAP 2015  | Colorado Springs |
| Potisek   | Validation of Patient Education Video on Labor<br>Analgesia.  | American Society of<br>Anesthesiologists Annual<br>Meeting 2014        | New Orleans, LA  |
| Potisek   | The Great Awakening. Unexpected and Sudden<br>Recovery From Toxic Metabolic Encephalopathy in<br>a 61-Year-Old Status Post Ivor Lewis<br>Esophagectomy and Wedge Resection,<br>Subsequently Found to Have a 10cm<br>Esophagopleural fistula | American Society of<br>Anesthesiologists Annual<br>Meeting 2014        | New Orleans, LA  |
| Dickerson | Patient Satisfaction with the use of Nitrous Oxide for Labor Analgesia  | SOAP 2015  | Colorado Springs |
| Judd      | Liver Transplantation in a Patient with Moderate<br>Portopulmonary Hypertension: When to Proceed<br>Versus Cancel   | American Society of<br>Anesthesiologists Annual<br>Meeting 2014        | New Orleans, LA  |

| Qadri  | Idiopathic Verapamil Sensitive Ventricular<br>Tachycardia After Transhiatal Esophagectomy                                       | IARS 2015 Annual<br>Meeting and<br>International Science<br>Symposium | Honololu, HI           |
|--------|---|---|------------------------|
| Shah   | Peripheral Nerve Block In A Child For Skin Grafting:<br>Playing With Fire?  | IARS 2015 Annual<br>Meeting and<br>International Science<br>Symposium | Honololu, HI           |
| Shah   | Obesity increases the risk of persistent moderate or severe overall pain 6 months and 1 year after motor vehicle collision      | American Society of<br>Anesthesiologists Annual<br>Meeting 2014       | New Orleans, LA        |
| Shah   | Intraoperative Pulmonary Embolism during<br>Mediastinoscopy: Medical and Ethical Decision<br>Making in the Midst of Catastrophe | American Society of<br>Anesthesiologists Annual<br>Meeting 2014       | New Orleans, LA        |
| Shah   | A Best Practice Guideline: An updated look at a protocol for anesthetic management for posterior spinal fusions                 | Society of Pediatric<br>Anesthesia Conference<br>2014                 | Fort Lauderdale,<br>FL |
| Suchar | Caudal Catheter Complication: The Dreaded<br>Epidural Abscess   | Society of<br>Pediatric Anesthesia<br>2015 Annual Meeting             | Phoenix, Arizona       |
| Suchar | Intravenous Dexmedetomidine in Dental<br>Rehabilitation: Cost Effectiveness Issues  | Society of Pediatric<br>Anesthesia 2014 Annual<br>Meeting             | Fort Lauderdale,<br>FL |
| Waller | Auditory Brainstem Implantation: What the Pediatric Anesthesiologist Needs to Know  | Society of<br>Pediatric Anesthesia<br>2015 Annual Meeting             | Phoenix, Arizona       |
| Willie | Children's Operating Rooms on the Ready: Pediatric<br>Perioperative Critical Event Training                                     | Society for Pediatric<br>Anesthesia Annual<br>Meeting                 | Phoenix, AZ            |
| Waller | Acute onset of Severe Neck and Facial Edema in the PACU: A Unique Presentation of Subcutaneous Emphysema                        | American Society of<br>Anesthesiologists Annual<br>Meeting 2014       | New Orleans, LA        |

# **Departmental Research Products**

### 1. Published Abstracts (in alphabetical order of first author)

Beaudoin FL, Gutman R, Peak DA, Jones JS, Swor RA, Domeier RM, Lee DC, Rathlev NK, Hendry PL, **McLean SA**. Treatment effects of opioids versus NSAIDs prescribed from the emergency department following motor vehicle crash: the impact on pain outcomes at 6 weeks. Accepted for publication/presentation to the 2015 meeting of the American Pain Society.

**Bortsov AV**, Velilla MA, Damiron K, Pearson C Jones JS, Hendry PL, Kurz MC, **McLean SA**. Vitamin D deficiency is associated with worse overall pain outcomes over time among African Americans experiencing motor vehicle collision. Accepted for publication/presentation to the 2015 meeting of the American Pain Society

**Bruno KA** Systematic Capture of Regional Anesthesia Quality Metrics for Labor Analgesia Presented 3/16/2015 at SOAP.

JS Byerley, K Gilliland, R Madanick, **C Enarson**. Threads and Coils: Building a Matrix for Integrated Curriculum Leadership. AAMC Innovations in Academic Medicine Poster Session Saturday November 8, 2014, Chicago, IL.

JS Byerley, **C Enarson**. Successful Change: Developing Shared Principles as the Foundation for Curriculum Redesign. AAMC Innovations in Academic Medicine Poster Session Saturday November 8, 2014, Chicago , IL.

**Hu J**, Bollen KA, Lane ST, **Bortsov AV**, Peak DA, Jones JS, Swor RA, Domeier RM, Lee DC, Rathlev NK, Hendry PL, **McLean SA**. Evaluation of the influence of stress-induced pain vulnerability and sociodemographic characteristics on acute pain after a motor vehicle collision using structural equation modeling. Accepted for publication/presentation to the 2015 meeting of the American Pain Society

**Hu J**, Kessler RC **Bortsov AV**, **Battles SR**, Peak DA, Jones JS, Swor RA, Domeier RM, Lee DC, Rathlev NK, Hendry PL, **McLean SA**. Evaluating musculoskeletal pain pathogenesis in the aftermath of motor vehicle collision in a multi-dimensional context. Accepted for presentation to the 2015 meeting of the American Pain Society

**Isaak R, Stiegler M, Martinelli S, Kolarczyk L, Arora H.** Mixed-fidelity Simulation for Assessment of ACGME Milestones and ABA APPLIED Exam Preparation. American Society of Anesthesiologists Annual Meeting, San Diego, CA, October 2015.

**HP Kirby**, **TP Rohman**, **RS Isaak**, **L Hance**, HJ Kim, **LM Kolarczyk**. Enhanced Recovery After Surgery (ERAS) clinical pathway for patients undergoing pancreatic surgery decreases hospital length of stay. ASA annual meeting. Accepted for oral presentation for Best of Abstract: Clinical Science session.

**Kirby HP**, **Rohman TP**, **Hance L**, **Isaak R**, Kim HJ, **Kolarczyk LM**. "Enhanced Recovery After Surgery (ERAS) clinical pathway for patients undergoing pancreatic surgery decreases hospital length of stay". American Society of Anesthesiologists Annual Meeting, San Diego, CA, October 2015.

**Lateef B**, **Liu AY**, **Hu J**, MO Martel, RR Edwards, Swor RA, Peak DA, Jones JS, Rathlev NK, Lee DC, Domeier RM, Hendry PL, **McLean SA**. Pain Catastrophizing as a Predictor of Opioid Administration in Patients Presenting to the Emergency Department (ED) After Motor Vehicle Collision (MVC) Accepted for publication/presentation to the 2015 meeting of the American Pain Society

**Linnstaedt SD**, **Riker KD**, Nyland JE, Zimny E, Lewandowski C, Hendry PL, Damiron K, Pearson C, Velilla MA, Jones J, Swor R, Domeier R, **McLean SA.** microRNA 320a is a potential mediator of chronic widespread hyperalgesia development after stress exposure. Accepted for presentation at the annual American Pain Society meeting in May 2015

Liu AY, Hu J, Platts-Mills TF, Lateef B, Qadri YJ, Wang HE, Velilla MA, Pearson C, Zimny E, Lewandowski C, Hendry PL, Damiron K, Domeier RM, Kaushik S, Feldman JA, Jones JS, Villard MA, McLean SA. Education status is not associated with opioid medication receipt among African American emergency department patients with acute pain. Accepted for publication/presentation to the 2015 meeting of the American Pain Society

**Mauck MC, Liu AY, Bortsov AV**, Jones S, Hwang J, Williams FN, Shupp JW, Karlnoski T, Smith DJ, Krishnan A, Wesp B, Gellatly M, Cairns B, **McLean SA**. Predictors of pain severity after major thermal burn injury vary according to phase of burn wound healing. Accepted for publication/presentation to the 2015 meeting of the American Pain Society

Nyland JE, **McLean SA**, Averitt DL. Combined serotonin and norepinephrine reuptake inhibition reduces the effects of stress on post-injury pain behaviors in a rat model of burn injury. Accepted for publication/presentation to the 2015 meeting of the American Pain Society

**Rohman TP, Kirby HP, Hance L, Isaak R**, Kim HJ, **Kolarczyk LM**. "Enhanced Recovery after Surgery (ERAS) clinical pathway for pancreatic surgical patients decreases unnecessary blood product administration." American Society of Anesthesiologists Annual Meeting, San Diego, CA, October 2015.

**Villard MA**, Beaudoin FL, **Hu J**, **Orrey D**, Peak DA, Jones JS, Swor RA, Domeier RM, Lee DC, Rathlev NK, Hendry PL, **McLean SA**. Few individuals at high risk of persistent musculoskeletal pain after motor vehicle collision receive early psychological or physiotherapy intervention. Accepted for publication/presentation to the 2015 meeting of the American Pain Society

# 2. Journal Articles (in alphabetical order of first author)

Buchbinder M, Wilbur R, Zuskov D, **McLean SA**, Sleath BL. Teachable moments and missed opportunities for smoking cessation counseling in a hospital emergency department: a mixed-methods study of patient-provider communication. *BMC Health Services Research* 2014, 14:651

Buchbinder M, Wilbur R, **McLean SA**, Sleath BL. "Is there any way I can get something for my pain?" Patient strategies for requesting analgesics. *Patient Educ Couns*. 2015 Feb;98(2):137-43

Dicus Brookes C, Berry J, Rich J, Golden BA, Turvey TA, Blakey G, **Kopp V**, Phillips C, **Anderson JA**. Multimodal Protocol Reduces Postoperative Nausea and Vomiting in Patients Undergoing Le Fort I Osteotomy. *J Oral and Maxillofacial Surg* 2015;37(2):324-332.

Garg AX, Sessler DA, **Kumar PA**, Devereaux PJ et al. Perioperative aspirin and clonidine and risk of acute kidney injury. *JAMA* 2014 Nov; 312(21):2254-2264

Halawa OI, Al-Diri I, **McLean SA**, Darnall BD. When I'm in Pain, I feel God is Testing Me: Differences in Middle Eastern and US Cancer Pain Experiences. *J Pal Med* 2015 epub ahead of print.

Hunold KM, Sochor MR, **McLean SA**, Mosteller KB, Fernandez AR, **Platts-Mills TF**. Ambulance transport rates after motor vehicle collision for older vs. younger adults: A population-based study. *Accid Anal Prev*. 73C:373-379, 2014.

**Isaak RS**, Furman W, Con: Patients at risk for spinal cord ischemia after thoracic endovascular aortic repairs should not receive prophylactic CSF drainage, *Journal of Cardiothoracic and Vascular Anesthesia*, http://dx.doi.org/10.1053/j.jvca.2015.05.191

Kessler RC, Rose S, Koenen KC, Karam EG, Stang PD, Stein DJ, Heeringa SG, Hill ED, Liberzon I, McLaughlin KA, **McLean SA**, Pennell BE, Petukhova M, Rosellini AJ, Ruscio AM, Shahly V. Shalev AY, Silove D, van Ommeren M, Zaslavsky AM, Angermeyer MC, Bromet EJ, Caldas de Almeida JM, de Girolamo G, de Jonge P, Demyttenaere K, Florescu SE, Gureje O, Haro JM, Hinkov H, Kawakami N, Kovess-Masfety V, Lee S, Medina-Mora ME, Murphy SD, Navarro-Mateu F, Piazza M, Posada-Villa J, Scott K, Torres Y, Viana MC. How well can post-traumatic stress disorder be predicted from pre-trauma risk factors? An exploratory study in the WHO World Mental Health Surveys. *World Psychiatry*. 2014 Oct;13(3):265-74.

**Koenig M, Kopp V** Relaxant-free intubation in children: what do we (really) know about it? Submitted to *Anesthesiology* 1/29/15

**Kopp V, Koenig M** Age-related oxygen supplementation in anaesthesia - letter to the editor. Submitted to *British Journal of Anaesthesia* 1/21/15

**PA Kumar, SM Martinelli, RW Kyle, H Arora.** Echocardiographic Discovery of Doubled Interatrial Septum: An Incidental Finding. *Semin Cardiothorac Vasc Anesth*. 2015 Apr 30.

**Linnstaedt SD, Hu J, Bortsov AV, Soward AC**, Swor RA, Jones JS, Lee DC, Peak DA, Domeier RM, Rathlev NK, Hendry PL, **McLean SA**. μ-Opioid Receptor Gene A118G Variants and Persistent Pain

Symptoms among Men and Women Experiencing Motor Vehicle Collision. *J Pain*. 2015 Jul;16(7):637-44

Musey PI, **Linnstaedt SD**, **Platts-Mills TF**, Miner JR, **Bortsov AV**, Safdar B, Bijur P, Rosenau A, Tsze DS, Chang AK, Dorai S, Engel K, Feldman JA, Fusaro AM, Lee DC, Rosenberg M, Keefe FJ, Peak DA, Nam CS, Patel R, Fillingim RB, **McLean SA**. Gender Differences in Acute and Chronic Pain in the Emergency Department: Results of the 2014 Society for Academic Emergency Medicine Consensus Conference Pain Section. *Acad Emerg Med*. 2014 Dec;21(12):1421-30.

Pereira GF, **McLean SA**, Tkacik TJ, Swor RA, Jones JS, Lee DC, Peak DA, Domeier RM, Rathlev NK, Hendry PL, **Platts-Mills TF**. Pain, distress, and anticipated recovery for older versus younger emergency department patients after motor vehicle collision. *BMC Emerg Med*. 2014 Dec 30;14:25.

**Qadri YJ, Bortsov AV**, Orrey DC, Swor RA, Peak DA, Jones JS, Rathlev NK, Lee DC, Domeier RM, Hendry PL, **McLean SA**. Genetic Polymorphisms in the Dopamine Receptor 2 Predict Acute Pain Severity after Motor Vehicle Collision. *Clin J Pain*. 2014 Nov 3.

Sellers KK, Bennett DV, Hutt A, **Williams JH**, Frohlich F. Awake versus Anesthetized: Layer-Specific Sensory Processing in Visual Cortex and Functional Connectivity between Cortical Areas. *J Neurophysiol*, 2015 113(10):3798-815.

Shin G, **McLean SA, Hu J**, Gotz D. Visualizing Temporal Patterns by Clustering Patients. Accepted *Workshop on Visual Analytics in Healthcare*. 2014 Nov 15.

**Smith KA**. What's New in Obstetric Anesthesia. *Audio Digest Anesthesiology*. Vol 56, Issue 48. Dec 28th, 2014. 0271-1265.

**Stiegler, MP**; Gaba DM. Editorial: Decision-Making and Cognitive Strategies. *Simulation in Healthcare* (in press)

Wang X, Xie H, Cotton AS, Tamburrino MB, Brickman KR, Lewis TL, **McLean SA**, Liberzon I. Early cortical thickness changes after mild traumatic brain injury following motor vehicle collision. *J Neurotrauma*. 2015 Apr 1;32(7):455-63.

D'Alonzo RC, Ryan JW, **Kumar PA**. Anesthesia for Robotic Cardiac Surgery. Chapter 4. In: WR Chitwood and K Kernstein (ed.). Robotic Cardiothoracic Surgery: Atlas and Guide (13 pages) Springer London Ltd; 2014

**Goswami S, Kumar PA**, Mets B. Anesthesia for Robotic Surgery. In: Ronal D. Miller (ed.). Miller's Anesthesia 8th edition Nov. 2014. Churchill Livingstone (Elsevier) (41 pages)

Hoffman BM, **Goetzinger A**, Blumenthal JA. Cardiovascular Disease. In: Andrasik F, Goodie JL, Peterson AL. *Biopsychosocial Assessment in Clinical Health Psychology*. New York: Guildford; 2015.

**Passannante AN**: Patient Safety: Does the Anesthesia Care Team Contribute to Infection Risk? Audio-Digest Anesthesiology 56(37) ISSN 0271-1265, October 2014

## 4. Grants and Grant Funding Salary Support

Title: Applying the Biopsychosocial Model to Post-MVC Pain Development in African Americans

Award Number: R01AR060852 Sponsor: National Institute of Arthritis Musculoskeletal Skin Disease Project Dates: 09/15/2011 – 08/31/2016 Principal Investigator: Samuel McLean

Title: The HELP PAIN Trial: Healing with Venlafaxine after motor vehicle collision Sponsor: Mayday Fund Project Dates: 12/8/2010-12/31/2016 Principal Investigator: Samuel McLean

Title: The Influence of microRNA in chronic pain development Sponsor: Mayday Fund Project Dates: 7/1/2012-6/30/2014 Principal Investigator: Samuel McLean

Title: Grant Funding Salary Support for Co-Investigators: Evaluations of Genetic Variance Pathway Related Neurosteroids on Outcomes after MVC Sponsor: Department of Veteran Affairs Project Dates: 09/01/2013-8/31/2014 Co-Investigators: Sarah Linnstaedt and Andrey Bortsov

TITLE: Influence of PTSD Symptoms on Chronic Pain Development after Sexual Assault Award Number: R01AR064700 Sponsors: NIAMS, NINDS, OD, NINR, NIMH, NICHD Project Dates: 2014-2019 Principal Investigator: Samuel McLean