LOMA LINDA UNIVERSITY

School of Medicine

*Center for Health Disparities and Molecular Medicine*

# 18th Annual Health Disparities Research Symposium


Education –Development – Research – Health Disparities – Community
NCMHD Research Center of Excellence

***PROGRAM, BIOS & ABSTRACTS***

Wednesday, August 1, 2018
12:00 pm – 7:30 pm
Wong Kerlee International Conference Center
Loma Linda University School of Medicine
Loma Linda, California


LOMA LINDA UNIVERSITY

School of Medicine

*Center for Health Disparities &*
*Molecular Medicine*

# LOMA LINDA UNIVERSITY SCHOOL OF MEDICINE

## *18th Annual Health Disparities Research Symposium*

**Wednesday, August 1, 2018**
**12:00 pm-7:30 pm, Wong Kerlee International Conference Center**

# Agenda

## Diversity and Health Disparities Panel

**Moderator: Marino De Leon, PhD** – Loma Linda University

**12:00 – 1:30 pm**

**Edwin Hernandez, PhD** – Adventist University of Health Sciences
**Carlos Casiano, PhD** – Loma Linda University
**Daisy De Leon, PhD** – Loma Linda University
**Magaly Hernandez, MPH** – Adventist University of Health Sciences
**Susanne Montgomery, PhD** – Loma Linda University

## Poster Session

**2:30 pm – 5:00 pm** **Poster Presentations by Research Fellows**

LLU-NIH IMSD, MD/PhD Program
Apprenticeship Bridge to College Program (ABC)
Undergraduate Training Program (UTP)
Medical Training Program (MTP)
Summer Undergraduate Research Fellowship (SURF)

**5:00 pm – 5:30 pm** **Flash Presentations by Selected Students**

**Johnny D. Figueroa, PhD**
Assistant Professor
Department of Basic Sciences
Member, CHDMM
School of Medicine

## Evening Program

**5:30 pm – 8:00 pm**

**Welcome** **Daisy D. De Leon, PhD**
Assistant to the Dean for Diversity
Professor of Physiology and Pharmacology
Department of Basic Sciences
Co-Investigator and Core Director, CHDMM
School of Medicine

**Invocation** **Julia Unternaehrer, PhD**
Assistant Professor
Department of Basic Sciences
School of Medicine

**Remarks** **Ronald Carter, PhD**
Provost
Professor of Earth and Biological Sciences
Professor of Theological Studies

**Remarks**

**H. Roger Hadley, MD**
Dean, School of Medicine
Executive VP, Medical Affairs, LLUAHSC
School of Medicine

**Remarks**

**Penelope Duerksen-Hughes, PhD**
Associate Dean for Basic Sciences Faculty & Translational Research
Chair, Department of Basic Sciences
Professor of Biochemistry
Member, CHDMM
School of Medicine

**Remarks**

**Marino De Leon, PhD**
Director, CHDMM
Director/PI, LLU-NIH IMSD Program
Professor of Physiology
Department of Basic Sciences
School of Medicine

**Introduction of Keynote Speaker**

**Marino De Leon, PhD**
Director, CHDMM

## Keynote Address

## Edwin I. Hernandez, PhD

President & CEO
Adventist University of Health Sciences

## *"Moral Communities as Health Havens: The Role of Religion in Modulating the Impact of Health Disparities"*

**Acknowledgement of Research Fellows**

**Carlos A. Casiano, PhD**
Associate Director, CHDMM
Professor of Microbiology and Molecular Genetics
Department of Basic Sciences
School of Medicine

**Daisy D. De Leon, PhD**
Assistant to the Dean for Diversity
Professor of Physiology and Pharmacology
Department of Basic Sciences
Co-Investigator and Core Director, CHDMM
School of Medicine

**Susanne B. Montgomery, PhD**
Associate Dean for Research
Professor of Social Work and Social Ecology
School of Behavioral Health
Director, Community Engagement and Education Core, CHDMM

**Kylie Watts, PhD**
Assistant Professor of Microbiology
Department of Basic Sciences
Director, SURF
School of Medicine

**Final Remarks and Acknowledgements**

**Marino De Leon, PhD**

## Keynote Speaker Biography

### Edwin I. Hernandez, PhD

President & CEO
Adventist University of Health Sciences

As the second President of Adventist University of Health Sciences (ADU), Edwin I. Hernández, PhD, is committed to extending the healing ministry of Christ through excellence in education, scholarship, and culture.

As ADU Provost from 2015 to 2017, Dr. Hernández improved the University's academic quality and stature by earning new accreditations for key programs and supporting both higher standards and increased support for faculty members. In 2017, he succeeded the University's founding President, Dr. David Greenlaw, as President.

A leading scholar and strong advocate for Christian education, Dr. Hernández is also an ordained minister in the Seventh-day Adventist (SDA) Church. After earning his Bachelor of Arts in Theology from Loma Linda University, Dr. Hernández earned his Master of Divinity (MDiv) at the Seventh-day Adventist Theological Seminary at Andrews University. He also holds a PhD in Sociology from the University of Notre Dame with a specialty in the Sociology of Religion.

Born in Glendale, California, Dr. Hernández grew up in an SDA family committed to education as the answer to serving the world and making a difference. His passion for bridging healthcare, education, and ministry is connected to his family's teachings.

Early in his career, Dr. Hernández served as chaplain at Hialeah Hospital in Miami, Florida; sociology instructor at Andrews University in Berrien Springs, Michigan; and researcher for Pew Charitable Trusts. He later served as Vice President of Academic Affairs at Antillean Adventist University in Puerto Rico, Program Officer for Pew Charitable Trusts, and founding Director of the Center for the Study of Latino Religion at the University of Notre Dame.

Prior to joining ADU, as Senior Program Officer with the Doug & Maria DeVos Foundation, he led a successful multi-million-dollar urban education philanthropic initiative and community engagement strategy in Grand Rapids, Michigan. Throughout his career, Dr. Hernández has remained an avid scholar and writer, authoring and contributing to five books and more than 60 articles and reports.

As an ordained minister since 1991, Dr. Hernández is a leader in the Adventist faith with a special interest in its impact on healthcare. Maggie, his wife of more than 30 years, is an adjunct Professor of Nutrition at ADU. They have two adult sons, Edwin Jr. and Michael.

# LOMA LINDA UNIVERSITY SCHOOL OF MEDICINE
# CENTER FOR HEALTH DISPARITIES AND MOLECULAR MEDICINE
# 18TH ANNUAL HEALTH DISPARITIES RESEARCH SYMPOSIUM

The Loma Linda University (LLU) Center for Health Disparities and Molecular Medicine (CHDMM) is a National Institutes of Health (NIH)-designated Center of Excellence in health disparities research and training. The CHDMM is funded in part by an award from the National Center on Minority Health and Health Disparities, NIH (P20 MD006988), and an educational research training award, the "Initiative for Maximizing Student Development" **(IMSD)** program, funded by the National Institute of General Medical Sciences, NIH, (2R25 GM060507). Integrating these programs at the CHDMM has provided synergy to our research and educational goals at the Loma Linda University School of Medicine (LLUSM). The CHDMM has four integrated cores: (1) Administration, (2) Research, (3) Research Training and Education, and (4) Community Outreach and Partnership.

The ultimate objective of the CHDMM is to eliminate health disparities by researching contributing biological factors, identifying and removing barriers that prevent underrepresented students from entering biomedical careers, and partnering with key community and government organizations. The focus of the biomedical translational research projects of the CHDMM is to explore the connection between the Augmented State of Cellular Oxidative Stress (ASCOS) and health disparities diseases such as certain cancers, diabetes and stroke.

A pivotal goal of the educational program is to increase the number of students from underrepresented groups and medically underserved communities that graduate with a PhD or MD/PhD degree in the biomedical sciences at LLU. The educational program supports highly qualified high school, undergraduate, graduate (PhD and MD/PhD), and medical students at LLU. Overall, the CHDMM supports a minimum of 50 students per year.

Promising high school and undergraduate students participate in the Apprenticeship Bridge to College **(ABC)** Program and the Undergraduate Training Program **(UTP)** respectively**,** during an 8-week summer research and academic experience. The programs incorporate scientific mentoring as well as participation in scientific seminars and lectures, with supplemental educational enrichment activities. In addition, students are given opportunities to attend national scientific meetings to make research presentations based on their summer experiences. Students are compensated competitively for participating in the program.

The Medical Training Program **(MTP)** provides research experiences for medical students at LLUSM who are interested in integrating biomedical research and health disparities research into the practice of medicine. Selected medical students are matched with prominent scientists in the basic science departments and collaborate jointly in scientific research projects. Students are required to attend scientific seminars, special lectures, and research colloquia.

Doctoral students in the basic science departments at LLUSM participate as NIH graduate fellows in the IMSD program. Successful applicants are awarded all tuition and fees in addition to a generous stipend/salary for living expenses. The program also incorporates participation in enrichment activities along with scientific seminars and special lectures. LLU-NIH IMSD fellows participate in well-structured research and educational activities that promote career development.

# ACKNOWLEDGEMENTS

We would like to acknowledge the contributions of all who were instrumental in making this 2018 Health Disparities Research Symposium successful. Teamwork, cooperation, and flexibility are just a few of the skills necessary to successfully implement such a dynamic research program.

## 2018 Faculty Research Mentors

Duane Baldwin, MD
Erik Behringer, PhD
Carlos Casiano, PhD
Maud Celestin, DrPH
Camille Clarke, MD
Daisy De Leon, PhD
Marino De Leon, PhD
Penelope Duerksen-Hughes, PhD
Johnny Figueroa, PhD
Hansel Fletcher, PhD
David Hessinger, PhD
Mary Kearns-Jonker, PhD
Salma Khan, PhD
Wolff Kirsch, MD
William Langridge, PhD
Eugenia Mata-Greenwood, PhD
Saied Mirshahidi, PhD
Subburaman Mohan, PhD
Susanne Montgomery, PhD, MPH, MS
Ying Nie, MD, PhD
Kerby Oberg, MD, PhD
Kimberly Payne, PhD
William Pearce, PhD
Christopher Perry, PhD
Lisa Roberts, DrPH
Ryan Sinclair, PhD
Salvador Soriano, PhD
Richard Sun, PhD
Julia Unternaehrer-Hamm, PhD
Charles Wang, MD, PhD
Kylie Watts, PhD
Christopher Wilson, PhD
Sean Wilson, PhD
Xiao-Bing Zhang, PhD

## Key Personnel

Marino De Leon, PhD, Principal Investigator, CHDMM Director
Carlos Casiano, PhD, Co-Investigator, Associate CHDMM Director
Daisy De Leon, PhD, Co-Investigator, Core Director
Susan Gardner, PhD, Writing Consultant, Professor of English, Walla Walla University
Susanne Montgomery, PhD, Co-Investigator, Core Director

## CHDMM Administrative Staff

Ann Bradshaw – CHDMM Manager
Daniela Soto Wilder – CHDMM Program Manager
Nannette Nevares – CHDMM General Operations
Debbie Rosenstock – Office Aide

## School of Medicine Office of Diversity

Venice Walsh – Administrative Assistant

This is by no means an exhaustive list. We wish to acknowledge all of the unsung heroes who contributed in very significant ways, too numerous to mention.

# 2018 Student Research Fellows

### *ABC – Apprenticeship Bridge to College*

Rafael Alvarez
Heidi Buri
Wendy Chow
Anthony Garcia
Mikayla James
Kevin Liu
Rosalia Marenco
Selorm Quarshie
Jacob Razzouk
Girish Senthil
DeAndre Siringoringo
Maya Townsend
Jennifer Tran
William Wang
Viviana Williams

### *UTP – Undergraduate Training Program*

Victor Campbell
Christine Castanon
Amy-Claire Dauphin
Shekinah Dosunmu
Karen Figueroa
Joshua Guerra
Isaac Kafeero
Annie Moretta
Krystal Santiago
Hannah Sukarloo
Alexis Townsend

### *MTP – Medical Training Program*

Miranda Berger Nordelo
Ninoshka Caballero-Colon
Edilberto Ocasio Feliciano
Marlene Rodriguez
Miguel Serrano Illan
Neera Shah
Alfonso Vera

### *IMSD – PhD/MD-PhD Graduate Fellows*

Ivana Alicea-Polanco
Victor Camberos
Katherine Concepcion
Alfonso Duran
Jerry Flores
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Jenniffer Licero Campbell
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Hiel Rutanhira
Evelyn Sanchez Hernández
Nicholas Sanchez
Julio Vega-Torres
Jonathan Wooten

### *Behavioral Health & Public Health*

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Amanda Mendez
Lauren Miller
Navdeep Randhawa
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### *SURF – Summer Undergraduate Research Program*

Nicolas Belliard
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Crystal Mariano
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Kari Roberts
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### *Guest Participants*
Eloisa Lopez
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## Institutional Affiliations of Research Fellows

### High Schools
Academy for Academic Excellence
Etiwanda High School
John F. Kennedy Middle College High School
Loma Linda Academy
Middle College High School
Ramona High School
Redlands High School
Western Central Academy

### Universities
Andrews University
Loma Linda University
Master's University
Oakwood University
Occidental College
Point Loma Nazarene
San Juan Bautista School of Medicine
Southern Adventist University
Southern California University of Health Sciences
Southern New Hampshire University
The College of New Jersey
University of California, Berkely
University of California, Los Angeles
University of California, Riverside
University of California, San Bernardino
University of California, San Diego
University of the Cumberlands
University of Nevada, Reno
University of Puerto Rico, Mayaguez
University of Texas, San Antonio
Valparaiso University
Walla Walla University

# LOMA LINDA UNIVERSITY SCHOOL OF MEDICINE

CENTER FOR HEALTH DISPARITIES RESEARCH
OFFICE OF STUDENT DEVELOPMENT IN THE BIOMEDICAL PROFESSIONS

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# Apprenticeship Bridge to College (ABC) High School Program

Rafael Alvarez
Heidi Buri
Wendy Chow
Anthony Garcia
Mikayla James
Kevin Liu
Rosalia Marenco
Selorm Quarshie
Jacob Razzouk
Girish Senthil
DeAndre Siringoringo
Maya Townsend
Jennifer Tran
William Wang
Viviana Williams

# RAFAEL ALVAREZ

## ABC PARTICIPANT 2018

I am an incoming senior at Ramona High School in Riverside, CA. Both of my parents immigrated to the United States from Mexico and have taught me to take advantage of the wonderful opportunities we are presented with in this country. I thank them for their guidance and for giving me the confidence to apply to this program.

My interest in becoming a doctor started in the eighth grade when I had to do a career project. The project consisted of researching the career and then writing a resume and cover letter. I chose to do my project on becoming an oncologist and was overwhelmed by how long it would take me to actually become a licensed physician. It consists of eight years of schooling, additional years of training, and multiple tests. I wasn't sure if I really wanted to devote so many years of my life studying to become a doctor, especially if I wasn't completely sure if I wanted to become one. That is why I am eternally grateful for being given the opportunity to be a part of this wonderful program. I was able to get a glimpse of how life in the biology field is, and it has confirmed my decision of pursuing a career in the medical field.

This summer I had the honor of working in Dr. Sean Wilson's lab. I'd like to thank him and everyone in his lab for welcoming me and helping me with any troubles I had.

# CHRONIC HYPOXIA HIGH ALTITUDE STRESS AFFECTS ANTIOXIDANT LEVELS IN SHEEP PULMONARY ARTERIES

Rafael Alvarez, Isaac Kafeero, Remy Bosviel, Michael La Frano, John Newman, Oliver Fiehn, Sean M. Wilson

Center for Health Disparities and Molecular Medicine, Department of Perinatal Biology, School of Medicine, Loma Linda University, Loma Linda, CA

Gestational Hypoxia is a common prenatal stress caused by high altitude living, smoking, and other prenatal disorders. It is associated with poor cognitive development and fetal growth restriction which puts newborns at an increased risk of developing pulmonary hypertension, respiratory distress, infant mortality, and cardiovascular diseases later in life. This work aims to determine how chronic high-altitude hypoxia alters primary metabolite profiles and provides mechanistic insight of this stressor on pulmonary vascular development and function. For this study, normoxic pregnant and non-pregnant sheep were obtained from Nebeker Ranch in Lancaster, CA, and were either sent to Loma Linda for study or sent to White Mountain Research Station at an altitude of 3800 meters to induce long-term high-altitude hypoxia (LTH). After 110+ days of gestation, sheep were transported to Loma Linda for study. Tissues from the pulmonary arteries of adult, newborn, and fetal sheep were prepared and frozen for analysis of primary metabolites. Our results revealed a metabolic pathway with several metabolites and intermediates acting as antioxidants, playing key roles in pulmonary vascular development and function through regulating Reactive Oxygen Species (ROS) and other prooxidants. Glutathione (GSH) works synergistically with ascorbic acid to detoxify Hydrogen Peroxide, an ROS produced as a waste product of metabolism. It also regulates the Nitric Oxide cycle, of which NO is an important signaling molecule in endothelium-dependent vasodilation. N-acetylcysteine (NAC), a GSH precursor and potent ROS scavenger, induces HIF-1α which promotes angiogenesis by inducing Vascular Endothelial Growth Factor (VEGF). Ascorbic acid and NAC inhibit Endothelin-1 induced ROS-dependent activation of MAP kinases in vascular smooth muscle cells. This study suggests that antioxidant levels decrease under LTH and are potential indicators of this prenatal stressor.

# HEIDI BURI

## ABC PARTICIPANT 2018

Throughout my life, I have been passionate about the study and discovery of science. This passion, specifically biology, constantly influences all aspects of my life. This coming year, I will enter my senior year of high school at the Western Center Academy located in Hemet, CA. I feel extremely fortunate to be returning to the ABC program as it has sparked my passion for research. In the future, I aspire to attend a UC school where I will earn an undergraduate degree in biology and then earn an MD/PhD degree at Loma Linda University.

I have always believed the body and mind coincide, which has influenced my decision to play tennis. Beginning my freshman year, I have played doubles on the Varsity team and advanced to CIF Team and CIF Individuals. Along with tennis, I have found comfort in my life by playing the piano. Through playing the piano in an assisted living home, I have been capable of sharing my gift in a pleasant manner. Playing for the many individuals in the home, I am brought countless joy as I observe the smiles the music brings to others' faces.

Another passion I have is traveling as I love experiencing the diversity and becoming immersed within different countries and cultures. Every new country I travel in, I am inspired by the new experiences, smells, tastes, and sounds.

I am thankful for my family and all the individuals in the breast cancer research lab including Dr. Daisy De Leon, Xousaen Helu, Qianwei Tan, and Vinodh Radhakrishnan for their immense amount of help and encouragement. Without their guidance, I would be lost in the diverse field of research.

# INHIBITION OF HER2 AND IGF2 IN JIMT1 CELLS WITH RESVERATROL AND CHROMECEPTIN RESULTS IN DECREASED CELL PROLIFERATION

Heidi Buri, Xousaen M. Helu, Daisy D. De León

Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, Loma Linda, CA

Breast cancer is a major issue among women as it is the second leading cause of cancer-related death in the world. Approximately 20% of breast cancer patients are found to have an overexpression of the Human Epidermal Growth Factor Receptor 2 (HER2). Although Transtuzumab, a recombinant monoclonal antibody that inhibits HER2 by binding to the HER2 receptors, has been demonstrated to slow tumor growth, about 30% of breast cancer patients do not respond to treatment. Previous results in our lab have demonstrated that JIMT1 HER2 positive breast cancer cells are resistant to Trastuzumab and also had higher levels of IGF2 compared to HER2 positive cells that responded to Trastuzumab. The hypothesis of this study is that cell viability and proliferation of the Trastuzumab resistant HER2+ JIMT cells will decrease in response to the treatment with Resveratrol and Chromeceptin. Both, Resveratrol and Chromeceptin, inhibit IGF2 while Resveratrol also inhibits HER2 and STAT3. We tested the effect of these IGF2 inhibitors in combination and at various concentrations to determine an effective dose and to assess if there are additive or synergistic effects when used in combination. There was a significantly visible decrease in the cell viability of the JIMT1 cells treated with the highest concentration of Resveratrol. Additionally, there was a significant change in the cell morphology of JIMT1 cells treated with the highest concentration of Chromeceptin. While combined, the cells seemed to react relatively the same to treatments on their own. These results indicate that treatment of the combination of Resveratrol and Chromeceptin are effective drugs in decreasing the cell viability and proliferation of HER2 Positive Trastuzumab-Resistant JIMT1 breast cancer cells. The separate treatments of high concentrations of Resveratrol and Chromeceptin effectively changed the cell morphology and decreased both the cell viability proliferation of HER2 Positive Trastuzumab-Resistant JIMT1 breast cancer cells.

# WENDY CHOW

## ABC PARTICIPANT 2018

I have not always loved learning. It was something I had to learn to love and then did. Science became a genuine passion of mine because this very subject explores how we work, what we don't know, and why the world is. This summer of 2018 has allowed me the opportunity to satisfy some of my curiosities and create many more.

This August I will be attending Ramona High School in Riverside for my fourth and final year. If the path I paved leads me well, I plan to obtain my Bachelor of Science in Biochemistry at UCR and continue to Loma Linda's School of Medicine. But my insatiable curiosity has also led me to pursue a great interest in the performing arts specifically on dance and piano. I was a shy girl who was scared of the idea of public speaking and negotiations, but subsequently I became the president of the Model United Nations (MUN) club. From there I was able to host the UNHCR Tent Walk for Refugees 2017 event, the Cultural Festival for Human Rights 70th Anniversary, and hold Ramona's first MUN conference. Familiarizing myself with the aspects of my environment and my home planet matters significantly.

I am very fortunate to have worked with the knowledgeable Dr. Eugenia Mata-Greenwood in her lab this summer. She taught me that school will be challenging but also that I have what it takes to put up a good fight. Her patience and belief in me sparked an even brighter fire for my passion to become a dependable family physician. Thank you for one of the best and most memorable experiences I've ever had.

# DEVELOPMENT OF A SURVIVAL SURGERY TO OVEREXPRESS VITAMIN D RECEPTOR (VDR) DURING PREGNANCY

Wendy Lee Chow, Eugenia Mata-Greenwood

Center for Health Disparities and Molecular Medicine, Center for Perinatal Biology, School of Medicine, Loma Linda University, Loma Linda, CA

Vitamin D sufficiency is considered essential for healthy pregnancy. The maternal plasma levels of active vitamin D increase during normal pregnancies, but the physiological and molecular mechanisms remain unknown. We hypothesize that pregnancy hormones lead to renal Vitamin D receptor (VDR) degradation that decreases VDR-dependent upregulation of CYP24a1, the vitamin D inactivation enzyme. To test this hypothesis, we delivered human VDR in the kidneys of pregnant CD1 rats using adenoviral vectors. At day 15 of pregnancy, 0.5 billion IFU adenoviral vectors containing hVDR or not (empty vectors) were injected into each kidney through the renal vein under anesthesia and according to IACUC protocols. Both empty and hVDR adenoviral vectors were tagged with GFP. Injected rats were allowed to recover, and 3 days later (pregnancy day 18), fetal/placental weights, plasma, and tissues (i.e., kidneys) were collected. There were no differences between our two groups (empty versus hVDR gene delivery) in pregnancy weight gain, litter size, fetal or placental weight. Renal gene expression of hVDR and GFP confirmed the success of adenoviral gene delivery. GFP was expressed in 8 of the 12 kidneys while hVDR was expressed in only 2 of the 6 kidneys of the hVDR-adenoviral injections, but not in any of the empty adenovirus injections. Adenoviral delivery of hVDR produced a non-significant decrease in the plasma levels of both 25-hydroxy and bioactive vitamin D as estimated by enzyme-immunosorbent assay. A colorimetric assay showed that hVDR delivery significantly decreased plasma calcium levels and non-significantly increased those in kidneys. In addition, hVDR gene delivery non-significantly increased the renal expression of rVDR and CYP24a1 mRNA. In conclusion, adenoviral delivery of hVDR in pregnant CD1 rats has the potential to alter vitamin D status and renal gene expression. To obtain statistically significant data, a higher adenoviral dose or an increase in rat number per group is needed.

# ANTHONY ALEXANDER GARCIA

## ABC PARTICIPANT 2018

I presently attend John F. Kennedy Middle College High School and Norco College where I'll be graduating with a high school diploma and four associate degrees next spring. In academia, I rank in the top 1% percent of my graduating class both in high school and college and superintend the College Honors program and the College STEM Scholars program. Being a nationally recognized Eagle Scout of America, I lead Crew 706 of Riverside as Venturing Crew President and was appointed by the Norco City Council to the NYAC. I'm the Senior Class Vice President, President of a national award-winning Academic Decathlon team, Regional President of the Future Medical Professionals of America, President of the Pre-Med Society at Norco College, music therapist at Kaiser Permanente, and rank regionally-nationally in the Brain Bee. I'm working in the CSUF SSRC as well as the UCR CGNI as a research assistant. Outside of school, my vast positions, and academic endeavors, I perform in the University of Redlands Youth Symphony Orchestra and the Jurupa Stake Orchestra as 1st violinist.

In the future, I aspire to attend Harvard College earning my BS/MS in neuroscience that will lead to my acceptance into the Harvard-MIT MD/PhD program, continuing my neuroscience studies. After graduating, I intend to enroll in a neurosurgery residency at Johns Hopkins and, subsequently, a brain fellowship.

I am grateful to Perla Ontiveros, Dr. Jo-Wen Liu, and Dr. Marino De Leon for their wise and beneficial expertise in neuroscience. I've been able to gain vast knowledge of neurophysiology. The most riveting part of the research I conducted was achieving the desire to develop a new method to treat neuropathic pain. The Apprenticeship Bridge to College program has affirmed my perpetual inclination to pursue a career in medicine and science.

# DOCOSAHEXAENOIC ACID AS A POTENTIAL REGULATOR OF AUTOPHAGIC FLUX IN AN *IN VITRO* MODEL OF LIPOTOXICITY

Anthony A. García, Perla Ontiveros Ángel, Manuel Montero,
Jo-Wen Liu, Marino De León

Center for Health Disparities and Molecular Medicine, School of Medicine,
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Autophagy, an important cellular process, maintains homeostasis by the segregation and delivery of cytoplasmic cargo for degradation through the lysosomal machinery. Dysregulated autophagic flux is detrimental to the cell. A previous report from our lab shows that docosahexaenoic acid (DHA) cellular neuroprotection against palmitic acid (PA)-induced lipotoxicity involves the activation of the autophagy pathway. The objective of this study is to characterize the expression levels of Microtubule-associated protein 1A/1B-light chain 3 (LC3B) and p62 (a receptor protein that binds to ubiquitin cargo, LC3 and its homologs) in this neuroprotective process. Differentiated pheochromocytoma 12 (PC12) cells were cultured under the following conditions: BSA (vehicle control), PA, DHA or PA+DHA. The expression levels of LC3B, p62 and cell viability were quantified after 18 and 48 hours respectively. ELISA assays used to quantify p62 showed a significant increase in cultures exposed to PA. This increase was reduced under cotreatment with DHA, confirming DHA facilitates autophagic flux to allow cell survival. The next series of experiments used flowcytometry to measure both LC3B and p62 in PC12 cells exposed to PA overload. These experiments showed a significant accumulation of p62 concomitantly with a decrease of LC3B, thus indicating a dysregulated autophagic flux. Treatment with DHA alone had little effect on p62/LC3B ratio. However, cultures co-treated with DHA and PA exhibited a p62/LC3B ratio similar to control. Furthermore, a direct correlation between a decrease of cell viability with elevated levels of p62 and p62/LC3B ratio was observed in the PA group. In contrast, high cell viability in these cultures was associated with normal levels of p62, and a normal p62/LC3B ratio was observed in the presence of DHA and DHA+PA. Our data is consistent with a role of DHA providing protection against lipotoxic injury by stimulating autophagy which includes the regulation of the expression levels of p62 and LC3B proteins.

# MIKAYLA JAMES

## ABC PARTICIPANT 2018

I like being challenged, so during my last semester at Redlands High School, I applied to the ABC program with a cheerful heart. However, during the interview, my hope started dwindling as I sized up the competition. I could practically see their scholarly auras. As if peer intimidation were not enough, I was positive my interviewers were not impressed with me as I finished earlier than those around me. It was with trepidation that I opened the e-mail from Daniela Soto-Wilder but was elated to see that it was an acceptance letter to the program. I was grateful for being selected and have learned lessons that will help me as I pursue my career.

I will be attending La Sierra University this fall. The ABC program has laid the foundation for the type of research that is a part of the University's honors program. I plan on working on research in public health and hope to one day be able to effectively reach out to underprivileged communities with a plan to help improve their living conditions, health education, and lifestyle. I also plan to be a student missionary while at La Sierra.

This summer, I compared Caspace-3, used to reveal apoptosis, with Fluoro-jade C, a stain used to detect neurodregradation. The idea of being a pioneer in my field of research is fascinating, and I thank Dr. William Pearce for encouraging me to ask questions, Dessy Carreon for guiding me, and Alejandra Beltran for being available whenever I had questions.

# FLUORO-JADE C AND CASPASE-3 DETECT SEPARATE BUT COMPLEMENTARY PATTERNS OF CELL DEATH INDUCED BY TRAUMATIC BRAIN INJURY

Mikayla James, Desirelys Carreon, Alejandra Beltran, William Pearce

Center for Health Disparities and Molecular Medicine, Center for Perinatal Biology, School of Medicine, Loma Linda University, Loma Linda, CA

In 2013, about 2.8 million Traumatic Brain Injury (TBI)-related emergency department visits occurred in the United States. TBI induces two types of cell death: necrosis, which happens immediately after impact, then apoptosis or programmed cell death, which occurs 1-12 hours after impact. Several sensitive and selective methods are available to detect cell death in the brain, including staining for caspase-3 and Fluoro-Jade C (FJC). Caspase-3 is an enzyme that is a final common mediator of apoptosis in all cell types. FJC is a fluorescent dye that stains degenerating neurons. Comparison of the extents of cell death measured by caspase-3 and FJC should help indicate the relative proportions of neuronal and non-neuronal cell death following TBI. To test this idea, we divided 10 rats into 2 groups: sham and mild TBI. The brains were collected 24 hours post injury and were stained with FJC and Caspase-3. Relative to shams, TBI caused a proportionately greater overall increase for caspase-3 than for FJC, indicating that TBI caused extensive non-neuronal apoptotic cell death. The caspase-3 signal was greater on the injury side of the brain than on the non-injury side. On the non-injury side of the brain, TBI-induced increases in the FJC signal were equal to or greater than the Caspase-3 increases, indicating that the majority of death on the non-injury side occurred in neurons. Overall, both Caspase-3 and FJC were strong indicators of TBI-induced brain injury and revealed very different patterns of injury. Ideally, any complete assessment of TBI-induced brain injury must take into account both neuronal and non-neuronal injury as well as apoptotic and non-apoptotic (necrotic) injury. Correspondingly, therapeutic strategies should take into account which cell populations are the primary target for rescue; such studies are excellent topics for future investigation.

# KEVIN LIU

## ABC PARTICIPANT 2018

Going into my senior year at Redlands High School, I have been involved in activities such as swimming and speech and debate. I have also taken a variety of classes centered on the field of science that have influenced my current plan to major in biology in college. I have always been intrigued and interested by science and its nuances. This summer program has given me the rare opportunity to observe and learn about the field of neuroscience in a laboratory setting that my previous experiences in science have lacked. My obsession with science is never-ending, and this experience has given me the chance to challenge myself in a way that I will be forever grateful for.

My accomplishments include being on the Varsity team for swimming for all years of high school so far; the team has been ranked first in the Citrus Belt League each of those years. On my free weekends, I choose to spend my time as a volunteer at the Palm Terrace Senior Center in Riverside in an effort to make a positive impact on my community and provide aid to the elderly.

This summer, I worked in Dr. Johnny Figueroa's laboratory under the supervision of Ivana Alicea Polanco and Julio Vega-Torres. We researched the effects of diet-induced obesity and palmitic acid and how these two factors impact the expression and function of key brain maturation. I would like to thank Dr. Figueroa's lab for giving me this unique opportunity and for helping me understand more about the brain and how stress reactivity is affected over time.

## HIGH-SATURATED FAT DIET-INDUCED NEUROINFLAMMATION AS A PATHWAY FOR STRESS VULNERABILITY DURING ADOLESCENCE

Kevin Liu, Keisha Jordan, Esmeralda Terrones, Ivana Alicea-Polanco, Julio D. Vega-Torres, Johnny D. Figueroa

Center for Health Disparities and Molecular Medicine, Department of Neuroscience, School of Medicine, Loma Linda University, Loma Linda, CA

Psychosocial stressors are a well-documented risk factor for mental illness. Neuroinflammation has been proposed to mediate this association. We have shown that consumption of diets rich in saturated fatty acids impairs cognitive function and heightens vulnerability to psychosocial stressors. The purpose of this study was to investigate the effects of a high-saturated fat diet (HSFD) on neuroinflammation in brain regions implicated in stress responsivity. Adolescent Lewis rats were fed a low-saturated fat control diet (LSFD, 13 kcal from fat) or a HSFD (41 kcal from fat). We assessed stress responsivity using a well-characterized fear-potentiated startle (FPS) paradigm. Further, we measured the mRNA levels of important neuroinflammatory biomarkers (NLRP3, TLR4, NFκβ, CX3CR1, IL1β, IL6, IBA1, TNFα, CDK5, and HMGB1) using real-time polymerase chain reaction. We found that LSFD-fed rats had an 87.5% decrease in post-extinction FPS when compared to pre-extinction FPS while the HSFD-fed rats had identical FPS magnitudes. These findings suggest that HSFD-fed rats had impairments in fear memory extinction which is an indication of greater manifestation of stress responsivity. We also found that the prefrontal cortex of HSFD-fed rats exhibited a significant reduction in the mRNA levels of CX3CR1 (24.4%) and NLRP3 (29.5%) genes when compared to LFSD-fed rats. Our findings support that consumption of a HSFD during adolescence can alter neuroinflammation markers in areas associated with stress responsivity.

# ROSALIA VITA MARENCO

## ABC PARTICIPANT 2018

Engaging in this prestigious program has opened my mind to how science has so much beauty and knowledge still being discovered today. I now realize how much passion, patience, and dedication it takes to put into the artwork of science. This program has truly taught me how to become a successful individual heading towards the medical route.

As a new graduate from The Lewis Center, I will now attend UC Riverside for my undergraduate degree majoring in entomology as a pre-medical student in the honors program. During my high school career, I was highly involved in community service and JROTC. Being an officer in JROTC has made me also become a better leader and an aid for others who are not recognized enough.

During my time in the program, my team consisted of Dr. David Hessinger, Matthew Kimble, and Selorm Quarshie. Putting our efforts together, we researched how we can inhibit all of the TRP channels on the sea anemone's nematocysts in order to cease the anemone's hunger response.

Being first generation of an immigrant family, I have also grown to realize how much my parents put into my family just so we could get a better education and lifestyle. My dream is to become the first medical doctor in my family and make other underprivileged individuals believe they also have a chance of reaching their dreams. The CHDMM has made me grow significantly as a scientist and individual. I would like to thank Dr. Hessinger for all the insight and opportunity he provided for my future endeavors. I would also like to praise God for opening this door for me. I am truly blessed (Proverbs 3:5-6).

## TRPV4 CHANNELS INVOLVED IN NEMATOCYST-MEDIATED PREY KILLING

Rosalia Marenco, Selorm Quarshie, Matthew Kimble, David A. Hessinger

Center for Health Disparities and Molecular Medicine, Division of Physiology and Pharmacology, School of Medicine, Loma Linda University, Loma Linda, CA

Three types of cnidocyte supporting cell complexes (CSCC) regulate and trigger nematocyst discharge against prey in sea anemone. Prey trigger discharge from Type Cs by directly stimulating a contact-sensitive mechanoreceptor (CSM) in order to trigger discharge. In Type Bs, prey must first chemosensitize the CSM to trigger discharge. Type As must undergo both chemosensitized and tune vibration-sensitive mechanoreceptors to trigger CSMs. Type As are inhibited by streptomycin and by N-acetylneuraminic acid-proline (NANA-Pro). While CSMs require $Ca^{2+}$ that work instantaneously, their identity is unknown. We suspect TRP channels function as CSMs because they conduct $Ca^{2+}$ and are known to be mechanically gated. Two TRP channel blockers, gadolinium ($Gd^{3+}$) and GSK2193874, dependently inhibit most, but not all, prey killing. $Gd^{3+}$ broadly inhibits TRP channels, but GSK is specific for TRPV4 channels. We hypothesize the unaffected CSCCs are Type As. We reason that if $Gd^{3+}$ and GSK inhibit Types B+C and not A, then we should achieve full inhibition in the presence of streptomycin or NANA-Pro. Using monoclonal *Haliplanella luciae* in a quantitative feeding assay, Gd+NANA-Pro and Gd+streptomycin fully inhibit, but GSK+streptomycin did not. Thus, GSK inhibits TRPV4 channels on either Types A+B or Types A+C. To test this, we utilized tetrodotoxin (TTX) together with GSK. Because TTX inhibits Types A+B, combining TTX and GSK will give less than full inhibition. Albeit, if GSK operates on Types A and C, then it will present full inhibition. Utilizing the feeding assay GSK with TTX, we conclude that GSK inhibits TRPV4 on Types A and B CSCCs.

# SELORM QUARSHIE

## ABC PARTICIPANT 2018

In June I graduated from Redlands High School. This fall I will attend Harvard University as a neuroscience major. Throughout my life I was always excited to learn about the complex mysteries associated with mathematics and science because, unlike other fields of interest, world problems brought forth to be answered by mathematics and science evolve with humankind. Whether it is disease or the necessity to find new energy sources, mathematics and science, just like people, always adapt.

Throughout my academic career I have been involved in various programs. I have participated in instrumental music programs as a brass player for the past seven years. I served as captain of my school's Academic Decathlon team and have won various awards ranging from Regional to Global recognition within Destination Imagination.

In my leisure time I really enjoy activities that allow me to refresh myself, including reading, playing video games, and playing the trumpet. I volunteer at my previous middle school as a coach for the school's MathCounts team while also leading a general advanced mathematics class for all students who want to challenge themselves and prepare for the American Mathematics Competition.

Within the ABC program I am researching satiety in *H.luciae,* a species of sea anemone, with colleagues Matthew Kimble and Rosalia Marenco, under the mentorship of Dr. David Hessinger. The research's focus on the nervous system and cell response to stimuli resonates with me personally, for it broadens my understanding of cell communication and, in turn, my understanding of fundamental biological concepts.

## TRPV4 CHANNELS INVOLVED IN NEMATOCYST-MEDIATED PREY KILLING

Selorm Quarshie, Rosalia Marenco, Matthew Kimble, David A. Hessinger

Center for Health Disparities and Molecular Medicine, Division of Physiology and Pharmacology, School of Medicine, Loma Linda University, Loma Linda, CA

Three types of cnidocyte supporting cell complexes (CSCC) regulate and trigger nematocyst discharge against prey in sea anemone. Prey trigger discharge from Type Cs by directly stimulating a contact-sensitive mechanoreceptor (CSM) in order to trigger discharge. In Type Bs, prey must first chemosensitize the CSM to trigger discharge. Type As must undergo both chemosensitized and tune vibration-sensitive mechanoreceptors to trigger CSMs. Type As are inhibited by streptomycin and by N-acetylneuraminic acid-proline (NANA-Pro). While CSMs require $Ca^{2+}$ that work instantaneously, their identity is unknown. We suspect TRP channels function as CSMs because they conduct $Ca^{2+}$ and are known to be mechanically gated. Two TRP channel blockers, gadolinium ($Gd^{3+}$) and GSK2193874, dependently inhibit most, but not all, prey killing. $Gd^{3+}$ broadly inhibits TRP channels, but GSK is specific for TRPV4 channels. We hypothesize the unaffected CSCCs are Type As. We reason that if $Gd^{3+}$ and GSK inhibit Types B+C and not A, then we should achieve full inhibition in the presence of streptomycin or NANA-Pro. Using monoclonal *Haliplanella luciae* in a quantitative feeding assay, Gd+NANA-Pro and Gd+streptomycin fully inhibit, but GSK+streptomycin did not. Thus, GSK inhibits TRPV4 channels on either Types A+B or Types A+C. To test this, we utilized tetrodotoxin (TTX) together with GSK. Because TTX inhibits Types A+B, combining TTX and GSK will give less than full inhibition. Albeit, if GSK operates on Types A and C, then it will present full inhibition. Utilizing the feeding assay GSK with TTX, we conclude that GSK inhibits TRPV4 on Types A and B CSCCs.

# JACOB RAZZOUK

## ABC PARTICIPANT 2018

The ABC program has given me the great opportunity to open my eyes to the many facets encapsulated within the medical research field. I would like most of all to thank Dr. Sean Wilson for allowing me to participate in his research studies; the collaborative nature of the work has been an immense privilege to learn from as we work on analyzing the fascinating reality surrounding athletes of USA cycling. The puzzling and, furthermore, alarming statistics that *over fifty percent* of new riders to the sport register for a USAC license but then do not choose to renew their license the following year, has been a stimulating, data-enriched labyrinth to navigate through, and I am once again grateful to Dr. Wilson for allowing me to be a part of his team.

I am a current student at Redlands High School where I will be a senior in the upcoming academic year. In my free time, I enjoy the hobbies of running, rock climbing, and basketball while also being a member of the Redlands Speech and Debate Team. Upon graduating from high school, I hope to attend a four-year undergraduate university and in the long-term—hopefully—attend medical school.

The most superlative of take-aways that I have sensed while interning at Loma Linda University is the emphasis on the holistic approach "To Make Man Whole," and with an ever-steady faith in the principles of loving one's neighbor and living a life of being a "cheerful giver," LLU truly imparts the sense that with dedication we can all strive to put these principles into practice and, by doing so, make our community, and *even* the world, a better place.

## RETENTION RATES AMONG USAC ATHLETES GOES DOWNHILL DURING EARLY COLLEGIATE YEARS

Jacob Razzouk, Drew Kogon, Hunter Wilson, Bill Leudeke, Sean M. Wilson

Center for Health Disparities and Molecular Medicine, Department of Perinatal Biology, School of Medicine, Loma Linda University, Loma Linda, CA

Cyclists who register their licenses with USA Cycling for the first time oftentimes do not renew their memberships the following year. The aim of this work was to test the hypothesis that there is a pronounced dropout rate among USA cycling athletes during their late-teens and early-twenties at the time when a large proportion of them would be enrolling in a collegiate institution or otherwise would be moving forward in life. Utilizing master yearly databases provided by USA Cycling, we analyzed retention rates of cyclists based on their license registration number. For certain years we examined the continuance and re-entry of junior riders (ages 15-18) as collegiate riders. We also examined crossover between USA Cycling and National Interscholastic Cycling Association (NICA) athletes who attended the regional championship event in 2018. Based on the population statistics, we find a change in the age demographics in the last several years with a pronounced increase in junior age ridership relative to previous years. However, there is a precipitous drop in total ridership as the ridership enters college. After this period, there is a steady rise in USAC participation among athlete populations who are in their late-twenties and on into adulthood. The results also show there is only about a 15% crossover between USAC and NICA ridership. Correspondingly, our work demonstrates that the shifting lifestyle circumstances around the early-twenties timeframe is acting as a source of stimuli and pressure engendering the trend of considerable drop-out rates among cycling athletes of this demographic as denoted by our USAC age distribution models. Secondarily, we do not find that these junior-aged athletes reenter the sport at least up through their mid-twenties.

# GIRISH N. SENTHIL

## ABC PARTICIPANT 2018

"The moment you doubt whether you can fly, you cease forever to be able to do it." This quote has guided me throughout my last year at Redlands High School and will continue to guide me at UCSD in the fall where I will be studying neurobiology. Along with taking AP classes, I also participated as a Varsity player on the boy's tennis team. Together we have won 3 CIF championships for the past 3 years. In addition to tennis, I also participated in clubs, including Gateway to Medicine and Cultures for Youth. These clubs have taught me to use the community in order to learn and connect with people. At the same time, programs such as the ABC have taught me much more than just school would have been able to.

This summer I have been doing research on prostate cancer (PCa) cells and how they are resistant to chemotherapy drugs such as Docetaxel. Currently, there is a large emphasis on proteins such as LEDGF/p75 and its role in metastatic castration resistant PCa (mCRPC). The main technique used to identify these proteins is immunoprecipitation which is very complex and precise. I am excited to be able to do it for my project. I have also done other techniques such as Western Blotting in order to characterize the expression of proteins relevant to the mechanisms behind mCRPC.

My goals are to excel at UCSD and ultimately be admitted to medical school. I would not have been able to do any of the work that is done in the lab without the help and patience of my mentors, Evelyn Sanchez and Greisha Ortiz, and I thank Dr. Carlos Casiano for giving me the opportunity to work in his lab this summer.

## THE TRANSCRIPTION FACTOR JPO2 IS UPREGULATED IN DOCETAXEL RESISTANT PROSTATE CANCER CELLS AND INTERACTS WITH LEDGF/P75

Girish Senthil, Greisha L. Ortiz-Hernandez, Shannalee Martinez, Carlos A. Casiano

Center for Health Disparities and Molecular Medicine, School of Medicine, Loma Linda University, Loma Linda, CA

Prostate cancer (PCa) is the most commonly diagnosed cancer and second leading cause of cancer-related male deaths in the United States. Current therapies for advanced PCa include androgen deprivation therapy and docetaxel (DTX) chemotherapy. Unfortunately, therapy resistance and disease progression are unavoidable, leading to patient mortality. Our group has demonstrated that the stress oncoprotein Lens Epithelium Derived Growth Factor protein of 75 kD (LEDGF/p75) is upregulated in clinical prostate tumors and contributes to DTX resistance in PCa cells. However, very little is known about the mechanisms by which LEDGF/p75 promotes chemoresistance. To explore these mechanisms we initiated a molecular analysis of protein-protein interactions (PPIs) between LEDGF/p75 and other nuclear proteins in DTX-sensitive and -resistant PCa cells. An emerging transcription factor, JPO2, has been linked to aggressive phenotypes in medulloblastoma through its binding with LEDGF/p75, but this interaction has not been explored in the context of PCa chemoresistance. Our hypothesis is that LEDGF/p75 interacts with JPO2 to induce the expression of stress survival genes that contribute to PCa chemoresistance. As a first step in evaluating this hypothesis, we assessed the protein expression of JPO2 through Western blotting in our DTX-sensitive and DTX-resistant PCa cell lines. Our data showed an upregulation of both JPO2 and LEDGF/p75 protein expression in the DTX-resistant cells compared to the sensitive cells. Also, preliminary data from immunoprecipitation experiments suggest an interaction between JPO2 and LEDGF/p75 in the chemoresistant PCa cells. Other techniques such as protein nuclear colocalization by immunofluorescence microscopy are being optimized to further determine to which extent LEDGF/p75 and JOP2 may be part of a transcription protein complex in chemoresistant cells. Our long-term goal is to establish the contribution of PPIs to LEDGF/p75-mediated upregulation of stress oncoproteins in the context of PCa chemoresistance and mortality disparities and target these interactions with small molecule inhibitors to re-sensitize chemoresistant PCa cells to DTX.

# DEANDRE SIRINGORINGO

## ABC PARTICIPANT 2018

"If your ship doesn't come in, swim out and meet it!" These words from the late comedian Jonathan Winters spurred me to apply for the ABC program here at Loma Linda University. When I first heard about this program and its focus on research immersion in the medical field for high school students who come from underrepresented demographics, I jumped at this opportunity right away. In order to be successful in achieving a goal, one must be actively searching to reach the goal, to swim out and meet the boat when the boat doesn't come in.

I am eighteen years old and just graduated from Etiwanda High School in Rancho Cucamonga. In high school, I was involved in Model United Nations, MedFutures, California Scholarship Federation as well as Chemistry Club working as a tutor for Honors and AP Chemistry students. Along with my academic extracurricular activities, I was a four-year Varsity tennis player during which I was captain my junior and senior year. After completing my undergrad, I wish to attend Loma Linda University's School of Medicine in hopes of becoming a physician.

This summer, I had the privilege to work with Dr. William Langridge and Mary Beth Yu researching methotrexate predictors for the treatment of rheumatoid arthritis patients. They were both patient and willing to guide me through this summer in my first research experience.

# IMMUNOASSAY FOR PREDICTING METHOTREXATE RESISTANCE IN RHEUMATOID ARTHRITIS PATIENTS

DeAndre Siringoringo, Mary Beth Yu, William H. R. Langridge

Center for Health Disparities and Molecular Medicine, Department of Immunology, School of Medicine, Loma Linda University, Loma Linda, CA

Rheumatoid arthritis (RA) is an incurable, chronic, systemic inflammatory disorder in which the immune system attacks the body's tissues. RA targets the joints causing a painful chronic inflammatory response. Methotrexate (MTX), a drug that interferes with folate metabolism, is frequently used to treat RA. Because MTX inhibits pro-inflammatory cytokine production, it gives relief to the swelling and pain of RA. However, there is significant individual variability in the clinical response to MTX. About 30%-50% of patients receiving MTX show little to no beneficial response. In this study, we hypothesize that the clinical response to methotrexate is directly related to the results of an *in vitro* assay used to measure MTX suppression of lymphocyte secretion of the pro-inflammatory cytokine interleukin-17 (IL-17). Increasing doses of MTX were added to peripheral blood leukocyte samples collected from new patients with active RA but not yet treated with MTX. The concentration of IL-17 in the leukocyte culture medium was measured by an enzyme linked immunosorbent assay (ELISA). In addition, we determined the concentration of another pro-inflammatory cytokine interferon-γ (IFNg), using the same method in a separate experiment. The addition of MTX to the patient samples showed a suppression of IFNg at high concentrations of MTX for three of the four patient samples tested. Based on our preliminary data, the *in vitro* IL-17 suppression assay may help to predict an accurate clinical response to MTX in RA patients. Thus, the MTX IL-17 suppression assay could become an important clinical method for protecting potentially resistant RA patients from three months of treatment with a potentially harmful drug likely to have no beneficial effect on reducing RA inflammation.

# MAYA TOWNSEND

## ABC PARTICIPANT 2018

I have always been dedicated to academics and furthering my education. I am an honor and AP student at Loma Linda Academy and will be entering my senior year this upcoming fall. After I graduate, I hope to attend the University of California, Davis, with a major in biochemistry and a minor in management. My long-term goals include earning a DDS/PhD and moving to New York where I will open my own practice in oral surgery to serve underprivileged communities.

Music has also been a passion of mine, and I have pursued it rigorously. At the age of six, I began taking violin lessons and gone on to play semi-professionally. I consider myself an accomplished musician, touring in New York, Pennsylvania, and Hawaii as principle viola in the Loma Linda Academy Symphony Orchestra. In my spare time, I enjoy watching films and collaborating with friends to make music as I also play guitar, ukulele, bass, and do vocals. As a soloist, I perform in churches, nursing homes, and concerts, hoping to inspire younger musicians. It is my belief that music and medicine work together toward healing the whole person.

Understanding my privileged upbringing and recognizing that not everyone has the resources I have had, I maintain a keen interest in giving back to my community. As part of this effort, I feed the homeless, make blankets for cancer patients along with my grandmother, and volunteer to help with Vacation Bible School programs at multiple churches.

My mentor, Dr. Salma Khan, and grad student partner, Eunice Nyasani, were tremendously helpful and inspired me every day. I am eternally grateful to have had this opportunity, and I believe it will continue to impact me as I continue my work in the field of dentistry.

## DIFFERENTIAL EXPRESSIONS OF C-SRC AND α-6 INTEGRIN IN WELL DIFFERENTIATED TO POORLY DIFFERENTIATED THYROID CANCER

Maya Townsend, Eunice Nyasani, Mia Perez, Nicole Mavingire, Ethan Frank, Suneetha Chintalapati, Yan Chen Wongworawat, Iqbal Munir, Anthony Firek, Salma Khan

Center for Health Disparities and Molecular Medicine, School of Medicine, Loma Linda University, Loma Linda, CA

Thyroid cancer is categorized into different entities: well-differentiated thyroid cancer (WDTC), poorly differentiated thyroid cancer (PDTC), and anaplastic thyroid cancer (ATC). WDTC includes follicular, papillary, and medullary thyroid cancer, whose characteristics are clearly noted with good prognosis. PDTC has a worse prognosis because the cancer cells grow and metastasize faster than WDTC cells. PDTC is also connected to a higher risk of recurrence. ATC presents the worst prognosis. Patients usually die within 6 months after diagnosis. This creates a need to find genes to cure PDTC/ATC. One of the targets is c-SRC because it is expressed in many cancer types, including thyroid cancer. C-SRC is a cytoplasmic non-receptor protein kinase-encoding gene responsible for cell proliferation, survival, motility, migration, cytoskeleton regulation, and oncogenesis by mediating downstream signaling pathways. Atypical amounts of SRC are associated with thyroid cancer aggression. SRC is activated by a series of signaling cascades like integrins. Integrins are proteins that join the cytoskeleton of a cell to the extracellular matrix. Alpha-6, an integrin designed for epithelial tissue, uses the SRC signaling pathway to stimulate invasion expression. The purpose of our experiment was to examine whether SRC/alpha-6 are differentially expressed in WDTC and PDTC/ATC by immunohistochemistry. This process included mounting tissue onto slides, deparaffinization, rehydration, antigen retrieval, antibody staining, hematoxylin counterstaining, dehydrating, stabilizing, and viewing the results with a microscope. Our results showed a higher expression of c-SRC in all subtypes of thyroid cancers. The strongest expression was observed with a6 integrin in PDTC and ATC compared to WDTC. This data showed that c-SRC expression along with a6 integrin can be used as prognostic markers for aggressive phenotypes of thyroid cancer. These can be targeted as future therapeutic strategies once we establish the interactions and signaling pathways of these oncoproteins.

# JENNIFER TRAN

## ABC PARTICIPANT 2018

I am an upcoming senior at Middle College High School and San Bernardino Valley College. Currently, I have over 40 college credits, and I plan on working towards an Associate's degree. I am planning on going to University of California, Los Angeles, for undergraduate and Loma Linda University for my graduate work in a biomedical major. I also want to work on my MD/PhD as I progress in graduate school.

What has inspired me to be in this internship is by volunteering at Totally Kids Rehabilitation Hospital. In this program, we interact with residents who are medically fragile and technologically dependent and give them the opportunity to engage with students that are similar in age to each other. I have been doing this community service since the fifth grade every summer until the end of last year; it took six summers for me to decide where I wanted to be today. As for myself, I love to draw using my artistic and creative side during my free time and as a stress reliever.

During this internship, I have been fortunate to work with Dr. Daisy De Leon in the breast cancer research lab. For my project, I worked with Qianwei Tan to research the clinical treatments by using pharmaceutical medicine to see what effects it has on breast cancer cells.

I am truly blessed to work under Dr. Daisy De Leon and my mentors Qianwei Tan, Xousaen Helu, and Vinodh Radhakrishnan for showing me the ways and the passion they have for research. I am fortunate to be in this internship, and I will hopefully continue this amazing experience and use it towards my future career.

# TREATMENT WITH IGF-II ANTIBODY INCREASES INTRACELLULAR IGF-II IN MDA-231 AND CRL 2335

Jennifer Tran, Qianwei Tan, Daisy D. De Leon

Center for Health Disparities and Molecular Medicine, School of Medicine, Loma Linda University, Loma Linda

Breast cancer (BC) is the most common malignancy observed in women from different ethnic groups. Previous studies demonstrated young African American (AA) women have a lower incidence of breast cancer but a higher mortality rate compared to Caucasians. Our research team has successfully identified IGF-II as an important biological factor contributing to higher breast cancer mortality among AA women. We showed that higher levels of IGF-II combined with higher INSR-A results in increased signaling which may contribute to higher breast density, more aggressive and rapid breast cancer progression, insulin resistance, and, possibly, type-2 diabetes. We also demonstrate there was a lower IGF-IIR expression in cells and "bioavailable IGF-II" and impaired glucose uptake contributing to increased important risk factors for AA women affected with breast cancer. This study was designed to determine the effect of using an IGF-II antibody to block antibodies that promote cell death. We used triple negative cell-lines, the MDA-231 cells obtained from a Caucasian woman and the CRL-2335 cell line obtained from an African American woman. We used real time QPCR and confocal microscopy to analyze the effect of the IGF-II blocking antibody in the mitochondria, nucleus, and cell morphology. We used real time QPCR to measure the changes of the IGF-II mRNA levels in control and in treated breast cancer cells. The CRL-2335 cells were more aggressive and proliferated even in the presence of the IGF-II antibody. In contrast, MDA-231 cells were dying after 24 hours of the antibody treatment. Changes in IGF-II regulated the shape of the mitochondria, cell morphology, and the nucleus. Treatment with the IGF-II antibody also increased IGF-II mRNA. Our results suggest decreased levels of extracellular IGF-II activate the intracellular production of this mitogen, possibly as a stress response. Since IGf-II prevents apoptosis, it's possible the stress response is a mechanism for cell survival and may explain the discouraging results of blocking antibodies in clinical trials.

# WILLIAM WANG

## ABC PARTICIPANT 2018

Ever since I was young, I have always been an avid learner of the sciences. When I was little, I would often dream about what the future would bring. For me, growing up in an Asian household, that was a future in medicine. Many people have stereotypes of Asians forced to be doctors and scientists, but my passion was with medicine. Ever since I received my first book on physics and biology, I was obsessed with learning more.

This obsession has culminated in the search for the ABC program. When I applied, I wanted hands-on lab experience to learn more about my desired field, and I was not disappointed. Following an intensive interview process, which only selected 15 members, I was introduced to a laboratory setting. This setting came as one of the best experiences of my life.

I have been working with my mentor, Dr. Kimberly Payne, and have done research on leukemia cells. My experiences have also been enhanced by my supervisors, Mavely Baez, Jacqueline Coats, Cornelia Stoian, and Xianmei Meng. Without these people, I could not have had the experiences I have had in the laboratory up until now.

# CHARACTERIZATION OF THE IL-7Rα RECEPTOR COMPONENT IN STANDARD-RISK AND HIGH-RISK B-ALL CELLS

William Wang, Jacqueline S. Coats, Cornelia Stoian, Hossam Alkashgari, Ineavely Baez, Kimberly Payne

Center for Health Disparities and Molecular Medicine, Division of Anatomy, School of Medicine, Loma Linda University, Loma Linda, CA

Leukemia is one of the deadliest cancers in the United States, claiming over 100,000 lives, and accounts for 26% of cancer cases in children under the age of 20 (Chan, 2010; Brown et. al 2018). More kids die of B-ALL than any other malignancy, and fewer than 1 in 3 kids with high-risk B-ALL survive. IL-7Rα is component of cell surface receptor complexes that have important roles in the JAK/STAT signaling pathway, which regulates cell division. Because leukemia is a proliferative disorder, it is important to understand what conditions alter IL-7Rα expression and potentially leukemia cell proliferation. Understanding these conditions can help develop target leukemia therapies against the JAK/STAT signaling pathway. We designed this study to evaluate IL-7Rα cell surface expression in high-risk CRLF2 and standard-risk B-ALL cells after incubation with the cytokines TSLP and IL-7, respectively. We cultured two standard-risk B-ALL cell lines with IL-7 for 24h and the CRLF2 B-ALL cell line with TSLP for 24 hrs. We then used immunophenotyping and flow cytometry to quantify the relative amounts of the IL-7Rα receptor component using the MFI (median fluorescence intensity) of the CD127 antibody. Flow cytometry data was collected on a MACSQuant Analyzer 8, analyzed in FlowJo 9.9.4 with statistical analyses done in Prism 7.0.a. We quantified the intensity of MFIs for cells and compared the treatment to the control groups. If IL-7Rα receptor expression is lower in the cytokine conditions, then the cancer cells will likely have reduced activation of the JAK/STAT pathway. As a result, we would expect reduced proliferation of the B-ALL cancer cells. Our next experiments will determine whether JAK/STAT signaling is shut down following the loss of IL-7Rα receptor expression.

# VIVIANNA WILLIAMS

## ABC PARTICIPANT 2018

I have been exposed to science since I was a little girl. Both of my grandparents are scientists, and my uncle is also a scientist. Naturally, I followed in their footsteps and discovered my own passion for science. Being accepted into the ABC program this summer has not only given me the opportunity to partake in what I love, but it also has given me the chance to expand my knowledge about the world around me.

I just completed my junior year at Loma Linda Academy, and I will be starting my senior year in August. Throughout my high school career, I have consistently played three sports, my favorite being either football or basketball. During lunch I participate in various clubs, my favorites being Friends Next Door Bible Club and Youth to Youth. As I neared the end of my junior year, many of my friends began to feel the pressure of school, so I aided them by offering free tutoring lessons. In the future, I hope to complete medical school and fulfill my dream of becoming an orthopedic surgeon. It is there I hope I can make a difference in the world, whether it is big or small.

I want to thank Dr. Carlos Casiano for trusting me to work in his lab as well as my mentor Evelyn Sanchez who taught me all I needed to know about the family of this lab. Together, I know that they brought me to my full potential in the lab this summer.

# OPTIMIZATION OF IMMUNOFLUORESCENCE MICROSCOPY STAINING OF GLUCOCORTICOID RECEPTOR IN PROSTATE CANCER CELL LINES

Vivianna Williams, Hannah Sukarloo, Evelyn Sanchez-Hernandez, Shannalee Martinez, Leanne Woods-Burnham, Carlos Casiano

Center for Health Disparities and Molecular Medicine, School of Medicine, Loma Linda University, Loma Linda, CA

Androgen deprivation therapy (ADT) and chemotherapy are standard-of-care treatments for advanced prostate cancer (PCa). However, resistance to these therapies occurs, and the underlying mechanisms are not completely understood. Synthetic glucocorticoids (GC) such as dexamethasone are administered to PCa patients to alleviate the side effects of chemotherapy. GCs exert their action by binding to the glucocorticoid receptor (GR) in the cytoplasm, leading to GR translocation into the nucleus where it activates gene expression. However, use of GCs in PCa therapy is currently being re-evaluated because GR has been shown to bypass androgen receptor (AR) blockade by ADT and enable activation of cancer-associated AR-targeted genes. African American (AA) patients with PCa are more likely to develop a more aggressive form of PCa and twice as likely to die from this malignancy than European American (EA) men. Also, AA men have higher circulating cortisol levels (endogenous GC) and increased GR sensitivity for GCs. These observations led to the hypothesis that enhanced GR signaling in AA men with PCa may prime them to develop increased resistance to therapy. As a first step in assessing GR protein expression in prostate tumor tissues from EA and AA men, it is necessary to optimize conditions to detect GR in PCa cells by immunofluorescence microscopy staining. We demonstrated that commercially acquired anti-GR antibodies react specifically with this protein in immunoblots of total protein from the PC3 and 22RV1 PCa cells. We have been optimizing immunofluorescence staining conditions to detect GR translocation to the nucleus of these cells upon dexamethasone treatment. We expect to observe GR immunofluorescence staining in the cytoplasm of untreated cells and nuclear staining in dexamethasone-treated cells. This optimization allows us to identify the proper anti-GR antibodies and conditions to assess GR expression in prostate tissue arrays from AA and EA PCa patients critical to understanding the role of GR signaling in PCa health disparities.

# Undergraduate Training Program (UTP)

Victor Campbell
Christine Castañón
Amy-Claire Dauphin
Shekinah Dosunmu
Karen Figueroa
Joshua Guerra
Isaac Kafeero
Annie Moretta
Krystal Santiago
Hannah Sukarloo
Alexis Townsend

# VICTOR CAMPBELL

## UTP PARTICIPANT 2018

As a biology major going into my junior year at Oakwood University in Huntsville, AL, I am anxiously awaiting the start of the school year so I can continue working with my research mentor Dr. Richardson. However, in my earlier years as a student, I wasn't interested in research. It was always a forced activity and never felt important. The clinical side of medicine was where my heart was. I wanted to become a neurosurgeon or cardiovascular surgeon and open my own practice in Liberia, Africa.

Things changed my sophomore year when I took microbiology. Dr. Vanterpool is one of the best instructors I've had. She designed the lab to be about the research she is doing personally, and I was able to experience real research that was enjoyable and felt important. Through this lab, I gained experience and a passion for research. I applied for the research program on campus, IMARI, and thus found out about Loma Linda University's Undergraduate Training Program (UTP).

Now officially being here, I see the importance of research. It starts with the question "WHY," and from then on the possibilities for discoveries that lead to saving lives are endless. This program has expanded my knowledge of science and human cells. Dr. Mary Kearns-Jonker has been a helpful and patient teacher helping me understand stem cells. My lab partners Larry, Pedro, Victor, Aaron, and Cole have been diligent in teaching the skills needed to work in this lab. Thanks to this program, I expect much more from the medical world and from myself. With hard work and meaningful research, we can change the world for the better.

Thank you, Loma Linda University UTP, for giving me this wonderful opportunity and thank you, Oakwood University, for teaching me and expecting greatness.

# EARLY-STAGE ISLET-1+ CARDIOVASCULAR PROGENITOR CELLS ISOLATED FROM THE HUMAN HEART EXPRESS CD56

Victor Campbell, Victor Camberos, Pedro Medina, Leonard Bailey, Nahidh Hasaniya, Mary Kearns-Jonker

Department of Pathology and Human Anatomy and Department of Cardiovascular and Thoracic Surgery, School of Medicine, Loma Linda University, Loma Linda, CA

Stem cells introduced for myocardial repair in clinical trials performed to date have the ability to facilitate cardiovascular repair but have limited ability to regenerate damaged tissue. In order to improve the outcome of these trials, retention of transplanted progenitors with the ability to differentiate *in vivo* into all cells of the cardiovascular lineage would be beneficial. Human embryonic stem cell-derived cardiovascular progenitor cells in the earliest stage of mesoderm commitment express CD56. The objective of this project was to address the hypothesis that early, clonal islet-1+ cardiovascular progenitor cells isolated from human patient-derived cardiac tissue express CD56. Using flow cytometry, we identified CD56 on neonatal cardiovascular stem cell clones. In order to determine whether islet-1+ CD56+ early stage cardiovascular progenitor cells express immunomodulatory factors that could enhance cell retention, we used PCR to demonstrate that indoleamine, a factor that promotes allogeneic cell survival, is expressed in these progenitors. The significance of this new data is that islet-1+ cells co-expressing CD56 isolated at the earliest stage of cardiovascular commitment may be promising as progenitors for cardiac repair and have the potential to be protected from immune rejection due to the expression of indoleamine.

# CHRISTINE PADILLA CASTAÑÓN

UTP PARTICIPANT 2018

Jeremiah 29:11 reads "'For I know the plans I have for you,' declares the Lord, 'plans to prosper you and not to harm you, plans to give you hope and a future.'" The Lord has surely provided for me beyond what I could ever imagine.

I am beginning my third year as an undergraduate student at UCLA to earn a degree in psychobiology with a minor in disability studies. At UCLA, I am actively involved at the University Catholic Center where I have been able to learn and grow in my faith and lead others in doing the same. Currently, I volunteer as a clinical medical Spanish interpreter and work in an autism research lab. Additionally, I teach ballet at a local middle school to help promote the importance of the performing arts within underfunded public education. After completing my undergraduate degree, I hope to attend medical school and become a physician working with patients that face health disparities and live in medically underserved areas. I also aspire to better provide healthcare to undocumented, non-English speaking patients.

I have been fortunate to participate in the ABC Program and Undergraduate Training Program for three summers. During this time, I have worked in Dr. Julia Unternaehrer's ovarian cancer research lab. This summer my research focused on using nanoparticles to target SNAIL in ovarian cancer cell lines and inhibit the epithelial-mesenchymal transition (EMT) pathway to prevent metastasis and increase tumor chemosensitivity.

Dr. Unternaehrer and my mentor, Evgeny Chirshev, have been beyond patient with me. No words explain how grateful I am for the time they have invested in my education and future. Their constant motivation and support have allowed me to grow as a student, researcher, and overall person.

## TARGETING CELL-SPECIFIC RECEPTORS TO DELIVER SISNAIL USING MESOPOROUS SILICA NANOPARTICLES

Christine Castañón, Evgeny Chirshev, Hanmin Wang, Ruining Wang, Carlotta Glackin, Yevgeniya Ioffe, Julia Unternaehrer

Center for Health Disparities and Molecular Medicine, Department of Biochemistry, School of Medicine, Loma Linda University, Loma Linda, CA

Targeting cell-specific receptors, this study aims to determine a method for delivery of siSnail to ovarian cancer cells. Ovarian cancer is the most lethal gynecological cancer due to current, ineffective treatment options caused by recurrent malignant tumor growth with relapse commonly attributed to cancer stem cells (CSC) found within tumors. Expression of Snai1 (Snail), an epithelial-mesenchymal transition regulator, has been linked to the acquisition of stem cell-like phenotypes. We are investigating the role of Snail in ovarian cancer cells by using tagged mesoporous silica nanoparticles (MSN) to knock down Snail using Snail-siRNA (siSnail). Cells used for the experiment include Ovcar8 and five ovarian cancer patient samples. MSNs were biocoated for optimal siSnail delivery to targeted sites. Using hyaluronic-acid (HA-MSN) tagged and folic-acid (FA-MSN) tagged MSN, we targeted different receptors specific to each sample. HA is the ligand for CD44, a cell surface adhesion receptor expressed in cancer cells, and FA is the ligand for folate receptors, a receptor upregulated in many cancer cells but expressed at low levels in normal tissue. After treating Ovcar8 with HA-MSNs for 24 hours, we observed a 97% decrease in Snail expression; at 48 hours, a 92% decrease; and at 72 hours, an 87% decrease as determined by RT-qPCR. We intend on running a Western blot to determine protein expression and conduct a wound healing assay with HA-MSN-siSnail treated Ovcar8 cells for migratory ability analysis. Additionally, we aim to treat patient samples with specifically targeted MSNs. We are now characterizing our patient samples with RT-qPCR for expression of the targeted receptors: CD44, folate receptor, and/or other receptor. We conclude MSNs successfully deliver siRNA to knock down Snail in ovarian cancer cells and expect this approach will effectively deliver the RNA therapeutic to patient-derived tumors in xenografts. Our long-term aim is to use MSNs as potential precision medicine treatment for ovarian cancer patients.

# AMY-CLAIRE DAUPHIN

## UTP PARTICIPANT 2018

Born in Utah and raised in Massachusetts, I am a junior at Oakwood University, Huntsville, AL, where I study biological sciences under the advisement of Dr. Juliet Penrod in preparation for a medical and research career. Prior to Oakwood, I attended Brandeis University in the Boston, MA, area.

As a holder of three Martin Luther King Jr. awards, I am committed to the welfare of the poor and marginalized with emphasis on medical research that informs evidence-based advocacy for health policy changes. Accordingly, while at Brandeis University, I helped manage the *Waltham Group*, a student organization that provides supplemental biological sciences education to underprivileged high school students. I also served as the minority representative on the Fund Allocations board, managing a $1.2 million budget in support of student organization activities. As a participant of Global Medical Brigades, I volunteered in Honduras in 2017, sensitizing rural communities on water, hygiene, and sanitation practices; on malaria and diabetes prevention; and contributing to building sanitation facilities alongside the local beneficiaries. At Oakwood, I serve as the Media Manager on the Oakwood Biomedical Association board.

Mentored by Ms. Alexia Ximinies, a PhD candidate in microbiology, I contributed to research aiming at characterizing the hypothetical protein PG0686 of *Porphyromonas gingivalis*. *P. gingivalis*, one of the causative agents of adult periodontitis, is a keystone pathogen of high virulence associated with other systemic diseases.

I am grateful for the patient teaching provided by Ms. Ximinies, my UTP mentor, and Dr Hansel Fletcher, the lead researcher, and for the outstanding research facilities and accommodation provided by LLU. I want to credit the CHDMM and Oakwood University for this research opportunity and for a sharper focus on a life of service to God and humankind.

# CHARACTERIZING THE ROLE OF HYPOTHETICAL PROTEIN, PG0686 IN *PORPHYROMONAS GINGIVALIS'* RESPONSE TO ENIRONMENTAL STRESS

Amy-Claire Dauphin, Alexia D. Ximinies, Hansel M. Fletcher

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*Porphyromonas gingivalis,* a black-pigmented, Gram-negative anaerobe is an important causative agent of adult periodontitis and associated with other systemic diseases. As a keystone pathogen, it subverts the host's immune system and can survive the harsh inflammatory environment of the periodontal pocket. The specific survival mechanisms employed by this pathogenic bacterium remain unknown, yet transcriptome analysis has identified the PG0686 gene as an important candidate in oxidative stress resistance. Our hypothesis is that PG0686 interacts directly with ROS and functions to protect *P. gingivalis* from multiple types of environmental stress. PG0686 was shown to be induced in *P. gingivalis* under $H_2O_2$- (7-fold), NO- (2-fold), and $O_2$-stress (4-fold). To determine sensitivity to NaClO stress, *P. gingivalis* strains W83 (wild-type), FLL361(PG0686::ermF), C361'(FLL361 containing pT-COW/PG0686 plasmid) were grown to O.D. 0.2 and exposed to 10mM NaClO; culture growth was monitored over a 24 hour period to determine the sensitivity of each strain. Gingipain activity assays were performed by incubating *P. gingivalis* cultures with BAPNA and ALNA, substrates of arginine (Rgp) and lysine-specific (Kgp) cysteine proteases, respectively. PG0686 bioinformatics identified 3 domains, including a hemerythrin domain, and the overexpressed and purified rPG0686 protein underwent UV-vis spectroscopy to observe the oxy and deoxy forms of hemerythrin present. When exposed to NaClO, W83 and FLL361 strains showed similar sensitivity while C361' was significantly more sensitive. Our work examined how PG0686 affects the virulence potential of *P. gingivalis*. In FLL361, Rgp activity was reduced by 40% at log and stationary phases while Kgp activity was reduced by 40% and 70% in log and stationary phases, respectively. The uv-vis spectra was similar to previously characterized hemerythrin proteins, suggesting the presence of the putative hemerythrin domain. Taken together, the data suggest PG0686 possesses a hemerythrin domain, which may contribute to its function in the oxidative stress response and influence the virulence in *P. gingivalis*.

# SHEKINAH DOSUNMU

## UTP Participant 2018

I have spent a large portion of my life in Michigan so when I received my acceptance letter for the UTP program here at Loma Linda University, I was humbled and overjoyed at the chance to spend my summer in California. I am currently studying biology at Andrews University, a small Christian university in southwestern Michigan. My future goals are to pursue an MD or an MD/PhD degree and to eventually become a missionary.

As an undergraduate student, I have been given many opportunities to serve my community and my local church. I have served as a Resident Assistant (RA) for the past two academic school years in the ladies' dormitory on campus. The diversity of Andrews University campus has exposed me to individuals who come from different cultures and backgrounds, and I believe the lessons that I personally have learned as an RA will equip me efficiently to work in the mission field in the future.

The research I am working on this summer is related to the role that copper plays in the onset of Alzheimer's disease. I have also been spending time working on isolating and culturing human endothelial cells.

This summer I have had the opportunity to work under the mentorship of Dr. Wolf Kirsh and Dr. Ying Nie. I would like to thank Dr. Nie and Dr. Kirsh's lab for helping me to develop stronger research skills and for aiding me in the development of my research project.

# VALIDATING SYNAPTIC VESSICLE ISOLATION PROTOCOLS TO DETERMINE COPPER DISREGULATION IN ALZEIHMER DISEASE

Shekinah Dosunmu, Nicholas Sanchez, Wolff M. Kirsch

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Alzheimer's disease (AD) is a neurodegenerative disease that affects those around the age of sixty-five or older. Previous work indicates that the brains of AD patients without cerebral amyloid angiopathy (CAA) contain a smaller measurement of copper in the neuronal synapses than someone without the disease. Currently, there is a gap in the literature concerning copper transport and its relation to AD. The purpose of this study is to further investigate copper dysregulation in the Alzheimer's brain. Synaptic vesicles were isolated utilizing a procedure adapted from previous studies conducted by Kamat et al. Frozen human brain samples were homogenized using sucrose-HEPES buffer and a series of progressive centrifugations to localize the synaptic vesicles in the supernatant. These samples were serially diluted to 1:100,000 and analyzed via MP-AES to determine the concentrations of copper in each sample. A Western blot of the synaptic vesicles was run to determine if the vesicles had been properly isolated. Protein determination was completed using a Bradford assay and a Pierce BCA assay. Preliminary results indicate there is a lower amount of copper in the synaptic vesicle sample of the Alzheimer's brain than that of the control. However, concrete conclusions about the differences in the copper concentrations of synapses in an Alzheimer's brain cannot be made. Future plans are to further modify the synaptic vesicle isolation procedure and compare it to previous procedures to determine the most efficient method.

# KAREN FIGUEROA

## UTP PARTICIPANT 2018

I graduated from Ramona High School in Riverside, CA, in 2013 and then attended the University of California, Los Angeles, where I obtained my BS in Biology. This is my seventh summer participating in research at Loma Linda University. In 2011, I stepped on LLU's campus for the first time as an ABC participant, knowing close to nothing about research; however, after eight intensive weeks, I left with the desire of someday obtaining an MD and conducting research as a physician.

I am grateful for the education I received at UCLA. I had the opportunity to learn about numerous subjects, experience different cultures, and meet people. As an undergraduate, I traveled to the Dominican Republic and provided medical services alongside local physicians to communities with no access to health care. I also volunteered in numerous health fairs as a Spanish translator which allowed me to serve my Latino community. As a Gates Millennium Scholar, I have felt the need to give back not only to my community but to the children who are part of underserved populations. As a scholar, I have become a mentor and tutor to many, including homeless youths, in the LA area. I strive to help others live healthy and prosperous lives.

Over the past few years I have had the privilege of working within Dr. Marino De Leon's lab. I am thankful for the supervision I have received from Dr. Magda Descorbeth and the guidance that my colleagues have given me.

# DOCOSAHEXAENOIC ACID (DHA) DECREASES PALMITIC ACID-INDUCED LIPOTOXICITY IN PRIMARY SCHWANN CELLS: ROLE OF PI3K/MTORC2/AKT

Karen Figueroa, Magda Descorbeth, Marino De Leon

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Saturated fatty acids overload like palmitic acid (PA) leads to lipotoxicity and cell death in non-adipose cells including neurons and Schwann cells (SC). Polyunsaturated fatty acids such as Docosahexaenoic acid (DHA) often show beneficial effects on tissues. We previously showed PA induced SC death, and co-treatment with DHA inhibited the loss of cell viability and apoptosis. In this study we investigated the potential role of PI3K/AKT and mTOR pathways in the protective effect of DHA on SC undergoing palmitic acid-induced lipotoxicity (PA-LTx). Primary SC were treated with PA:BSA (300 µM: 150 µM) in absence or presence of DHA (50 µM). Protein expression was determined by Western blot, and cell viability examined using crystal violet. We found PA induced a decrease in AKT-Ser473 and AKT-Thr308 phosphorylation. However, in the presence of DHA, the p-AKT levels were restored to the control level, suggesting that DHA regulates AKT phosphorylation. Next, we examined by crystal violet the effect of PI3K inhibitors LY294002 and BKM120 in DHA protection on SC undergoing PA-LTx. We found PA decreased cell viability while co-treatment with DHA increased cell viability. However, the presence of LY294002 and BKM120 diminished the protective effect of DHA under PA-LTx suggesting the involvement of the PI3K/AKT pathway. It is known that mTORC2 regulates p-AKT at the Ser site. In order to study its implication in the protective effect of DHA, cells were treated with Torin 1, an mTORC1/mTORC2 inhibitor and Rapamycin an mTORC1 inhibitor. Torin 1 decreased the protective effect of DHA but not Rapamycin suggesting the implication of mTORC2 in DHA protection of SC undergoing PA-LTx. Furthermore, treatment of the cells with Torin 1 under PA/DHA condition decreased phosphorylation of AKT-Ser473 but not AKT-Thr308 while Rapamycin had no effect on p-AKT levels under these conditions. In conclusion, our results suggest that DHA protects SC against PA-LTx by modulating p-AKT through PI3K and mTORC2.

# JOSHUA GUERRA

## UTP PARTICIPANT 2018

When I was younger, I viewed research as just something successful people at my high school joined in on. It wasn't until I pursued research myself that I realized its tremendous value. My high school senior year I researched with Dr. Sunil Ahuja on an immunogenetic project. During this time, we investigated single nucleotide polymorphisms within genes that code for immune cell receptors related to HIV pathogenesis. From this experience I grew a passion and thirst for knowledge in the realm of biomedical research.

I am now entering my third year at the University of Texas at San Antonio where I study both public health and sociology with a minor in biology. At UTSA this past year I successfully completed my Honors Thesis which addressed the stigmas seen among treatment workers within addiction medicine as we tackled treatment stigmas and disparities within the opioid crisis. This paper, now co-authored with Dr. Erin Madden, has been accepted by the 2018 Society for the Study of Social Problems Annual Meeting for their "Critical Dialogue: Harm Reduction" session. My future plans entail becoming a researching physician with a possible focus on epigenetic or epidemiological research. In addition to research, I work towards expanding opportunities for students within the Honors College at UTSA through my leadership role as we redesign the Honors curriculum.

I would like to extend my gratitude and thanks to Dr. William Langridge and Mary Beth Yu for their mentorship in a new realm of science and allowing me to work in their lab this summer. This experience has allowed me to grow as a student and future researcher.

# THE ROLE OF EXTRACELLULAR VIMENTIN IN HUMAN DENDRITIC CELL ACTIVATION

Joshua Guerra, Mary Beth Yu, William Langridge

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Vimentin is an intermediate filament protein that anchors the position of the organelles in the cytosol, allowing flexibility and integrity within the cell. While intracellular vimentin has a well-known structural function, the role of extracellular vimentin in conditions such as cancer and necrosis have not been widely studied. Previous studies have shown that vimentin plays a role in the innate immune system by affecting neutrophils, monocytes, and macrophages. This study aimed at understanding the role of extracellular vimentin in dendritic cell activation using polyinosinic-polycytidylic acid (poly I:C), an immunostimulant used to simulate viral infections. Poly (I:C), structurally similar to double-stranded RNA, is present in a number of viruses and was used to mimic viral infections that cause tissue damage where extracellular vimentin is often released. Previous literature has shown that poly (I:C) generally increases DC expression of CD86, a costimulatory factor for T cell activation. In this study, poly (I:C) was combined with vimentin and cultured with DCs. This experiment showed a decrease in poly (I:C)-induced expression of CD86 as assessed by flow cytometry. In another experiment, DC secretion of anti-inflammatory IL-10 and pro-inflammatory IL-12 cytokine secretion was also measured. Cytokine analysis by enzyme-linked immunosorbent assay (ELISA) showed an increase in IL-10 secretion when immature DCs were cultured with poly (I:C). However, when DCs were cultured with vimentin + poly (I:C), no change in IL-10 secretion was observed in comparison with the controls. Under both culture conditions, IL-12 was undetectable in the majority of independently repeated experiments. Based on our experimental data, vimentin + poly (I:C) was shown to cause a greater reduction in the immunostimulatory response than poly (I:C) alone, suggesting vimentin may play a role in preventing autoimmunity, hindering the immune response to viral infection, and inhibiting effective immune responses against cancer.

# ISAAC KAFEERO

## UTP PARTICIPANT 2018

I am a junior biology major at Oakwood University located in Huntsville, AL. As an aspiring medical scientist, I have been an active member of the biology department, serving in the capacities of lab assistant, teaching assistant, and, most recently, Public Relations Coordinator of the Oakwood Biomedical Association. I also serve in the Huntsville community as a volunteer at the local rescue mission.

Being a part of the UTP program this summer has helped me appreciate the research environment on top of making the most of the sunny southern California weather. Being a member of Dr. Sean Wilson's lab has given me the opportunity to not only gain valuable research skills but also expand my knowledge of cardiovascular physiology and disease. I am now further intrigued and motivated to continue undergraduate research in this field and will highly consider specializing in this area of the body in my graduate studies.

Whether my aspirations lead me back to the southside of Chicago or as far as central Uganda, I wish for my past and future experiences to translate into something beneficial to the field of science, especially to alleviate the health disparities among underserved populations.

# CHRONIC HYPOXIA HIGH ALTITUDE STRESS AFFECTS ANTIOXIDANT LEVELS IN SHEEP PULMONARY ARTERIES

Isaac Kafeero, Rafael Alvarez, Remy Bosviel, Michael La Frano, John Newman, Oliver Fiehn, Sean M. Wilson

Center for Health Disparities and Molecular Medicine, Department of Perinatal Biology, School of Medicine, Loma Linda University, Loma Linda, CA

Gestational Hypoxia is a common prenatal stress caused by high altitude living, smoking, and other prenatal disorders. It is associated with poor cognitive development and fetal growth restriction which puts newborns at an increased risk of developing pulmonary hypertension, respiratory distress, infant mortality, and cardiovascular diseases later in life. This work aims to determine how chronic high-altitude hypoxia alters primary metabolite profiles and provides mechanistic insight of this stressor on pulmonary vascular development and function. For this study, normoxic pregnant and non-pregnant sheep were obtained from Nebeker Ranch in Lancaster, CA, and were either sent to Loma Linda for study or sent to White Mountain Research Station at an altitude of 3800 meters to induce long-term high-altitude hypoxia (LTH). After 110+ days of gestation, sheep were transported to Loma Linda for study. Tissues from the pulmonary arteries of adult, newborn, and fetal sheep were prepared and frozen for analysis of primary metabolites. Our results revealed a metabolic pathway with several metabolites and intermediates acting as antioxidants, playing key roles in pulmonary vascular development and function through regulating Reactive Oxygen Species (ROS) and other prooxidants. Glutathione (GSH) works synergistically with ascorbic acid to detoxify Hydrogen Peroxide, an ROS produced as a waste product of metabolism. It also regulates the Nitric Oxide cycle, of which NO is an important signaling molecule in endothelium-dependent vasodilation. N-acetylcysteine (NAC), a GSH precursor and potent ROS scavenger, induces HIF-1α which promotes angiogenesis by inducing Vascular Endothelial Growth Factor (VEGF). Ascorbic acid and NAC inhibit Endothelin-1 induced ROS-dependent activation of MAP kinases in vascular smooth muscle cells. This study suggests that antioxidant levels decrease under LTH and are potential indicators of this prenatal stressor.

# ANNIE MORETTA

## UTP PARTICIPANT 2018

Research has always held a special place in my heart, especially most recently as our family has experienced first-hand the other side of the work of researchers. My mother was recently diagnosed with a rare type of liver cancer, placing her in clinical trials, exams, and biopsies. We were faced with what seemed like a million questions and uncertainty about the future, and I realized there are families all around the world asking the same questions. I want to be able to answer these questions, and cancer research has amazing potential to do so.

I am currently a student at Andrews University in Michigan, studying biology and music. The mind and the body fascinate and inspire me to study the intricacies of physiology meeting consciousness and how we are truly and wonderfully made. In the future, I hope to enroll in the MD program at LLU and integrate research into my training. I hope to be able to serve underprivileged communities here in the United States and abroad as a medical missionary.

This last year I had the privilege to serve in a few free clinics specializing in an incredible degree of dental and medical care. I had the opportunity to meet several families who were in need as a result of uncontrollable circumstances, and I want to be able to not only provide medical care but also show families and individuals the kindness and love of Jesus. Wherever God continues to lead in my life, I know that there are people in need, and that is where I need to be.

I want to truly thank Dr. Saied Mirshahidi for patiently working with me and giving me the opportunity to learn and be challenged in this research program.

# EFFECTS OF INDOMETHACIN INDUCED APOPTOSIS IN HUMAN OSTEOSARCOMA CRL-1547 TUMOR CELLS

Annie Moretta, Lee M. Zuckerman, Mark E. Reeves, Saied Mirshahidi

Department of Basic Sciences and Biospecimen Laboratory, Cancer Center, Center for Health Disparities and Molecular Medicine, Department of Orthopedic Surgery, Division of Surgical Oncology, Loma Linda University, Loma Linda CA

Osteosarcoma (OS) is the most common malignant bone tumor in children and teenagers. Unfortunately, 25-30% of OS patients presented with metastatic disease have a 5-year event free survival (EFS) rate of less than 20%. Nonsteroidal anti-inflammatory drugs (NSAIDs), widely used in orthopedic surgery to reduce pain and inflammation, have also been shown to be toxic to certain malignancies including colorectal, breast, and pancreatic cancers. The aim of this study was to assess whether indomethacin, a nonselective cyclooxygenase (COX) inhibitor and NSAID, could induce apoptosis in human osteosarcoma cells and to explore the underlying mechanism. Human osteosarcoma cell line (CRL-1547) was treated with various concentrations of indomethacin. Cell viability, apoptosis induction, surface expression of PD-L1, and the expression of apoptosis-related proteins were examined by MTT assay, flow cytometry, and Western blot, respectively. The results indicated that indomethacin significantly decreased viability and induced apoptosis of OS cells in a dose-dependent manner. Apoptosis was confirmed by cell morphology and Annexin V+ cells. Molecular data showed indomethacin could significantly downregulate the expression of anti-apoptotic proteins such as Bcl-2, survivin and pro-caspase-3, PARP, and upregulate the expression of both cleaved caspase-3 and PARP as well as the Bax/Bcl-2 ratio. Overall, the results suggested the inhibitory effects of indomethacin on OS cells were correlated to cell apoptosis. In addition, we showed that indomethacin could downregulate the expression of PD-L1 on OS tumor cells, a ligand associated with not only progression but also poor prognosis of survival. Indomethacin treatment did not downregulate COX-2 which, when overexpressed, can be correlated with poor prognosis in several tumor lines. This finding indicated that the mechanism to decreased cell viability and increased apoptosis was COX-independent. These findings offer initial optimism that indomethacin can be used as neoadjuvant or an adjuvant treatment before and after tumor removal.

# KRYSTAL R. SANTIAGO

## UTP PARTICIPANT 2018

D'Angelo once said, "Develop a passion for education because if you do, you will never cease to grow." Aiming to achieve academic excellence with the help of God is one of my priorities. Thus, in 10th grade I decided to attend the Centro de Oportunidades Educativas de Mayaguez, a boarding school specializing in mathematics and sciences. There I was able to take advanced specialized classes as well as college credit courses. This fall I will be starting my third year as an undergraduate at the University of Puerto Rico at Mayaguez (UPRM) doing a BS in Industrial Microbiology. I hope to further my education by earning a PhD to fulfill my dream of being a researcher.

Throughout my middle school and high school years, I also attended an academy specializing in music and the arts during the evenings and learned to play the flute and trained my voice. I am now part of the Coral Universitaria, a choir representing the UPRM nationwide.

I believe my purpose in this world is to serve others, and I have exemplified this conviction in many ways. After Hurricane Maria, my friends and I helped rebuild houses and feed the homeless. I also volunteered as a nanny in a house for abused children. It is my duty to reflect God's image through my actions.

I want to thank Dr. Salma Khan for welcoming me into her lab and teaching me science related to cancer and Eunice Nyasani, Nicole Mavingire, and Amber Gonda for teaching me techniques used in the lab. I have been given the opportunity to have hands-on lab experience and understand the complexity of the miRNAs in different subtypes of thyroid cancer. This study will impact the thyroid cancer health disparities research field tremendously.

# DIFFERENTIAL EXPRESSION OF MICRORNA IN THYROID CANCER HEALTH DISPARITIES

Krystal R. Santiago, Eunice Nayasani, Hanmin Wang, Yan Chen Wongworawat, Mia C. Perez, Iqbal Munir, Salma Khan

Center for Health Disparities and Molecular Medicine, Department of Biochemistry, School of Medicine, Loma Linda University, Loma Linda, CA

Filipino Americans are known to have higher rates of thyroid cancer incidence and disease recurrence than European Americans. They are also known to be 2 times more likely to die of thyroid cancer. Thyroid cancer has been linked to multiple factors, one of them being acculturation stress-induced obesity. Studies have shown that Filipino immigrants have a higher obesity rate than Filipinos who were born in the US, which leads us to the hypothesis that acculturation stress-induced obesity increases microRNAs (miRNAs) that lead to the thyroid cancer health disparities. Acculturation stress increases obesity that can increase exogenous stress leading to endogenous stress and induces microRNA expression, which contributes to cancer development. When deregulated, miRNAs can function as tumor suppressant genes or as oncogenes. One of the miRNA families of let is let-7, which is a family of 13 genes located on 9 different chromosomes and is one of the most expressed miRNAs in normal thyroid glands. Therefore, the let-7 family carries an important role in thyroid development and functionality. In this study, we expect to see the expression of let-7 and use this gene as a diagnostic, prognostic and predictive biomarker in thyroid cancer. In order to study this, we used QIAGEN's DNA and miRNA extraction kits. Results from these extractions showed high quality and quantity DNA and miRNA obtained from paraffin-embedded thyroid tissues. We then proceeded to do miRNA qPCR assays to profile the let-7 miRNA expression. We found lower let-7 expression in Filipino American versus European American thyroid cancer tissues. In the future, we will do a miRNA-array analysis to distinguish miRNA profiles in Filipino Americans versus European Americans thyroid cancer tissues.

# HANNAH SUKARLOO

## UTP PARTICIPANT 2018

The great philosopher Plato once said, "Music is a more potent instrument for any other education." For me, this is physics. I grew up loving music. I played at every opportunity that I got: in orchestras, in band, and in churches. I thought there was nothing that I could love more than music until I discovered physics and bioengineering.

A couple years ago, I was watching an interesting documentary on Christian scientists. What caught my attention the most was a scientist who said, "The Earth was put in the exact place, so that we are able to make discoveries." God wanted us to make discoveries about the earth and about the incredible universe that He made. Both physics and engineering are about learning why and how things work, but they are about so much more than that. These sciences give us a glimpse into how God works. This is why I want to be an astrophysicist. Astrophysicists use physics and other sciences to discover the beauties of the world. Along with my interest in astrophysics, I would also like to do research in space medicine and bioengineering.

I am so grateful to have been given the opportunity to participate in the UTP program this summer, to learn more about other sciences, and for the invaluable research experience I have gained. I would like to thank Dr. Carlos A. Casiano for welcoming me into his lab and allowing me to learn more about biology and prostate cancer. I would also like to thank my mentors Evelyn Sanchez Hernandez and Greisha Ortiz Hernandez. Thank you so much for everything you have taught me and for all your kindness.

# OPTIMIZATION OF IMMUNOFLUORESCENCE MICROSCOPY STAINING OF GLUCOCORTICOID RECEPTOR IN PROSTATE CANCER CELL LINES

Hannah Sukarloo, Vivianna Williams, Evelyn Sanchez-Hernandez, Shannalee Martinez, Leanne Woods-Burnham, Carlos Casiano

Center for Health Disparities and Molecular Medicine, School of Medicine, Loma Linda University, Loma Linda, CA

Androgen deprivation therapy (ADT) and chemotherapy are standard-of-care treatments for advanced prostate cancer (PCa). However, resistance to these therapies occurs, and the underlying mechanisms are not completely understood. Synthetic glucocorticoids (GC) such as dexamethasone are administered to PCa patients to alleviate the side effects of chemotherapy. GCs exert their action by binding to the glucocorticoid receptor (GR) in the cytoplasm, leading to GR translocation into the nucleus where it activates gene expression. However, use of GCs in PCa therapy is currently being re-evaluated because GR has been shown to bypass androgen receptor (AR) blockade by ADT and enable activation of cancer-associated AR-targeted genes. African American (AA) patients with PCa are more likely to develop a more aggressive form of PCa and twice as likely to die from this malignancy than European American (EA) men. Also, AA men have higher circulating cortisol levels (endogenous GC) and increased GR sensitivity for GCs. These observations led to the hypothesis that enhanced GR signaling in AA men with PCa may prime them to develop increased resistance to therapy. As a first step in assessing GR protein expression in prostate tumor tissues from EA and AA men, it is necessary to optimize conditions to detect GR in PCa cells by immunofluorescence microscopy staining. We demonstrated that commercially acquired anti-GR antibodies react specifically with this protein in immunoblots of total protein from the PC3 and 22RV1 PCa cells. We have been optimizing immunofluorescence staining conditions to detect GR translocation to the nucleus of these cells upon dexamethasone treatment. We expect to observe GR immunofluorescence staining in the cytoplasm of untreated cells and nuclear staining in dexamethasone-treated cells. This optimization allows us to identify the proper anti-GR antibodies and conditions to assess GR expression in prostate tissue arrays from AA and EA PCa patients critical to understanding the role of GR signaling in PCa health disparities.

# ALEXIS TOWNSEND

## UTP PARTICIPANT 2018

I have had a passion for education for as long as I can remember. However, participating in this program, as well as in the ABC program in 2016, has solidified my love for scientific knowledge. This program is of particular interest to me because it emphasizes the prevalence of health disparities and how we can work to help our surrounding community to overcome these disadvantages.

I recently finished my first year of college at Oakwood University, a small HBCU in Alabama, where I am a biology major and a fixture on the Dean's list. In the future, I will get my MD, and then I hope to become an OB/GYN and open my own fertility clinic. I plan to place special emphasis on minority communities who often do not have access to such treatment options.

I have a passion for helping others, which can be seen through my professional aspirations but also through my participation in a program where we go out and feed the homeless every first Saturday of the month.

This summer I worked in the Sinclair lab where I examined bacteria concentrations in people's homes and silver's antimicrobial properties. The most interesting part of research is after gathering the results of a project, that moment when all the information learned and the procedures you performed finally "click," and you fully understand the significance of the project. In this program I was able to experience the "click," and I hope my explanation also inspires this feeling in my listeners.

I would like to thank Dr. Christopher Perry and Dr. Ryan Sinclair for allowing me to work in their labs this summer and increasing my overall knowledge.

# SURVIVAL RATES OF *E. FAECALIS* AND *P. AERUGINOSA* ON SILVER TREATED FABRIC WHEN SUBJECTED TO A COLD-WATER WASH

Alexis Townsend, Elaine Leslie, Ryan Sinclair, Christopher Perry

Center for Health Disparities and Molecular Medicine, School of Medicine and School of Public Health, Loma Linda University, Loma Linda, CA

Fabrics containing small amounts of silver are known to have antimicrobial properties. If they are used in cold water laundering, these fabrics could offer an energy-efficient alternative to hot water washes and traditional disinfectants. The purpose of this study was to test the survival rates of various microorganisms (*Enterococcus faecalis* and *Pseudomonas aeruginosa*) on silver-treated fabric in a cold-water household washing machine. The fabrics used were 12.5% silver-treated pillowcases, 30% silver-treated privacy curtains, and control non-Ag sheets, all cut into 3 $in^2$ swatches. The swatches were inoculated with a known bacteria concentration and then washed in a cold water cycle with three sterile 1 $m^2$ ballast white bed sheets (non-Ag) and one artificially soiled 1 $m^2$ bed sheets (non-Ag). Results were collected by comparing colony growth by number of colonies on an initial concentration, pre-wash, washed, and air-dried samples. Our results showed a 4 log reduction (LR) on the 30% curtain and a 0.8 LR on the 12.5% pillowcase in the concentration of the gram positive *E. faecalis* after the wash. The gram negative *P. aeruginosa* showed a 7.74 LR and did not survive on silver-treated fabric in a cold-water wash; however, the washing machine without the silver had a similar LR on *P. aeruginosa*. Our work suggests that silver treatment and cold-water washes may be a suitable alternative to using expensive heat and disinfectants for cases when *P. aeruginosa* and low contamination of *Enterococcus* (also VRE) are of concern. Future ongoing work is using silver-treated ballast fabric in the washing machine to increase the ratio of silver-treated to non-silver-treated fabrics in the wash. This change and a longer wash time may prove to have greater antimicrobial effects.

# Medical Training Program (MTP)

Miranda Berger Nordelo
Ninoshka Caballero-Colon
Edilberto Ocasio-Feliciano
Marlene Rodriguez
Miguel Serrano Illan
Neera Shah
Alfonso Vera

# MIRANDA K. BERGER NORDELO

## MTP PARTICIPANT 2018

Coming from a little island called Puerto Rico to the big state of California is a cultural shock of great proportions, but it allowed me to integrate the spirit of curiosity and learning to this opportunity in the Medical Training Program. An intern in the Center for Genomics in Dr. Charles Wang's laboratory, I am presented with the opportunity to see beyond the human anatomy to the macromolecules and the changes they undergo with respect to the environment we are in. As a second year medical student in San Juan Bautista School of Medicine, with my sub-mentor Teddie Liu, I am able to integrate what I learned this summer in the project of differential expression of miRNA in aging with the biology of the human body.

For most of my teenage years, I volunteered as a catechism teacher for young children and later on in the Veterans Affairs Caribbean Healthcare System where communication, techniques, and care were shown to work intrinsically. With these experiences, I started to aspire to take my medical degree to these populations, and while I am yet undecided as to where I will finally mark my ground, I know that all the opportunities given to me, and earned by my hard work and dedication, will lead me there.

I thank Dr. Wang's lab for allowing me the opportunity to learn under patient eyes, answering my questions, and guiding me in my endeavors.

# THE ROLE OF DIET ON MAINTAINING HEALTH AND LONGEVITY THROUGH CIRCULATING MIRNA MODULATION

Miranda Berger-Nordelo, Tiantian Liu, Charles Wang

Center for Health Disparities and Molecular Medicine, School of Medicine, and
Center for Genomics, Department of Basic Sciences,
Loma Linda University, Loma Linda, CA

Current studies suggest diet plays an intricate role in aging and age-associated diseases, including the increased susceptibility to cardiovascular disease, cancer, and cognitive decline. The molecular mechanism of how this is achieved has not been comprehensively studied. Recently an epigenetic regulatory connection between lifetime vegetarian diet and human health span has been established through DNA methylome. However, the effect of diet on miRNA expression and its subsequent influence on aging remains unclear. The purpose of this study is to explore different miRNA expression in long-term vegetarians vs non-vegetarians and its potential role in aging. We hypothesize a long-term vegetarian diet modulates circulating miRNA expression which affects health span by regulating gene expression involved in nutrient sensing pathways. To test this hypothesis, we exploited the participants of a large (N = 96,000) and long-standing cohort, the Adventist Health Study-2, with detailed clinical, dietary and health outcomes follow-up data over years. We collected plasma from 103 subjects in this cohort from two different dietary groups, extracted circulating miRNA, and constructed miRNA-seq libraries from 35 samples (21 vegetarian and 14 non-vegetarian) using QIAgen miRNeasy Serum/Plasma kit and QIAseq miRNA Library kit, respectively. All libraries were sequenced on Illumina NextSeq 550 and analyzed through Qiagen Data Analysis Center portal. Results showed there were five microRNAs that were significantly differentially expressed ($p<0.05$) in the vegetarian diet: miR-223-5p, miR-215-3p, miR-4467, miR-1303, and miR-26b-5p. These miRNAs have been implicated in innate immunity pathways and the proliferation of certain cancers. In addition, we detected six piwi-interacting RNAs that were upregulated ($p<0.05$) in the vegetarian group. This finding deserves further exploration as it may shed light on the role of piRNA in epigenetic regulation. Our study suggested dietary pattern, specifically a long-term vegetarian diet, plays a role in modulating circulating miRNA expression, and some of these miRNAs can serve as potential biomarkers for age-associated diseases.

# NINOSHKA M. CABALLER0-COLON

## MTP PARTICIPANT 2018

I am a second-year medical student at San Juan Bautista School of Medicine in Caguas, Puerto Rico, currently participating in the Medical Training Program (MTP) in the Center for Health Disparities and Molecular Medicine. I work in Dr. Marino De Leon's laboratoy on the lipotoxicty caused by saturated fatty acids on the nervous system. I believe research is the means by which our understanding of disease and the quality of care we give to our patients can be improved.

I graduated from the University of Puerto Rico at Humacao with a Bachelor's degree in general biology and engaged in research as an undergraduate student in the areas of neuroscience, molecular and developmental biology, and genetics. I picture myself in the future practicing medicine as a pediatric neurologist, conducting research, and working towards the development of policy on health disparity issues. The seminars this program offers have been of great help to enhance my awareness and judgement on this topic.

Another goal I have is to establish a multidisciplinary healthcare center for children and collaborate with other health professionals such as school psychologists, physical and occupational therapists, and speech language pathologists in order to provide a place for parents where they have access to different services their children may need. My hobbies include practicing yoga and going to the gym.

Being an MTP student has been very valuable because it has provided me with more experience in biomedical research and enhanced my clinical and critical thinking, team work, and communication skills which, overall, will strengthen my commitment to pursue a career in medicine and be a better physician in the future. I would like to thank Dr. De Leon's lab for their guidance this summer.

# NECROPTOSIS: THE CASPASE INDEPENDENT-CELL DEATH PATHWAY IN DIFFERENTIATED PC12 CELLS UNDER PALMITIC ACID-INDUCED LIPOTOXICITY

Ninoshka M. Caballero-Colón, Manuel Montero, Jo-Wen Liu, Carlos A. Casiano, Marino De León

Center for Health Disparities and Molecular Medicine, School of Medicine, Loma Linda University, Loma Linda, CA

Programmed cell death pathways may include either a lytic or non-lytic morphology, depending on the signaling pathway involved. Apoptosis is a non-lytic, non-inflammatory cell death mechanism while necroptosis is a lytic, inflammatory cell death process. Under conditions where caspase activity is inhibited, cells may divert to necroptosis as a backup mechanism for programmed cell death. This cell death process can be directly activated by stimuli that induce the expression of death receptor ligands observed during ischemia-reperfusion injury and neurodegenerative diseases. Necroptosis starts with death receptor activation, followed by phosphorylation of kinases RIP1 and RIP3 (Receptor Interacting Proteins 1 and 3) and recruitment of MLKL (Mixed Lineage kinase domain-like) leading to the formation of the necroptosome. We have shown that nerve growth factor-differentiated pheochromocytoma (NGFDPC12) cells treated with the pan-caspase inhibitor carbobenzozy-valyl-alanyl-aspartyl-[O-methyl] fluoromethylketone (ZVAD) fails to protect from palmitic acid lipotoxicity (PA-LTx)-induced cell death but instead may activate necroptotic cell death pathway. To further study this process, NGFDPC12 cells were treated with BSA (vehicle control), ZVAD, PA, PA+ZVAD and PA+ZVAD+Necrostatin-1 (Nec-1) for 18, 24, and 30 hours. Cell viability experiments show that ZVAD alone failed to increase cell survival. However, combinatory treatment with ZVAD and Nec-1 (necroptosis inhibitor) significantly increased cell viability in NGFDPC12 cells exposed to PA. This finding supports a role of necroptosis during the PA+ZVAD treatment. Next, we analyzed by immunoblotting the activation of MLKL, a key protein of the necroptosis pathway. We report that treatment with PA+ZVAD increased the expression of phosphorylated (activated) MLKL compared to controls. Thus, while PA-LTx primarily involves an apoptotic process, ZVAD treatment to inhibit caspases result in a caspase independent-cell death, necroptotic process. Our finding provides valuable information for therapeutic targeting in pathologies involving lipotoxicity and cell death.

# EDILBERTO J. OCASIO-FELICIANO

## MTP PARTICIPANT 2018

My journey from being a kid born and raised in Puerto Rico to being an intern doing research at Loma Linda University is quite long, but it has been worth every sacrifice. Difficulties have been always present, but it is the desire and passion about science and health that have driven me through this entire process.

I went to the University of Puerto Rico in Aguadilla where I majored in biomedical sciences. Actually, I am a medical student in my second year at San Juan Bautista School of Medicine. My goal is to finish the MD program and continue to a residency in internal medicine. After that, I want to enter a fellowship program in endocrinology.

The most important aspect in the clinical research setting is that, as a scientist, I can produce knowledge in order to improve the quality of health of my future patients. That is why research in health disparities is relevant because it helps those that are not being treated with equity to achieve similar results with the same treatment. Before I started this research, I did not understand what a health disparity was, but now it is one aspect that I look to when reading scientific literature.

I want to thank Dr. Daisy De León for being a person to look up to, for her passion towards science, and for providing me the opportunity to grow as a person and scientist. It has been a challenging summer, but it's worth it.

## ROLE OF NATURAL IGF2-ANTISENSE IN TRIPLE NEGATIVE BREAST CANCER CELLS

Edilberto J. Ocasio Feliciano, Vinodh Kumar Radhakrishnan, Daisy de León

Center for Health Disparities and Molecular Medicine, Breast Cancer Lab, School of Medicine, Loma Linda University, Loma Linda, CA

Breast cancer (BC) is the most common cancer in women, independent of race or ethnicity, and it is also the second cause of death from cancer in women. IGF2 plays a major role in breast cancer survival because it prevents cell death and promotes rapid tumor growth and metastasis. Our research team previously demonstrated that IGF2 levels are higher in breast cancer tissues from African American (AA) than in Caucasians (CA). Furthermore, higher IGF2 levels were expressed in normal tissues of AA women than in CA women. Since methylation regulates the IGF2 gene, we analyzed differentially methylated regions (DMRs) of the IGF2 gene to assess if it corresponded to IGF2 protein levels in paired (Normal/Tumor) breast tissues as well as in breast cancer cell lines. We identified a novel region with differential methylation that we named the IGF2 DVDMR. Surprisingly, this Differential Methylated Region (DMR) corresponds to a region in exon 3 of the IGF2-Antisense transcript. In this project, we studied the role of the IGF2-Antisense transcript variants in triple negative breast cancer cells (TNBC): MDA-MB-231, MDA-MB-468, Hs578T and CRL-2335. We designed primers using intron spanning assay to differentiate the different IGF2-Antisense splice variants. The mRNA gene expression studies were performed using qPCR to amplify the IGF2 and IGF2-Antisense splice variants, and the methylation levels were measured using Methyl Sensitive Restriction Enzymes (MSRE). Our data revealed that the DVDMR is hypomethylated in aggressive TNBCs which also expressed higher levels of the IGF2 transcript. The IGF2-Antisense is a non-translatable mRNA and may play a critical role in regulating the expression of IGF2 in correlation with the methylation.

# MARLENE B. RODRIGUEZ HERNANDEZ

## MTP PARTICIPANT 2018

As a Hispanic woman and a future physician, I want to take an active role in health disparities as an advocate for underserved communities. This summer as a participant in the Medical Training Program has helped me understand the abundant health dipartites not only in the terms of health access and disease but also as a social construct that has created gaps in health and that not enough efforts are created to improve the quality of life for minorities.

I am a second-year medical student at San Juan Bautista School of Medicine located in Puerto Rico, and during this summer I worked with Dr. Salvador Soriano in his efforts to reveal the true cause of late-onset Alzheimer's disease affecting our elderly by defying the scientific beliefs of the amyloid hypothesis. With the help of Karina Mayagoitia and Sam Shin, we studied the effects of high cholesterol diets that cause neuroinflammation and, as a result, triggers immune response that could lead to the neurodegeneration seen in Alzheimer's disease. These efforts will contribute to the search for better treatments in Alzheimer's disease that affects almost every family in the United States.

I wish to join Dr. Soriano and other scientists by continuing my medical career as a neurology physician and to keep involved in the ongoing research for better health quality and equality. There is more to do for underserved communities. That is why I wish for more opportunities like this one to empower these communities and aid in decreasing the healthcare gap that limits minorities from quality health care.

I want to thank Dr. Soriano's lab for welcoming me, for their guidance, and for patiently teaching me techniques that will be useful in my medical career and also in future research.

# NEUROINFLAMMATION AS A RESULT FROM CHOLESTEROL DYSREGULATION LEADS TO NEURODEGENERATION

Marlene B. Rodriguez, Samuel Shin, Karina Mayagoitia, Salvador Soriano

Center for Health Disparities and Molecular Medicine, Department of Human Anatomy, School of Medicine, Loma Linda University, Loma Linda, CA

Cholesterol dysregulation leads to inflammation in neurodegenerative conditions such as Alzheimer's disease, Parkinson's disease, Niemann Pick type C disease and amyotrophic lateral sclerosis. One example of cholesterol dysregulation is the accumulation of the proinflammatory oxysterol 27-hydroxycholesterol. Our laboratory has shown that the amyloid precursor protein (APP), a transmembrane protein highly expressed in the brain, is protective, in vitro, against neuroinflammation and neuronal cell death caused by the accumulation of 27-OHC. To explore whether 27-OHC accumulation leads to neuroinflammation pathways that are common to different neurodegenerative conditions, we will measure inflammatory markers in two mouse models of cholesterol dysregulation that lead to 27-OHC accumulation, neuroinflammation and cognitive decline: Niemann Pick type C disease mice and mice fed a high-cholesterol diet. Both models will be investigated in the presence or absence of the neuroprotective APP gene. Using immunological assays such as Luminex and immunohistochemistry, as well as bioinformatic tools, we will identify inflammatory pathways common to both cholesterol dysregulation models and determine the specific role of APP in modulating those pathways. With this approach, we can open a new window of treatments to optimize inflammatory responses in the brain that occur in a wide number of neurodegenerative conditions.

# MIGUEL SERRANO ILLAN

## MTP PARTICIPANT 2018

Hi there! If you are reading this, well, here is a literary high-five for your willingness to take the time. Since I am supposed to tell you about myself, here are a few things you may want to know about me: I love homemade cookies with a reckless passion. I also enjoy science and medicine, and I always have. While a kid growing up in Mexico, I used to dream of becoming a mad scientist, a radio talk show host, or a baker. Fortunately for my mother, I ended up choosing the first option with a few tweaks: I added medicine and mostly subtracted the mad feature.

As the years go by, my childhood dreams have evolved a bit, and I have now added other dreams as well, like that of using science and medicine to contribute to the healing and teaching ministry of Christ among the people who need it most. This past year I got to experience the partial fulfillment of that dream as I completed my first year of medical school at Loma Linda University, and this summer I'm hoping to fulfill my last requirement in order to graduate from the PhD program as well.

One of my most cherished awards during my tenure on this earth is the prestigious "favorite uncle award" given to me by my two nieces. Apparently, they appreciate bear hugs and overly animated bedtime stories, which are two of my spiritual gifts.

I dream of one day using my scientific, medical, and superb uncle skills to inspire the next generation of young people to use their own talents and gifts for the benefit of others and to make this world a little richer both in knowledge and in kindness.

## LONG-CHAIN FATTY ACID REGULATION OF PMP22 IS CORRELATED WITH CELL SURVIVAL AND PROLIFERATION IN SCHWANN CELLS.

Miguel Serrano-Illán, Magda Descorbeth, Amelia Padilla, Marino DeLeon

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Schwann cells (SCs) play a prominent role in axonal growth and repair during peripheral nerve regeneration. Myelin proteins, such as peripheral myelin protein 22 (PMP22), are critical for SC integrity and proper myelin formation, maintenance, and structure. Dysregulation of PMP22 can lead to peripheral neuropathies. Upregulation in the expression of PMP22 can lead to cell arrest and death while the opposite contributes to an increased SC proliferation and survival. We have shown that palmitic acid (PA)-induced lipotoxicity leads to cell death in SCs while docosahexaenoic acid (DHA) is able to reverse this detrimental effect. Our hypothesis is that PMP22 is down-regulated by DHA to prevent PA-induced decreases in cell viability and proliferation, thus playing a neuroprotective role in SCs. In this study we examined the changes of PMP22 and cell proliferation in cultured SC treated with BSA (vehicle control), PA, DHA and PA+DHA. Analysis using quantitative real time polymerase chain reaction (RT-PCR) and Western blot following *in vitro* treatment with PA/BSA at a 2:1 ratio (300:150uM) showed a significant upregulation in PM22 mRNA and protein levels at 36 and 48 hours post-treatment. In contrast, DHA/BSA (50:150uM) treatment induced PMP22 mRNA and protein downregulation at 48 hours post-treatment. Furthermore, PA and DHA co-treatment resulted in pre-treatment levels of PMP22. Next, BrdU analysis showed a significant decrease in proliferation following PA treatment in SCs beginning at 12 hours and was most dramatic at 48 hours. Conversely, DHA prevented this decrease in proliferation when administered along with PA while increasing proliferation when given by itself. Taken together, these data suggest that DHA confers neuroprotection in the event of PA-induced lipotoxicity by preventing SC death and increasing proliferation, a process correlated with the regulation of PMP22.

# NEERA SHAH

## MTP PARTICIPANT 2018

I am a second-year medical student here at Loma Linda University School of Medicine. I am hoping to pursue a career in neonatology, which incorporates clinical practice with research. The best part of research for me is the juxtaposition of routine with curiosity and investigation. I enjoy analyzing how experiments work and why certain things are the way they are. At the same time, I really value the human connection that is central to the practice of medicine.

I am particularly drawn to babies for their unique physiology, incredible resilience, and, of course, their adorable features. I have spent time shadowing in the NICU where I hope to work one day, and the only other place I have felt so at home with regards to my future is in my current lab.

I have been working with Dr. Kerby Oberg, Charmaine Pira, and recent graduate Dr. Billy Watson in the field of developmental biology since February 2017. I love basic science research and am excited to continue to incorporate it into my schooling and career in the future. I also participated in a translational research program last year that focused on neonatology, and I learned more about how basic science research can affect clinical medicine. To me, the thought of doing something like that is incredible. I know that what I have learned here will take me a long way as I continue my journey. I am very grateful to Dr. Oberg and my lab mates for welcoming me into their family and teaching me more than I ever expected!

## MECHANISM OF FGF-MEDIATED LHX2 UPREGULATION

Neera M. Shah, Billy A. Watson, Charmaine U. Pira, Kerby C. Oberg

Center for Health Disparities and Molecular Medicine, Department of Pathology and Human Anatomy, School of Medicine, Loma Linda University, Loma Linda, CA

During development, fibroblast growth factors (FGFs) secreted from the apical ectodermal ridge (AER) direct limb outgrowth. FGFs also coordinate limb patterning through cross-talk with other signaling molecules. The LIM homeobox transcription factor LHX2 is a suspected regulator of patterning cross-talk, is expressed at the distal tip of the limb bud subjacent to the AER, and is a primary response target of FGF. FGF regulates cell function through the Jak/Stat, PLCγ, AKT, and Ras/MEK intracellular pathways; however, the mechanism by which FGF regulates LHX2 is unknown. Based on the suspected roles of each signaling pathway, we hypothesize that FGF mediates LHX2 upregulation through the Ras/MEK pathway. To determine whether the Ras/MEK pathway is involved in the FGF-mediated LHX2 regulation, we implanted FGF soaked beads adjacent to beads laden with a chemical inhibitor of the Ras pathway into the limb bud of Hamburger Hamilton (HH) stage 23-24 chicken embryos. The embryos were harvested 4 hours after bead implantation and processed via whole mount *in situ* hybridization for *LHX2* expression. Inhibition of the Ras/MEK pathway has not been confirmed yet through these bead implant experiments. Injections of Ras inhibitor into HH stage 21-22 limbs stunted limb growth and supports the continued experimentation of Ras/MEK pathway inhibitors with bead implants. Inhibition of the entire FGFR1 pathway resulted in markedly decreased *LHX2* expression. These results confirm that FGF is a mediator of *LHX2* upregulation, but further work is needed to clarify the intracellular pathway used to accomplish this regulation.

# ALFONSO VERA

## MTP PARTICIPANT 2018

I never quite understood the notion of graduate school until my sophomore year of college, especially since no one in my entire family history had ever graduated from college. A compassionate professor mentored me throughout the process and conveyed that not only was I going to graduate college, but I was capable of achieving medical school. Therefore, I did my best by dedicating time to study even if the path felt strange and unknown. I applied and was accepted to the UTP, and this is where a new horizon and appreciation of science bridged the gap between the social and scientific aspect of medicine. The motivation and desire to pursue medicine rose exponentially after completing the UTP program, which ultimately led me on the track to be accepted into medical school.

I attend UC Riverside School of Medicine where my goal is to become a child psychiatrist. My experience as a child counselor in an at-risk youth group home and a behavioral interventionist for children with autism spectrum disorder have led me in this direction. Seeing these kids overcome difficulties and striving regardless of the circumstances has led me to become a better person. Another goal is to model behavior for children of this community and help facilitate programs to direct those from underserved backgrounds into STEM-related fields.

Apart from studies, I do many outdoor activities that involve mostly hiking and basketball. The sweetest gift of all is to hang out with my 13-year-old little brother, Daniel. I love spending time with my family and growing in my spiritual beliefs.

I want to thank Dr. Subburaman Mohan's Lab for allowing me to receive exceptional training. I appreciate the personnel's willingness in being kind and patient with me while explaining complex techniques and procedures.

# DIFFERENTIAL EFFECTS OF THYROID HORMONE RECEPTORS ALPHA AND BETA IN ADIPOCYTE DIFFERENTIATION

Alfonso Vera, Richard Lindsey, Subburaman Mohan

Center for Health Disparities and Molecular Medicine, School of Medicine,
Loma Linda University, and Musculoskeletal Disease Center,
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Obesity, a public health concern, is associated with co-morbidities such as hypertension, type II diabetes, and stroke. Although many therapies have been suggested to treat obesity, none has been effective, and obesity continues to increase in prevalence. Obesity develops from an increase of lipid storage in white adipose tissue (WAT) due to excess caloric intake. By contrast, brown adipose tissue (BAT) has non-shivering adaptive thermogenesis capabilities through uncoupling effects that dissipate excess energy as heat without producing ATP. Therefore, current research has focused on converting WAT into brown-like beige adipose tissue, a process known as "browning," as a potential therapeutic strategy for treating obesity. In previous work, we found thyroid hormone (TH) deficiency increased total body fat mass and bone marrow adiposity (BMA). In addition, TH treatment increased expression of BAT makers in WAT. However, increased TH can have significant adverse effects by causing hyperthyroidism, so a more specific therapeutic target is needed. Based on recent studies which implicate TH receptor (TRβ) signaling in regulating BMA, we evaluated the effects of TRs α and β in adipocyte differentiation. We hypothesized that TRβ-specific agonist GC-1 would act on TRβ to regulate WAT and BAT marker gene expression differently from triiodo-L-thyronine (T3) in marrow mesenchymal cell lines. We, therefore, treated primary mouse bone marrow stromal cells (BMSCs) and a murine marrow stromal cell line (C3H10T1/2) with adipocyte differentiation factors IBMX, dexamethasone, and insulin followed by T3 or GC-1. We found that T3, acting primarily through TRα in these marrow mesenchymal cells, mainly upregulated WAT genes and downregulated BAT/browning genes while GC-1 did not. Conclusions: 1) T3 and GC-1 exerted differential effects on the expression of adipocyte differentiation markers, and 2) further optimization of conditions to promote browning of WAT via activation of TRβ signaling without inducing white adipocyte differentiation could provide a potential therapeutic strategy for ameliorating obesity.

# Initiative to Maximize Student Development (IMSD)

Ivana Alicea-Polanco
Victor Camberos
Katherine Concepcion
Alfonso Duran
Jerry Flores
Xousaen Helu
Jenniffer Licero Campbell
Richard Lindsey
Greisha Ortiz Hernández
Foluwasomi Oyefeso
Hiel Rutanhira
Evelyn Sanchez Hernández
Nicholas Sanchez
Julio Vega-Torres
Jonathan Wooten

# IVANA M. ALICEA-POLANCO

## IMSD PARTICIPANT 2018

I was born and raised in Puerto Rico where I studied and graduated from Antillean Adventist University in 2015 with a BS in Biology. Soon after, I was accepted into Loma Linda University to pursue a PhD degree in physiology. I have had the privilege of serving my community through leadership and volunteering, which has made me passionate about finding ways to serve others and provide positive change wherever it's needed. Biomedical research is a powerful tool that gives young, driven, and motivated young people the opportunity to serve society in long-lasting ways.

I am a proud member of Dr. Johnny Figueroa's lab where I study the interplay between diet consumption during development and stress behaviors. In particular, I'm looking at potential mechanisms that might be playing a role in this relationship. I am so grateful to be a part of this lab with my labmate Julio Vega and my mentor, Dr. Figueroa. It has been a pleasure to be part of such an amazing team of scientists who, like me, share a passion for the topics of nutrition and mental health.

I would like to start by thanking my labmate, Julio Vega, for challenging and supporting me when I have needed it. I also want to thank my mentor and PI, Dr. Figueroa, for leading and encouraging me and for his unbelievable patience and kindness. I am forever grateful to my team.

## HIGH-SATURATED FAT DIET-INDUCED NEUROINFLAMMATION AS A PATHWAY FOR STRESS VULNERABILITY DURING ADOLESCENCE

Ivana Alicea-Polanco, Kevin Liu, Keisha Jordan, Esmeralda Terrones, Julio D. Vega-Torres, Johnny D. Figueroa

Center for Health Disparities and Molecular Medicine, Department of Neuroscience, School of Medicine, Loma Linda University, Loma Linda, CA

Psychosocial stressors are a well-documented risk factor for mental illness. Neuroinflammation has been proposed to mediate this association. We have shown that consumption of diets rich in saturated fatty acids impairs cognitive function and heightens vulnerability to psychosocial stressors. The purpose of this study was to investigate the effects of a high-saturated fat diet (HSFD) on neuroinflammation in brain regions implicated in stress responsivity. Adolescent Lewis rats were fed a low-saturated fat control diet (LSFD, 13 kcal from fat) or a HSFD (41 kcal from fat). We assessed stress responsivity using a well-characterized fear-potentiated startle (FPS) paradigm. Further, we measured the mRNA levels of important neuroinflammatory biomarkers (NLRP3, TLR4, NFκβ, CX3CR1, IL1β, IL6, IBA1, TNFα, CDK5, and HMGB1) using real-time polymerase chain reaction. We found that LSFD-fed rats had an 87.5% decrease in post-extinction FPS when compared to pre-extinction FPS while the HSFD-fed rats had identical FPS magnitudes. These findings suggest that HSFD-fed rats had impairments in fear memory extinction which is an indication of greater manifestation of stress responsivity. We also found that the prefrontal cortex of HSFD-fed rats exhibited a significant reduction in the mRNA levels of CX3CR1 (24.4%) and NLRP3 (29.5%) genes when compared to LFSD-fed rats. Our findings support that consumption of a HSFD during adolescence can alter neuroinflammation markers in areas associated with stress responsivity.

# VICTOR CAMBEROS

## IMSD PARTICIPANT 2018

I am a third year IMSD graduate student at Loma Linda University working on my PhD in physiology. Upon completing my PhD, I hope to find work in a university or hospital setting doing clinical research. Ideally, I would like to work in a children's hospital doing oncology research. Currently, I work under the mentorship of Dr. Mary Kearns-Jonker using human cardiac progenitor cells to investigate novel treatments for heart failure patients. Our goal is to be able to manipulate these cells to become more regenerative so that we can use them therapeutically to replenish lost cardiomyocytes in patients who have experienced a myocardial infarction.

One of the studies we are pursuing involves investigating the effect of spaceflight and microgravity on cardiac progenitor cells and searching for ways we can reproduce these effects more efficiently in a laboratory setting for therapies on Earth. The most interesting thing about the research I do is that we work with NASA and SpaceX to launch our cells to the International Space Station where they are cultured by an astronaut and returned to us for further studies and analysis. Since I first started culturing stem cells as an undergrad at UC Riverside, I have been fascinated by them because stem cells offer so much potential for treating diseases and they allow us to obtain a deeper understanding of how the cells in our body work.

I would like to thank Dr. Kearns-Jonker for welcoming me into her lab and giving me the opportunity to be a part of exciting research while working on my PhD.

# EARLY-STAGE ISLET-1+ CARDIOVASCULAR PROGENITOR CELLS ISOLATED FROM THE HUMAN HEART EXPRESS CD56

Victor Camberos, Victor Campbell, Pedro Medina, Leonard Bailey, Nahidh Hasaniya, Mary Kearns-Jonker

Center for Health Disparities and Molecular Medicine, Department of Pathology and Human Anatomy and Department of Cardiovascular and Thoracic Surgery, School of Medicine, Loma Linda University, Loma Linda, CA

Stem cells introduced for myocardial repair in clinical trials performed to date have the ability to facilitate cardiovascular repair but have limited ability to regenerate damaged tissue. In order to improve the outcome of these trials, retention of transplanted progenitors with the ability to differentiate *in vivo* into all cells of the cardiovascular lineage would be beneficial. Human embryonic stem cell-derived cardiovascular progenitor cells in the earliest stage of mesoderm commitment express CD56. The objective of this project was to address the hypothesis that early, clonal islet-1+ cardiovascular progenitor cells isolated from human patient-derived cardiac tissue express CD56. Using flow cytometry, we identified CD56 on neonatal cardiovascular stem cell clones. In order to determine whether islet-1+ CD56+ early stage cardiovascular progenitor cells express immunomodulatory factors that could enhance cell retention, we used PCR to demonstrate that indoleamine, a factor that promotes allogeneic cell survival, is expressed in these progenitors. The significance of this new data is that islet-1+ cells co-expressing CD56 isolated at the earliest stage of cardiovascular commitment may be promising as progenitors for cardiac repair and have the potential to be protected from immune rejection due to the expression of indoleamine.

# KATHERINE CONCEPCION

## IMSD PARTICIPANT 2018

Before coming to Loma Linda, my mission was clear to me: to practice medicine at the bedside while creatively doing everything I could to eradicate disease on a larger scale. It is this passion that influenced my desire to become a physician-scientist.

Patients and their families affected by preventable diseases are what drive me every day, both clinically and in the lab. Previous to coming to Loma Linda University, I spent every free period involved in translational research in labs that had the passion to treat patients as an end goal. My constant through the years has been my heightened interest in perinatal biology. It is this patient population that pushes me to persevere in my research and medical studies with passion and patience. These patients have called me to not only be involved in research but advocate for them in policy, in education, and on administrative levels. I am looking forward to one day being a pediatric physician and, more specifically, a neonatologist who finds clinical solutions through research.

I am currently in Loma Linda University's MD/PhD IMSD program. Finishing the first two years of medical school, I have a desire to search for clinical problems close to the bedside and find solutions in the lab. My hope is to bridge the gap between medical and graduate students and be a facilitator for creating research projects that directly answer clinical questions. I am currently working with Dr. Lubo Zhang in the Center for Perinatal Biology to develop an effective model to study brain ischemic injury and inflammation in neonatal rats. My hypothesis is that both glucocorticoid and mineralocorticoid receptors decrease inflammation post-hypoxic ischemic injury in the neonatal rat.

# HYDROCORTISONE PROTECTS THE BRAIN FROM HYPOXIC-ISCHEMIC INJURY IN NEONATAL RATS

Katherine R. Concepcion, Yong Li, Lubo Zhang

Center for Health Disparities and Molecular Medicine, Center for Perinatal Biology, Division of Pharmacology, School of Medicine, Loma Linda University, Loma Linda, CA

Hypoxic-ischemic encephalopathy (HIE) is a major cause of neonatal disability and mortality. Infants acquiring HIE are at risk for developing other neuronal diseases such as severe cerebral palsy, mental retardation, seizures, and other neurodevelopmental disabilities. HIE brain damage is largely due to perinatal asphyxia and hypoxia prior to or after birth. Inflammation has been shown to play a critical role in neonatal brain damage and is an important contributor to the pathogenic cascade. Inflammation can both sensitize, as seen in perinatal infections, and participate in the injury response to a hypoxic insult as well as in the recovery process after insult. In the present study, we modified a Rice-Vannucci model in rat pups to better understand the consequences of inflammation and epigenetic regulation during fetal and postnatal life. Previous studies have shown that pretreatment with dexamethasone, an anti-inflammatory steroid medication, in neonatal HI brain injury demonstrates a neuroprotective effect and decreases HI insult-induced brain infarct size. Because dexamethasone has many detrimental side effects, we explored the potential therapeutic use of hydrocortisone. The aim of this project was to develop a model to study the effects of post-HI treatment with hydrocortisone. Our results demonstrated that rat pups treated with hydrocortisone 4 hours post-HI showed a decrease in brain infarction size. We then used LPS to mimic the infections acquired in the womb or post-birth. Our results demonstrated increased HI-induced brain infarction and the mortality rate in rat pups treated with LPS. We also showed that intracerebroventricular injection of hydrocortisone significantly decreased HI-induced brain injury in the pups receiving LPS. Of importance, we demonstrated that intranasal delivery of hydrocortisone after HI insult showed a significant reduced brain infarction size. Our results suggest a potential therapeutic effect of hydrocortisone for HIE in neonates. Further studies are needed to investigate the mechanisms by which hydrocortisone acts in neuroprotection in the developing brain.

# ALFONSO DURÁN

## IMSD PARTICIPANT 2018

When graduating from medical school, I thought most of my academic career was over. However, in my second year of residency, I found myself somewhat disheartened with the future impact I could have on a community's health. Even though helping patients on a one-to-one basis can change their lives dramatically, changing a community's health is almost impossible, especially when dealing with chronic diseases such as obesity, diabetes, etc.

Thus, I elected to put residency on hold and pursue a PhD in physiology. My current research focus involves metabolomics studies of Latinos with chronic diseases. Using metabolomics, we can identify key bio-markers and elucidate major metabolic pathways involved in the pathophysiology contributing to health disparities. Further, in the context of health disparities, metabolomics can inform researchers about mechanisms that underlie variation in response to interventions/treatments and direct the development of effective interventions for at-risk communities. Therefore, metabolomics provides a powerful tool to investigate current health disparities in the Latino population.

Currently, the delivery of healthcare lacks a patient-centered focus and many times misses addressing causative agents of disease. My future goal is to develop a comprehensive evidence-based health center that focuses on integrative care and translational research in underserved communities. Moreover, the focus of the health center would be on developing new forms of healthcare delivery and formulating novel clinical research aimed at solving chronic diseases.

# OMEGA-3 POLYUNSATURATED FATTY ACID SUPPLEMENTATION AMELIORATES PAINFUL DIABETIC NEUROPATHY SYMPTOMS AND DECREASES ELEVATED SPHINGOSINE LEVELS IN MEXICAN-AMERICANS WITH TYPE 2 DIABETES

Alfonso Durán, Justin Câmara, W. Lawrence Beeson, Anthony Firek, Zaida Cordero-MacIntyre, Marino De León

Center for Health Disparities and Molecular Medicine, School of Medicine, Loma Linda University, Loma Linda, CA

Our objective was to determine whether dietary-supplementation with omega-3 polyunsaturated fatty acids (PUFAs) reduces painful diabetic neuropathy (DN) symptoms in Mexican-Americans with type 2 diabetes. Forty volunteers with type 2 diabetes enrolled in the "*En Balance*-PLUS" program which provided weekly nutrition-diabetes education classes and daily supplementation with 1000 mg docosahexaenoic (DHA)/400 mg eicosapentaenoic acid over 3 months. The study 1) assessed neuropathic pain symptoms pre/post intervention using the short-form McGill pain questionnaire (SF-MPQ), 2) monitored clinical laboratory values at baseline/3 months, and 3) performed baseline/3 month metabolomics analysis of plasma samples. We found twenty-six participants self-reported painful DN symptoms at baseline; after three months of omega-3 PUFA supplementation, participants expressed significant improvement on the SF-MPQ scores (sensory, affective, and visual analogue scale) ($P < 0.001$, $P = 0.012$, and $P < 0.001$, respectively). Untargeted metabolomics analysis revealed that participants in the moderate-to-high SF-MPQ group had the highest relative plasma sphingosine levels at baseline compared to the low SF-MPQ group ($P = 0.0127$) and the non-pain group ($P = 0.0444$). Omega-3 PUFA supplementation increased plasma DHA and reduced plasma sphingosine levels in participants reporting painful DN symptoms ($P < 0.001$, and $P < 0.001$, respectively). Increased plasma DHA levels significantly correlated with the improved SF-MPQ sensory scores ($r = 0.425$, $p = 0.030$). However, improved SF-MPQ scores did not correlate with standard clinical values. These findings support that using omega-3 supplementation as part of a balanced diet may reduce neuropathic pain symptoms in individuals with type 2 diabetes.

# JERRY FLORES

## IMSD PARTICIPANT 2018

I attended the University of California, Riverside (UCR) where I majored in biology. After my second year of undergrad, I attended Loma Linda University's (LLU) summer program where I was exposed to scientific research. During this program, I learned how our bodies have molecular mechanisms and how these pathways can be manipulated to produce beneficial outcomes in various pathophysiologies. Through this program, I met Dr. John H. Zhang who took me on as a research student after graduating UCR. In Dr. Zhang's laboratory, I was introduced to the field of neuroscience where I learned how to model cerebral vascular diseases (stroke) and construct experimental designs.

I recently completed my first year of the PhD program at Loma Linda University and supported by the IMSD program. Currently, I have 2 first and 18 co-authored publications under the guidance of Dr. Zhang. Because of my productivity as a graduate student, I was given the "Excellence in Publications" award at LLU.

My research is based on the germinal matrix (GMH) model, the leading cause of morbidity and mortality in preterm infants in the United States with no available therapeutics. GMH is defined by the rupture of immature blood vessels within the subependymal (or periventricular) germinal matrix. I specifically focus on the upregulation of endogenous immunomodulatory pathways that upregulate macrophage phagocytosis of hematoma, resulting in hematoma clot clearance. The clearance of hematoma results in better outcomes in the short and long-term by decreasing hydrocephalus.

With this experience and continued mentoring, my long-term goal is to be awarded a pre-doctoral grant, publish, and use this acquired knowledge to establish my very own laboratory in the future.

# N-FORMYL PEPTIDE RECEPTOR 2 ACTIVATION VIA ANNEXIN A1 UPREGULATES HEMATOMA RESOLUTION AFTER GERMINAL MATRIX HEMORRHAGE

Jerry Flores, John H. Zhang

Center for Health Disparities and Molecular Medicine, Center for Neuroscience Research, Physiology, School of Medicine, Loma Linda University, Loma Linda, CA

Germinal matrix hemorrhage (GMH) is the leading cause of morbidity and mortality in preterm infants in the United States with little progress made in its clinical management. Survivors are often afflicted with long-term neurological sequelae, including cerebral palsy, mental retardation, and post-hemorrhagic hydrocephalus. Blood clots disrupting normal cerebrospinal fluid circulation and absorption after germinal matrix hemorrhage are key contributors towards post-hemorrhagic hydrocephalus development. N-formyl peptide receptor 2 (FPR2), a G-protein-coupled receptor, has been associated with the activation of scavenger receptor CD36. CD36, a trans-membrane glycoprotein, plays an important role in microglia phagocytic blood clot clearance after GMH and its upregulation has been shown to enhance hematoma resolution and attenuate post-hemorrhagic hydrocephalus. Currently, FPR2's role in blood clot clearance after hemorrhagic stroke is unknown. We hypothesize that FPR2 activation by Annexin A1 will enhance hematoma resolution via upregulation of the CD36 signaling pathway, thereby improving short- and long-term neurological outcomes. Bacterial collagenase (0.3 U) was infused intraparenchymally into the right hemispheric ganglionic eminence in P7 rat pups to induce GMH. Annexin A1 and FPR2 Inhibitor (Boc2) were given at 1 hour post-GMH via intranasal administration. Short-term neurological deficits were assessed using negative geotaxis test. Hematoma volume was assessed using hemoglobin assay. Protein expression was assessed using Western blots. Long-term neurocognitive deficits and motor coordination were assessed using Morris water maze, rotarod, and foot fault tests. We have demonstrated that Annexin A1 treatment enhances hematoma resolution and improved neurological deficits in the short and long-term. Our findings may lead to a safe and non-invasive therapeutic target for the reduction of blood clots early in the pathophysiology to reduce post-hemorrhagic hydrocephalus, which would be essential in the management of GMH.

# XOUSAEN HELU

## IMSD PARTICIPANT 2018

Ever since I participated in a summer research program here at Loma Linda University back in 2002, I knew I wanted to pursue a career in scientific research. As a graduate student in the MD/PhD program at LLU, I am training to attain that goal. I attended La Sierra University in Riverside, CA, and obtained my bachelor's degree in biochemistry in 2007. I had the opportunity to attend a summer research program, the Undergraduate Scholarship Program (UGSP) at the National Institutes of Health (NIH), after completing my bachelor's degree. Afterwards, I joined the MD/PhD program at Loma Linda University School of Medicine in August of 2007.

My current research topic is the interaction of IGF2 and HER2 in trastuzumab-resistant breast cancer under the mentorship of Dr. Daisy De Leon. My career goals include heading my own lab and working in close collaboration with clinicians to help develop new therapies against cancer.

Outside of the lab, I enjoy watching movies with my wife, walking my dog Juno, and cooking. The IMSD program and my mentors, Drs. Marino and Daisy De Leon, have been instrumental in my development as a scientist. I appreciate their efforts and guidance, and I look forward to the time when I can help mentor and guide the next generation of scientists.

# INHIBITION OF HER2 AND IGF2 IN JIMT1 CELLS WITH RESVERATROL AND CHROMECEPTIN RESULTS IN DECREASED CELL PROLIFERATION

Xousaen M. Helu, Heidi Buri, Daisy D. De León

Center for Health Disparities and Molecular Medicine, School of Medicine,
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Breast cancer is a major issue among women as it is the second leading cause of cancer-related death in the world. Approximately 20% of breast cancer patients are found to have an overexpression of the Human Epidermal Growth Factor Receptor 2 (HER2). Although Transtuzumab, a recombinant monoclonal antibody that inhibits HER2 by binding to the HER2 receptors, has been demonstrated to slow tumor growth, about 30% of breast cancer patients do not respond to treatment. Previous results in our lab have demonstrated that JIMT1 HER2 positive breast cancer cells are resistant to Trastuzumab and also had higher levels of IGF2 compared to HER2 positive cells that responded to Trastuzumab. The hypothesis of this study is that cell viability and proliferation of the Trastuzumab resistant HER2+ JIMT cells will decrease in response to the treatment with Resveratrol and Chromeceptin. Both, Resveratrol and Chromeceptin, inhibit IGF2 while Resveratrol also inhibits HER2 and STAT3. We tested the effect of these IGF2 inhibitors in combination and at various concentrations to determine an effective dose and to assess if there are additive or synergistic effects when used in combination. There was a significantly visible decrease in the cell viability of the JIMT1 cells treated with the highest concentration of Resveratrol. Additionally, there was a significant change in the cell morphology of JIMT1 cells treated with the highest concentration of Chromeceptin. While combined, the cells seemed to react relatively the same to treatments on their own. These results indicate that treatment of the combination of Resveratrol and Chromeceptin are effective drugs in decreasing the cell viability and proliferation of HER2 Positive Trastuzumab-Resistant JIMT1 breast cancer cells. The separate treatments of high concentrations of Resveratrol and Chromeceptin effectively changed the cell morphology and decreased both the cell viability proliferation of HER2 Positive Trastuzumab-Resistant JIMT1 breast cancer cells.

# JENNIFFER C. LICERO

## IMSD PARTICIPANT 2018

Jenniffer Licero, a name which some have correlated with the feelings bubbly and happy, is a courageous, humble, hardworking, devoted, focused and happy 28-year-old. I am an incessant questioner of paradigms and theories who daily strives to unearth the unknown through scientific discovery. I am a worshipper. I am God's daughter. I am a Christian. I am Venezuelan, even while recognizing that my grandparents' Colombian blood runs through my veins. I am likely in the smallest of minorities as a Christian, Hispanic, female scientist who wants to change the world and help people live better lives. I am a girl who has defied the odds and looks forward to the challenges ahead. When all is said and done, I would say I am a servant of God that has been used to show that seemingly impossible dreams are not impossible for Him.

My current challenge involves changing paradigms in the field of spinal cord injury with the help of my mentor Dr. Marino De Leon. I am presently conducting studies in the area of inflammation post spinal cord injury and am finding that it takes special skill to coax the unknown out of its comfortable home. In addition to research, I have somehow found the time to complete the major class requirements for a degree in human anatomy. Having recently entered my 6$^{th}$ year as a PhD student, I cannot wait to move forward in my career and continue to contribute to the greater body of thinkers who want to learn more about the world and make it a better place.

## SIGNIFICANT GENE EXPRESSION OF FATTY ACID BINDING PROTEIN 4 FOLLOWING SPINAL CORD INJURY IN RATS

Jenniffer Licero Campbell, Miguel Serrano Illán, Kathia Cordero, Alfonso Duran, Johnny Figueroa, Marino De Leon

Center for Health Disparities and Molecular Medicine, School of Medicine, Loma Linda University, Loma Linda, CA

The pathology of traumatic spinal cord injury (SCI) results from both the initial mechanical insult and the secondary processes that occur over hours and days following injury. This secondary insult represents an important window for intervention and is characterized by a marked deregulation in lipid metabolism leading to inflammation. The present study investigates the expression and roles of fatty acid-binding protein 4 (FABP4) in rats post spinal cord injury. The multicenter animal spinal cord injury study (MASCIS) injury model was used to generate a contusion to the T-10 spinal segment of rats. Spinal cord samples were collected at 1, 3, 7, 14, and 28 days post-injury and analyzed to determine the spatiotemporal expression of FABP4 using immunohistochemistry and real-time RT-PCR. Here, we show that injury to the spinal cord results in a dramatic up-regulation in the mRNA and protein levels of FABP4. Notably, this expression was most prevalent in bone marrow derived M1 macrophages and microglia. To investigate the potential role of this protein in functional recovery after SCI, the rats received intrathecal administration of the FABP4 inhibitor BMS 309403. We show that animals receiving the FABP4 inhibitor exhibited improved locomotion after injury when compared to vehicle-treated rats. Interestingly, this beneficial effect was not associated with the regulation of pro-inflammatory cytokines mRNA levels in the injured spinal cord. Altogether, our findings are the first to show a robust increase in protein and mRNA levels of FABP4 following SCI and a possible functional role in this context. These data suggest that FABP4 may play a major role in hyper-acute inflammatory responses and functional recovery after injury, representing an attractive target for intervention.

# RICHARD LINDSEY

## IMSD PARTICIPANT 2018

I am a seventh-year student in Loma Linda University's MD/PhD program, having completed two years of medical school and four years of the PhD program. In 2012, I graduated from Biola University with a degree in biochemistry, and I am a perpetual member of Biola's Torrey Honors Institute, a great books program taught in the Socratic style. I intend to use my education from both Biola and LLU to pursue a career in endocrinology research with an eye toward understanding and eliminating health disparities. Moreover, I am interested in Christian theology and philosophy of science, and I want to contribute both to science and to the way people perceive and relate to science. In an effort "to glorify God and to enjoy him forever" (*Westminster Shorter Catechism*), I want to ensure that Man's conquest of Nature does not become Nature's conquest of Man (CS Lewis, *The Abolition of Man*). Over the past year, my interests in data science, R programming, and reproducible research have continued to expand. For recreation, I enjoy reading (currently Roberts & Wilson's *Echoes of Exodus* and Hansen's *Our Secular Age*) and digital typesetting, and I've recently been tinkering with programming in Go and Racket.

Over the years, I have participated in the UTP, MTP, and IMSD programs, and this is my ninth year presenting at the CHDMM's annual symposium. Additionally, this is my ninth summer working with Dr. Subburaman Mohan in the Musculoskeletal Disease Center at the VA Loma Linda Healthcare System, and I am truly grateful for the support and learning opportunities he has given me. I have learned much from Dr. Mohan over the last year through the processes of speaking at conferences and submitting grants, and I look forward to completing my PhD in Dr. Mohan's lab.

# SKELETAL EFFECTS OF NON-GENOMIC THYROID HORMONE RECEPTOR (TR) β1 SIGNALING IN MICE

Richard C. Lindsey, Catrina Godwin, Subburaman Mohan

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Thyroid hormone (TH) levels increase rapidly during the prepubertal growth period in mice, and studies have shown that TRβ1-mediated activation of Indian hedgehog signaling is necessary for endochondral ossification of the epiphyses. In addition to its traditional genomic signaling role as a transcription factor, TRβ1 can also exert non-genomic effects by interacting with other signaling molecules such as PI3K. To investigate the role of non-genomic TRβ1 signaling in endochondral ossification, we evaluated the skeletal phenotype of TRβ147F mutant mice in the TRβ1–PI3K interaction is disrupted. These TRβ147F mice exhibit a normal genomic response of TRβ1 to TH, but the non-genomic response through the PI3K pathway is impaired. Using microCT, we found that 13-week-old TRβ147F mice had significantly less trabecular bone mass in the distal femoral secondary spongiosa compared to control mice, and trabecular BV/TV at the tibial epiphyses was also decreased. The mutants' reduced trabecular bone mass was primarily due to decreased trabecular thickness. Histomorphometric analyses revealed decreased measures of bone formation. To explore the mechanisms of these TRβ1 effects in osteoblasts, we measured changes in mRNA expression caused by TRβ-specific agonist GC-1 in calvarial osteoblasts of mutant and control mice. We found that GC-1 increased *Alp* expression in control osteoblasts (1.55-fold, $P = 0.01$) but not TRβ147F mutant osteoblasts. Since canonical β-catenin signaling has been implicated in mediating PI3K non-genomic signaling in other cell types, we evaluated the GC-1 effect on β-catenin protein levels in MC3T3-E1 pre-osteoblasts. GC-1 treatment, however, did not significantly alter β-catenin levels, suggesting TRβ1–PI3K modulation of β-catenin is not likely involved in mediating GC-1 effects on osteoblast differentiation. Together, these results suggest TH acting through TRβ1 regulates endochondral ossification in part via non-genomic signaling in mice. Further investigation of this non-genomic mechanism of TRβ1 signaling could lead to novel therapeutic targets for promoting endochondral ossification.

# GREISHA L. ORTIZ HERNÁNDEZ

## IMSD PARTICIPANT 2018

Growing up on the beautiful island of Puerto Rico (PR), I discovered that my biggest passion, other than food and the outdoors, is the sciences. But anything that comes that easy, as Zig Ziglar said, "You don't have to be great to start, but you have to start to be great."

After my Bachelor's graduation in biology from Universidad Metropolitana in PR, I was ready to apply for graduate school at Loma Linda University (LLU). When doing so, however, my family and I received heartbreaking news. My grandfather, whom I used to call "Guelo," would die in three months because of a head-neck cancer. So far, it was the most difficult moment of my life. But God's plans are perfect, and we greatly enjoyed the last days of my Guelo. This was a process where I learned to enjoy every path in my life and be grateful for it. Spring 2015 I reapplied for the LLU graduate program, and I was finally accepted and awarded through the IMSD program. Being exposed to my grandpa's death to cancer confirmed my choice of pursuing a career in cancer research.

After completing my first year of required lab rotations, I decided to join Dr. Carlos A. Casiano's prostate cancer (PCa) research laboratory. Recently, I passed my comprehensive examination for the Pharmacology program and just finished the required classes for it. My plan for the summer is to develop the necessary preliminary data for the first aim of my proposal for this coming fall quarter. My long-term goal with my research project is to explore the contribution of protein-protein interactions to LEDGF/p75-mediated upregulation of stress oncoproteins to tumor aggressiveness and chemoresistance in the context of PCa health disparities.

# THE TRANSCRIPTION FACTOR JPO2 IS UPREGULATED IN DOCETAXEL RESISTANT PROSTATE CANCER CELLS AND INTERACTS WITH LEDGF/P75

Greisha L. Ortiz-Hernandez, Girish Senthil, Shannalee Martinez, Carlos A. Casiano

Center for Health Disparities and Molecular Medicine, School of Medicine, Loma Linda University, Loma Linda, CA

Prostate cancer (PCa) is the most commonly diagnosed cancer and second leading cause of cancer-related male deaths in the United States. Current therapies for advanced PCa include androgen deprivation therapy and docetaxel (DTX) chemotherapy. Unfortunately, therapy resistance and disease progression are unavoidable, leading to patient mortality. Our group has demonstrated that the stress oncoprotein Lens Epithelium Derived Growth Factor protein of 75 kD (LEDGF/p75) is upregulated in clinical prostate tumors and contributes to DTX resistance in PCa cells. However, very little is known about the mechanisms by which LEDGF/p75 promotes chemoresistance. To explore these mechanisms we initiated a molecular analysis of protein-protein interactions (PPIs) between LEDGF/p75 and other nuclear proteins in DTX-sensitive and -resistant PCa cells. An emerging transcription factor, JPO2, has been linked to aggressive phenotypes in medulloblastoma through its binding with LEDGF/p75, but this interaction has not been explored in the context of PCa chemoresistance. Our hypothesis is that LEDGF/p75 interacts with JPO2 to induce the expression of stress survival genes that contribute to PCa chemoresistance. As a first step in evaluating this hypothesis, we assessed the protein expression of JPO2 through Western blotting in our DTX-sensitive and DTX-resistant PCa cell lines. Our data showed an upregulation of both JPO2 and LEDGF/p75 protein expression in the DTX-resistant cells compared to the sensitive cells. Also, preliminary data from immunoprecipitation experiments suggest an interaction between JPO2 and LEDGF/p75 in the chemoresistant PCa cells. Other techniques such as protein nuclear colocalization by immunofluorescence microscopy are being optimized to further determine to which extent LEDGF/p75 and JOP2 may be part of a transcription protein complex in chemoresistant cells. Our long-term goal is to establish the contribution of PPIs to LEDGF/p75-mediated upregulation of stress oncoproteins in the context of PCa chemoresistance and mortality disparities and target these interactions with small molecule inhibitors to re-sensitize chemoresistant PCa cells to DTX.

# FOLUWASOMI OYEFESO

## IMSD PARTICIPANT 2018

By the time I finished high school, my future direction was set in stone. Over the years I developed an immense love for science with its complexities and secrets. Although my interests changed numerous times, my original motivation for this field may resemble many of my peers. In 2004, the day after Christmas, I lost my young cousin to leukemia. The progression of the disease was slow, but the impact was significant. I began to study different diseases to understand them in hopes of treating terminal/chronic illnesses.

After some decision making, I decided on pursuing a bioengineering degree at Walla Walla University in part because of my desire to stay in a Christian community. Almost immediately after familiarizing myself with the campus, I began to ask my science professors how I could become involved in research. Between classes, serving in officer positions, and playing for the University soccer team, I found time to work on tissue scaffold engineering and 3D printing projects with the Biology Department.

During my summer vacations I would alternate between lab research and returning home to Los Angeles for work as a STEAM coordinator at the Santa Monica Boys & Girls Club. I have a strong desire to give the youth in my hometown the opportunities to join STEAM programs that I never had. In the future I plan to create STEAM programs for socially or financially disadvantaged youth. The path God is leading me on has given me the chance to achieve that goal. I am now attending the Loma Linda University PhD program with a focus in bioengineering.

I am grateful to Dr. Michael Pecaut and my lab partner Nina Nishiyama for their mentorship in radiation research as I investigate the fields of neuroscience and regenerative medicine.

# DEVELOPING A RADIATION BIODOSIMETER USING EXOSOMAL MIRNA ISOLATED FROM MURINE BRAIN TISSUE

Foluwasomi Oyefeso, Nina Nishiyama, Amber Gonda, Nathan Wall, Michael Pecaut

Center for Health Disparities and Molecular Medicine, Biomedical Engineering Sciences, School of Medicine, Loma Linda University, Loma Linda, CA

Exosomes are small vesicles (30-150 nm) released from the cell by exocytosis during normal cell function. They have been reported to carry proteins, viral components, and nucleic acids. Further, they may have functionally diverse roles including cell-cell communication, disease transfer, and cell waste management. Still, much is unknown about the specific function of exosomes, and isolating exosomes from excised tissue is a relatively new research approach compared to traditional techniques. We are investigating the possibility of using the content of exosomes as a dose-specific radiodosimeter, focusing specifically on exosomal miRNA of brain tissue. We will compare the exosomal miRNA signature found in brain tissue with a similar profile characterized in the blood. We believe this biomarker will ultimately allow us to quickly assess any potential risks for radiation-induced neural tissue damage due to exposure during combat situations or nuclear disasters (e.g., Fukushima and Chernobyl). Our parameters for this research are sex (male and female), whole-body gamma-radiation dose (0, 2, and 4 Gy), and time after exposure (4 and 48 hours).

As a first step, we tested two independent methods for isolating exosomes from brain tissue and determined which method would give us a higher yield and greater sample purity. We began by homogenizing tissue from a mouse hemi-brain and using step-wise centrifugation to remove large cell components. Using the selected protocol, this step was followed by ultracentrifugation to pellet exosomes. The ultracentrifugation steps required a sucrose gradient (layered 2.5 M, 1.3 M, and 0.6) to purify exosomes apart from cell debris and other extracellular vesicles (Vella et al., 2018). After resuspending the exosome pellets, we compared the isolation methods by quantifying size, quantity, and purity using Nanoparticle Tracking Analysis (Malvern Panalytical). The research is ongoing, but we have successfully isolated exosomes within the acceptable size range. Following completion of exosome isolation, we will proceed to isolate total RNA from exosomes to characterize miRNA type and quantity.

# HIEL RUTANHIRA

## IMSD PARTICIPANT 2018

I am a 5th year PhD student in Dr. Hansel Fletcher's lab at Loma Linda University in the Department of Microbiology & Molecular Genetics and a member of the LLU IMSD program. Our lab's research focuses on periodontal disease and microbes, *Porphyromonas gingivalis* and *Filifactor alocis,* which potentiate disease progression.

I was born in Zimbabwe, Africa, and my parents brought us to the United States for a better education, and this move forced me to focus on school. I attended Mount Vernon Academy in Ohio for high school, and there Mrs. C, my science teacher, made me fall in love with biology. This love for biology led me to decide to major in biology with a biomedical emphasis. My interest in microbiology began in college at Southern Adventist University where I was able to do research which led me down this career path.

During my time at Southern Adventist University, I was inducted into the Tri-Beta Biological National Honor Society which piqued my interests in other areas of biology besides medicine. Upon acceptance into Loma Linda, I began working for Dr. Fletcher where I was partnered with Dr. Yuetan Dou, who has been pivotal to all the knowledge I have gained since the start of my program. My project is titled "The Role of Putative Membrane Transporters in Regulation of Oxidative Stress in *Porphyromonas gingivalis*." My short term goal is to continue writing my first author publication in hopes of being published next year.

When I'm not in the lab, I'm at the gym, playing sports, or singing for the church praise team. I have a passion for science and helping people, and I hope I can accomplish that in my career.

# THE ROLE OF PUTATIVE MEMBRANE TRANSPORTERS IN REGULATION OF OXIDATIVE STRESS RESISTANCE IN *PORPHYROMONAS GINGIVALIS*

Hiel Rutanhira, Yuetan Dou, Hansel Fletcher

Center for Health Disparities and Molecular Medicine, Department of Microbiology and Molecular Genetics, School of Medicine, Loma Linda University, Loma Linda, CA

Periodontal disease presents with chronic inflammation, bone destruction, and loss of the supporting structures of the teeth. *Porphyromonas gingivalis*, a Gram-negative anaerobic bacterium, causes periodontal disease in synergy with other oral microbes. The survival of *P. gingivalis* in the periodontal pocket requires an unknown mechanism(s) to overcome oxidative stress in addition to other environmental changes. Extracytoplasmic function (ECF) sigma factors are known to play a role in adaptation to environmental conditions via transcriptional regulation. In an overexpression strain of ECF sigma factor PG0162, we observed an upregulation of *PG1660,* another ECF sigma factor*,* along with the *PG1662-PG1663-PG1664-PG1665* (PG1662-PG1665) gene cluster. The *PG1662* to *PG1665* gene cluster, confirmed to be an operon, encodes an ABC transporter and is located downstream of ECF sigma factor *PG1660*, implicated in virulence and oxidative stress resistance. The upregulation of *PG1662-PG1665* operon and its downstream location in reference to *PG1660* suggests it could play a role in virulence or oxidative stress resistance mechanisms regulated by ECF sigma factors PG0162 and PG1660. PG1663, annotated as ABC transporter ATP binding protein in this ABC tansporter operon, shows about 40% sequence homology to the YecC, ATP binding protein, described in *Escherichia coli* as being involved with cystine transport. Cystiene metabolism has been shown to play a role in oxidative stress resistance in bacteria. We will test the hypothesis that the *PG1662-PG1665* operon encoding a putative ABC transporter is involved in cystine transport and could play a role in oxidative stress resistance in *P. gingivalis*. Isogenic mutant FLL500 (ΔPG1662-PG1665) defective in this operon was created by allelic exchange mutagenesis using *ermF* cassette. FLL500 showed increased sensitivity to oxidative stress compared to W83 parent. We observed significant decrease in gingipain activity in the isogenic mutant FLL500 compared to W83. Our observations suggest that this operon, *PG1662-PG1663-PG1664-PG1665* may play a role in virulence regulation and stress adaptation in *P. gingivalis*.

# EVELYN S. SANCHEZ-HERNANDEZ

## IMSD PARTICIPANT 2018

I graduated from California State University, Northridge (CSUN) in May 2017 with a Bachelor of Science in Cell and Molecular Biology. I recently completed my first year as a PhD student here at Loma Linda University. I chose one of the new programs being offered which is Cancer, Development and Regenerative Biology (CDRB).

Throughout my undergraduate career, experiences shaped my purpose in life. Having the opportunity to conduct research as a MARC scholar at CSUN allowed me to discover my passion for conducting biomedical research. Also, observing a member of my family being affected by cancer made me realize the importance of biomedical research in our society. Many patients' lives depend on the answers that scientists seek in their laboratories. I want to contribute to increase our understanding on complex diseases such as cancer.

After completing my third lab rotation during my first year, I chose Dr. Carlos A. Casiano's laboratory. Dr. Casiano's project focusing on the role of glucocorticoid receptor (GR) signaling in prostate cancer and its contribution to chemotherapy resistance interests me the most. I want to continue working on his project which also incorporates a health disparity component that affects the African American population more compared to European American patients. My goal is to contribute to elucidating the mechanism by which GR may drive chemoresistance in prostate cancer.

This summer I enjoyed working with Vivianna Williams and Hannah Sukarloo focusing on studying the expression of GR in primary as well as in metastatic prostate cancer tissues.

# OPTIMIZATION OF IMMUNOFLUORESCENCE MICROSCOPY STAINING OF GLUCOCORTICOID RECEPTOR IN PROSTATE CANCER CELL LINES

Evelyn Sanchez-Hernandez, Hannah Sukarloo, Vivianna Williams, Shannalee Martinez, Leanne Woods-Burnham, Carlos Casiano

Center for Health Disparities and Molecular Medicine, School of Medicine, Loma Linda University, Loma Linda, CA

Androgen deprivation therapy (ADT) and chemotherapy are standard-of-care treatments for advanced prostate cancer (PCa). However, resistance to these therapies occurs, and the underlying mechanisms are not completely understood. Synthetic glucocorticoids (GC) such as dexamethasone are administered to PCa patients to alleviate the side effects of chemotherapy. GCs exert their action by binding to the glucocorticoid receptor (GR) in the cytoplasm, leading to GR translocation into the nucleus where it activates gene expression. However, use of GCs in PCa therapy is currently being re-evaluated because GR has been shown to bypass androgen receptor (AR) blockade by ADT and enable activation of cancer-associated AR-targeted genes. African American (AA) patients with PCa are more likely to develop a more aggressive form of PCa and twice as likely to die from this malignancy than European American (EA) men. Also, AA men have higher circulating cortisol levels (endogenous GC) and increased GR sensitivity for GCs. These observations led to the hypothesis that enhanced GR signaling in AA men with PCa may prime them to develop increased resistance to therapy. As a first step in assessing GR protein expression in prostate tumor tissues from EA and AA men, it is necessary to optimize conditions to detect GR in PCa cells by immunofluorescence microscopy staining. We demonstrated that commercially acquired anti-GR antibodies react specifically with this protein in immunoblots of total protein from the PC3 and 22RV1 PCa cells. We have been optimizing immunofluorescence staining conditions to detect GR translocation to the nucleus of these cells upon dexamethasone treatment. We expect to observe GR immunofluorescence staining in the cytoplasm of untreated cells and nuclear staining in dexamethasone-treated cells. This optimization allows us to identify the proper anti-GR antibodies and conditions to assess GR expression in prostate tissue arrays from AA and EA PCa patients critical to understanding the role of GR signaling in PCa health disparities.

# NICHOLAS SANCHEZ

## IMSD PARTICIPANT 2018

After earning my bachelor's degree in medical biology from the University of California, Riverside, I was fortunate enough to be afforded the opportunity to continue my education through Loma Linda University. As a PhD student at this institution, I have been absorbing the experience necessary to succeed in pursuing a career in science policy and research. During my studies here at LLU, I have been working in Dr. Wolff Kirsch's lab on a breadth of projects spanning across multiple disciplines. My efforts have been focused on the pathogenesis of neurodegenerative diseases, specifically on copper dysregulation, its role in the onset of dementia, and this dysregulation may lead to the development of Alzheimer's disease. This is a contested field where all ideas are hotly debated and scrutinized with established researchers lining up on a radiant of opposing viewpoints. Working in this environment is intimidating yet brings its own excitement from being so dynamic.

My project has previously earned the Alzheimer's Greater Los Angeles Young Investigators Award, placing it among few projects recognized in Southern California for this field. Having done my thesis proposal, I'm working towards gathering data to test my project's hypothesis and determine the further direction of my work.

Outside of my work as a young scientist, I find my peace in long distance running, digging into a well told story, and finding the best way to spend time with my family. Along with everything else in my life, I feel quite fortunate how I am surrounded with those who provide support and to be in an institution that allows me to thrive.

# COPPER TRANSPORT DYSREGULATION AND NEUROTOXICITY IN ALZHEIMER'S DISEASE: PROGRESS

Nicholas Sanchez, Shekinah Dusunmu, Wolff M. Kirsch

Center for Health Disparities and Molecular Medicine, Neurosurgery Center for Research, Training and Education, Department of Biochemistry, School of Medicine, Loma Linda University, Loma Linda, CA

Therapeutic approaches focused on preventatively clearing amyloid-beta, the peptide name in the prominent theory in Alzheimer's disease (AD) pathogenesis, have neither decelerated disease progression nor achieved improved cognition. Building from an established correlation between copper dysregulation and neurodegenerative disorders, our lab has previously shown the accumulation of copper in neuronal axons in AD-affected human brain samples as compared with controls, with a proteomic screening showing increased expression of copper transport proteins, specifically the dynactin subunit p62. Taken together, these results suggest an abnormality in copper trafficking in this context. We hypothesized the dysregulation of the copper transport system is a key step in AD pathogenesis due to APOE4 expression. This project aims to understand and reveal the potential pathway to this debilitating disease. We have begun three distinct approaches in looking at Cu and AD: 1) Synaptic vesicle isolation protocol was examined using AD and control human brain samples for comparison, 2) SH-SY5Y neuroblastoma cell line was used to test a siRNA transfection protocol to knock down the Atox1 copper transporter, using Western Blot for validation, and 3) Copper movement in live SH-SY5Y cell culture was imaged to test TM4-157 probe viability as well as tissue staining using Wilson's Disease (WD) brain and control brain comparisons. Preliminary tests have revealed the need for troubleshooting our chosen protocols. Further results from these experiments will help determine the direction we move forward with regards to copper and its role in the emergence of Alzheimer's disease.

# JULIO D. VEGA-TORRES

## IMSD PARTICIPANT 2018

I am currently a PhD candidate in the Department of Physiology with a specific focus on neuroscience and psychological disorders such as post-traumatic stress disorder (PTSD). My main interest is to understand the implications that nutrition has on stress, fear, dopamine, and brain circuitry. More importantly, my long-term goal is to be an important part in improving the quality of psychological disorders management and addressing mental health disparities in at-risk populations.

I have the privilege of being part of FigNeuro Lab Inc (Dr. Johnny D. Figueroa's laboratory). The lab has been blessed with the contribution of many summer students throughout the years. This summer we have a high school student, Kevin Liu, with great interest in research. His hard-working attitude and great ability for critical thinking motivates me to continue mentoring the future generation of scientists.

Besides being in the lab, I love spending time with my wife and friends, playing the saxophone, playing tennis, playing pickleball, and training for mountain bike races. I thank God for the opportunity of being part of LLU and, most important, the Center for Health Disparities and Molecular Medicine.

"True success in education, as in everything else, is found in keeping the future life in view" (Ellen Gould White).

## JUVENILE OBESITY LEADS TO ABNORMAL NEURAL AND BEHAVIORAL SUBSTRATES UNDERPINNING FEAR AND ANXIETY

Julio D. Vega-Torres, Elizabeth Haddad, Jeong Bin Lee, Priya Kalyan-Masih, Leonardo López Pérez, Darla M. Piñero Vázquez, Yaría Arroyo Torres, José M. Santiago Santana, Andre Obenaus, Johnny D. Figueroa

Center for Health Disparities and Molecular Medicine, Department of Basic Sciences, School of Medicine, Loma Linda University, Loma Linda, CA, and University of California Irvine, Department of Pediatrics, Irvine, CA; University of Puerto Rico Carolina, Carolina, Puerto Rico; Metropolitan University, San Juan, Puerto Rico

Obesity has been identified as a major risk factor for anxiety disorders. Fear conditioning has long been considered a central pathogenic mechanism in anxiety disorders. The objective of this study was to determine the impact of an obesogenic Western-like high-fat diet (WD) on fear conditioning. We hypothesized that consumption of a WD during adolescence impairs conditioned fear as revealed by the magnitude of startle response to an auditory stimulus. Adolescent Lewis rats were fed for eight weeks with either the experimental WD diet (41.4% kcal from fat) or the control diet (16.5 % kcal from fat). Acoustic startle reflex (ASR) and fear-potentiated startle (FPS) responses were assessed to determine fear, attentional processing, and startle plasticity. We found that rats that consumed a WD during adolescence exhibited reduced acoustic startle responses. Notably, the FPS paradigm revealed that WD-fed rats exhibited marked impairments in fear-associative learning. We showed that the rats that consumed the WD exhibited increased background anxiety to the acoustic stimuli. These behavioral effects were associated with a robust disruption in the medial prefrontal cortex and amygdalar structural integrity and connectivity as revealed by diffusion tensor imaging (DTI) indices. Altogether, our findings demonstrate that adolescent WD consumption has a profound impact in the neural and behavioral substrates implicated in anxiety. This study is important because it prepares the ground to delineate the mechanistic links between obesity and anxiety disorders. We anticipate that our research will inform the path to needed biomarkers and interventions for improving the quality of stress and anxiety management, particularly in a growing obese population.

# JONATHAN WOOTEN

## IMSD PARTICIPANT 2018


I am an alumnus of Oakwood University in Huntsville, AL, where I majored in chemistry. It was at this institution that I had my first exposure to basic science research studying nanoparticles as potential anti-cancer agents. During my time as a student, I also had the opportunity to do an internship at the Centers for Disease Control and Prevention (CDC). This experience gave me insight into the variety of research possibilities available for applying chemistry to the public health environment.

After completing my Bachelor of Science in Chemistry, I acquired a Master's degree in Chemistry at Georgia State University (GSU) in Atlanta, GA. My research experience at GSU inspired me to pursue a career involving drug synthesis, testing, and evaluation in relation to human health. Considering this interest, I am pleased to say I am on track to achieving this goal, having recently completed my third year as a PhD Pharmacology student here at Loma Linda University. Albeit a challenging program, the resources and mentorship provided at this institution have taken my knowledge and research skills to the next level. I am currently working with Dr. Eileen Brantley, Assistant Professor in the Division of Pharmacology. I am working on a fascinating research project which focuses primarily on determining the potential anticancer actions of aryl hydrocarbon receptor (AhR) agonists and related signaling mechanisms.

With the experiences, knowledge, and skills gained both at the CDC and Loma Linda University, my long-term career goal is to work for the CDC, performing cutting-edge research focused on elucidating the effects of various drugs on human health.

# PLANT ISOLATE DIBENZYL TRISULFIDE POTENTLY INHIBITS CYTOCHROME P4501 ENZYME ACTIVITY AND THE GROWTH OF BREAST CANCER CELLS DERIVED FROM AFRICAN AMERICAN PATIENTS

Jonathan Wooten, Shaniece Wauchope, Nicole Mavingire, Petreena Campbell, JéAnn Watson, Maxine Gossell-Williams, Rupika Delgoda, Eileen Brantley

Center for Health Disparities and Molecular Medicine, Department of Basic Sciences, School of Medicine, Loma Linda University Health, Loma Linda, CA and Natural Products Institute, University of the West Indies, Mona, Jamaica

Triple negative breast cancer (TNBC), characterized by tumors that lack expression of the estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2), carries a poor prognosis. African American women develop TNBC at disproportionately higher rates than women from other ethnic groups. Dibenzyl trisulfide (DTS), found expressed in the Jamaican plant *Petiveria alliacea*, has been shown to inhibit the growth of several cancer types. However, little is known about whether this plant isolate displays anticancer activity in TNBC cells derived from African American patients or modulates cytochrome P450 1 (CYP1) enzyme activity. This work, as part of an on-going ethnopharmacology-based bioactivity screening, was designed to fill this deficit. African American TNBC (AA-TNBC) cells HCC1806 and MDA-MB-468 were treated with varying concentrations of DTS for 48 h and cell viability assessed using the Alamar Blue assay. DTS potently inhibited the growth of HCC1806 and MDA-MB-468 cells, producing $IC_{50}$ values of 10.6 ± 1.2μM and 10.3 ± 2.0μM, respectively. Additionally, we discovered that DTS induced apoptosis in these cells. Furthermore, we investigated the ability DTS has to impact the activities of the CYP1 family of enzymes which are known to convert procarcinogens to carcinogens. The $IC_{50}$ values obtained for CYPs 1A1, 1A2 and 1B1 were 1.68 ± 0.3μM, 1.9 ± 0.2μM and 1.29 ± 0.3μM, respectively. These data indicate that DTS exhibits potent inhibition of the activities of these enzymes. In particular, DTS was able to bind to CYP1A2 in accordance with irreversible kinetics. In addition, DTS reduced CYP1 mRNA expression in both cell lines. Our findings provide a rationale for *in vivo* evaluations of DTS as a potential candidate for chemoprevention and for treating AA-TNBC patients.

# School of Behavioral Health & School of Public Health

Raveena Chara
Shevel DaCosta-Davis
Simone Deshields
Akinchita Kumar
Marisol Lara
Nipher Malika
Amanda Mendez
Lauren Miller
Navdeep Randhawa
Rajhvir Singh

# RAVEENA CHARA

## BEHAVIORAL HEALTH PARTICIPANT 2018

The bridge between health and psychology has always intrigued me. Early in my life I learned that physical wounds often receive attention and usually heal whereas psychological wounds often do not. This reality piqued my interest in studying human behavior, and I soon discovered my passion in the field of psychology. Currently, I am pursuing my Bachelor of Arts in Psychology at California State University, San Bernardino. While in college, I have had the opportunity to work in many different settings with diverse groups of people, ranging from working in an adult medical clinic to tutoring high school students and working with children as a child development intern. Each of my experiences has reaffirmed my interest in improving mental health to benefit the person as a whole.

While I am generally interested in minority mental health and health disparities, I have a specific interest in the experiences of the Punjabi community. As a member of the Punjabi community, I have seen how mental health is ignored and rarely considered a priority, especially among women. My goal in continuing my education and training is to be able to reach out to the women of my community to find how I can assist them in their journey towards good mental health and wellbeing.

My training experience in Dr. Susanne Montgomery's lab has been invaluable. The opportunities I have been able to participate in have helped me broaden my knowledge and understanding of mental health disparities. Thanks to the guidance of Dr. Montgomery and my lab mentor, I feel more prepared for further research in psychology. In the future, I would like to combine my love for my community and raising mental health awareness.

# EXPLORING SATISFACTION WITH LIFE AMONG PUNJABI SIKH WOMEN IN CALIFORNIA

Raveena K. Chara, Guljinder K. Chera, Akinchita Kumar, Navdeep K. Randhawa, Lisa Roberts, Susanne Montgomery

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Anxiety and depression can be important indicators of one's subjective wellbeing. Furthermore, subjective wellbeing often affects one's satisfaction with life. Recently a few studies have noted an increased risk of negative mental health experiences for Punjabi Sikh Asian-Indian (AI) women in the US including higher rates of anxiety and depression. For Punjabi women, the literature points to joint-family households serving both as protective buffers against and risk factors for negative mental health experiences. However few studies have explored women's level of life satisfaction in this regard. Our aim was to explore differences on the Satisfaction with Life Scale (SWLS) between Punjabi Sikh women (N =154) who did (48%) vs. did not (50%) live in joint-family households. Participant women (*M*=36) lived in the US for an average of 18 years; most women were married (85 %), completed the survey in English (74%), and were highly educated (86% BA >). Bivariable results indicate that satisfaction with life (SWL) was higher in women who lived in joint-family households, were born in India, older, and married. Moreover, higher SWL was also significantly associated with lower levels of depression and anxiety. Simple multivariate regression results, however, revealed that only depression remained significantly negatively related to SWL, explaining 21.6% of the variance. Our results point to lifestyle and cultural nuances that affect the subjective SWL of Punjabi Sikh women in CA. It is noteworthy that, unlike the general US population, many Punjabi Sikhs still live in joint-family homes and this living situation is protective for this AI subgroup. Mental health professionals working with Punjabi women should be aware of the potential relationship between family structure and life satisfaction. They should also take their patients' larger family into account to meet their mental health needs. Further research exploring the influence of family structure on Punjabi women's life satisfaction and other measures of wellbeing is recommended.

# SHEVEL DACOSTA-DAVIS

## BEHAVIORAL HEALTH/PUBLIC HEALTH PARTICIPANT 2018

Medical school has been a journey. While on this journey, I am learning that even though doctors are here to help alleviate patients' pain, it is important to remember how critical food is to medicine. My desire is to be a physician that has the knowledge to educate my patients on healthy living by using the most cutting-edge research available. I am a Loma Linda University (LLU) graduate with a Master's in Biomedical Sciences and now a second-year medical student at LLU. I also volunteer my time tutoring middle school students in the City of San Bernardino.

I am very passionate in giving my service to underserved communities because I grew up in one myself. As a medical student, I am realizing how interconnected research, medicine, and health are. It is hard for the medical field to thrive without scientific research, and it is impossible to stay healthy without first taking care of one's health. I am currently working with Drs. Camille Clarke and Susanne Montgomery in their research project on the "The Full Plate Diet" for Latinos.

"The Full Plate Diet" is an innovative way of eating healthy by including more fiber-rich fruits and vegetables in one's diet alongside an increase in water consumption. In this adaptation, we also address emotional resiliency in eating and staying healthy. Through this research, I am learning how critically important a person's emotions are in wanting to become and stay healthy. I also learned that consuming just 40 grams of fiber in one's daily diet can make a difference in losing weight.

I want to thank Dr. Clarke's research team for facilitating, guiding, and educating me this summer in the importance of resiliency and eating healthy to better one's health.

# A DEEPER LOOK AT MENTAL HEALTH AND LIFESTYLE HABITS AMONGST LATINOS

Shevel DaCosta-Davis, Maud Joachim-Celestin, Marisol Lara, Lauren Miller, Simone DeShields, Susanne Montgomery, Camille Clarke

School of Medicine, Loma Linda University, Loma Linda, CA

Studies have shown that people with poor mental health (i.e., depression and anxiety) have a higher prevalence of obesity. Hispanics have the highest prevalence of obesity in the US, tend to enroll less in weight loss programs, lose less weight than non-Hispanic whites, and are more likely to regain weight at follow-up. Moreover, weight loss studies tend to exclude patients with a diagnosed mental illness because of adherence concerns. Few studies have been conducted on the relationship of mental health and weight loss, specifically for Latinos. Our poster aims to evaluate the correlation between anxiety and depression and Latino participants' readiness to change dietary patterns. A pilot survey was collected from Latino participants (N=50) residing in Southern California. Quantitative data analysis was conducted using SPSS v. 24. Participants were asked questions regarding perceived weight status (normal, overweight, obese), reported weight, depression (PHQ9), and anxiety (GAD7). The majority (52%) of our participants were overweight or obese. Those who had mild anxiety had a marginally statistically significant lower weight when compared to those with severe anxiety ($p=.06$). When performing Post-Hoc analysis, there was a statistically significant difference in weight between those with no depression and those with moderate depression ($p=.02$). Although our results showed no significant correlation between mental health and readiness to change, our findings highlighted that those who reported higher weights scored higher on the anxiety ($p=.06$) and depression ($p=.02$) scales. Many lifestyle interventions fail to address the potential impact depression and anxiety may have on weight loss. It is important to address and provide solutions for Latino participants who might suffer from depression and anxiety during their weight loss journey. Further studies need to be done to address behavioral mechanisms to help weight loss participants manage their mental health, such as the Community Resiliency Model, that can help participants cope with their anxiety and depression to achieve maximum health.

# SIMONE DESHIELDS

## BEHAVIORAL HEALTH/PUBLIC HEALTH PARTICIPANT 2018

Born in Brooklyn and raised in Loma Linda, I graduated from Redlands Adventist Academy in 2011. In 2015, I received a BS in Psychobiology and a minor in Society & Genetics from UCLA. This fall I will be entering my sophomore year of medical school at Loma Linda University (LLU). I am very passionate about serving the community and take any opportunity I can to serve. Last year, I served as site coordinator for LLU Community-Academic Partners in Service (CAPS) as well as a tutor at Indian Springs High School. I aspire to become a well-rounded physician that listens and cares for the needs of my patients. Recently, my interest has been in Family Medicine with a subspecialty in Preventive Medicine or Urgent Care. Although medical school is time consuming, I enjoy spending leisure time with family and friends, traveling, and practicing yoga.

Currently, I am working on an obesity research study, adapting "The Full Plate Diet" (FPD), in partnership with local community health workers to a more culturally meaningful context for Latinos. Our new version of the FPD involves a comprehensive health approach including culturally aligned motivational aspects. Unlike many diet plans, it is very simple. The focus is to increase the intake of dietary fiber indirectly by encouraging fiber-rich fruit and vegetable consumption using familiar foods and dishes along with drinking more water.

I truly appreciate Dr. Camille Clarke, Dr. Susanne Montgomery, and Dr. Maud Joachim-Celestin for their guidance, knowledge, and patience throughout this process. I also appreciate the collaboration and companionship of my classmates, Shevel Dacosta-Davis and Lauren Miller. It has been a valuable growing experience allowing me to serve the community in a meaningful way.

# A LATINO-CULTURAL PERSPECTIVE: HOW DOES ACCULTURATION AFFECT INTENTION TO ADOPT A HEALTHY LIFESTYLE?

Simone DeShields, Maud Joachim-Célestin, Lauren Miller, Shevel DaCosta-Davis, Marisol Lara, Susanne Montgomery, Camille Clarke

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A balanced diet is essential for a healthy lifestyle and may be heavily influenced by one's cultural background and ethnicity. In the United States, Latinos make up the largest minority group and have the highest prevalence of obesity. Research has shown acculturation and country of origin are associated with a decrease in the "healthiness" of the Latino diet, including a reduction in fiber intake. Furthermore, less acculturated Latinos tend to consume more fruit, rice and beans and less sugar and sweetened beverages. The purpose of this poster is to examine the association between acculturation and intent to change one's diet in order to achieve a healthy lifestyle. A survey was administered to Latinos (N=50) residing in Southern California to determine the relationship between acculturation (ability to write, read and speak English, the use of English to communicate, and country of origin: US born or not) and intent to improve diet and exercise (measured on a Likert scale 1-5, recoded into agree, neutral and disagree). One-way ANOVA and Spearman's correlations were used to analyze data. Results indicate that US birth was significantly associated with increased intent to eat healthy ($p<.01$) and exercise ($p<.05$). When language was used, the relationship with intent to exercise more and eat healthier became stronger ($p<.001$). These results are of importance as Latinos have among the highest frequency of obesity, which is often a precursor for lifestyle-based diseases including diabetes, heart disease, and cancer. To address obesity in this population, it is important to understand their willingness to initiate a healthy lifestyle may be influenced by their place of birth; ability to write, read and speak English; and the use of English to communicate with their social network. Since these measures of acculturation influenced intent to adopt healthier behaviors, health educators and healthcare providers working with Latinos would benefit from assessing acculturation prior to making lifestyle recommendations.

# AKINCHITA KUMAR

## PUBLIC HEALTH PARTICIPANT 2018

I recently graduated with a Master of Science in Public Health with a specialization in Global Health from Southern New Hampshire University. Previously I received a Bachelor of Arts in Psychology from University of California, San Diego. I have gained experience in developing and implementing community-based initiatives, health equity research, and health education and promotion programming to address social and public health issues affecting culturally and linguistically marginalized populations. I have a personal interest in exploring health disparities and feel it is especially important for ethnic communities to create narratives that explore multiple factors of community health within the complex dynamics of culture, language, and gender. I am planning to attend medical school this upcoming year and expand my experiences in contextual social/medical research to help better prepare me as a physician in a diverse society.

My training experience in Drs. Susanne Montgomery and Lisa Roberts' lab has been irreplaceable. Our team works on research exploring health disparities in Punjabi Asian-Indian communities within the Inland Empire. This research allowed me to get to know the narratives of the Punjabi community and the hardships they face integrating into American society. I am eternally grateful for the local Punjabi community, their stories, and the profound influence they have had on my life and future career. They have helped me realize that people are much more complex and nuanced than a set of symptoms. They have identities and feelings to account for when treating their emotional, mental, and spiritual health.

Drawing on my training and experience in the fields of public health, psychology, healthcare, and social and behavioral research, I am excited to continue my commitment to addressing health disparities in low-income communities through a cross-disciplinary approach.

# EXPLORING DISCRIMINATION AND MENTAL HEALTH IMPLCIATIONS FOR PUNJABI YOUNG ADULTS IN POST 9/11 AMERICA

Akinchita Kumar, Semran K. Mann, Lisa Roberts, Susanne Montgomery

School of Behavioral Health, Loma Linda University, Loma Linda, Ca

Recent studies on Punjabi Asian-Indians (AI) point to higher rates of mental distress experienced because of the conflicting tensions between familial expectations and societal expectations of integration into the dominant culture. The post-9/11 climate further increased the threat of violence for Punjabi AIs, adding instances of misidentification and discrimination, to their integration burden. Few studies have explored these issues among American Punjabi young adults. Our aim was to explore the relationship between sociocultural and integration factors, misidentification, discrimination, and mental distress among young adult Punjabi AI's in California. We conducted mixed-methods community-based participatory research using semi-structured key informant interviews (n = 8), focus groups (n = 17), and a self-administered anonymous survey (n = 99) to explore correlates of depression and anxiety. A survey that included the Patient Health Questionaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7) as well as a measure for discrimination was given to young adults ages 18-25. Results indicated four main themes that point to multiple challenges experienced by young adult Punjabi AIs: (a) misidentification; (b) discrimination; (c) pressures to assimilate, integrate, and be accepted in American society; and (d) mental health consequences resulting from multiple burdens. Our quantitative results verified these themes and indicated mild to moderate anxiety ($M$=6.60, SD 5.57) and depression ($M$=6.01, SD 5.57). At the bivariate level, discrimination correlated with Punjabi language preference, fewer years lived in the US, and non-US place of birth. Linear regression models run to explore explanatory factors for anxiety and depression indicated that a model exploring discrimination significantly predicted both anxiety ($R^2$=.324) and depression ($R^2$=.332). We recommend expansion of culturally appropriate health education, including providing inclusive mental health promoting practices to increase awareness and alleviate distress in this community.

# MARISOL LARA

## PUBLIC HEALTH PARTICIPANT 2018

My journey to public health has been one of many discoveries and adventures. For years I unknowingly aligned my purpose to Owen Arthur's message: "For he who has health has hope; and he who has hope, has everything." I have always loved serving people. Health and medicine have always intrigued me, yet I also knew health and healing were not confined to medicine alone. Just as our cells function together to keep us healthy and thriving, so must a network of health professionals and the community come together to create a healthy, thriving society.

My MPH program at Loma Linda University challenged me to identify what health meant to me, to my career, and to those whom I will be serving. I spent my time as a graduate student exploring "health" from the perspective of those in the poorest health conditions while conducting a health fair in Zimbabwe, gaining a new understanding of "health" working with homeless women on feminine hygiene, and working with Latino community health workers on an obesity prevention program. I realized how diverse "health" can be and that culture is critically important. Although the term "health" has been different in each context, I believe that the hope and excitement to improve one's health—when provided with the means and knowledge—is shared across international and cultural borders. My hope is to continue to explore avenues that bring hope and healing to individuals through continued research, pursuing my medical degree, and active engagement with the communities I wish to serve.

I want to thank Dr. Camille Clarke, Dr. Susanne Montgomery, and Dr. Maud Joachim-Celestin for providing me with an incredible opportunity to learn and work alongside them as they bring hope and healing to individuals, families, and communities.

# EXAMINING THE FEASIBILITY AND EFFECTIVENESS OF A COMMUNITY-BASED MODEL FOR PREVENTION OF OBESITY AMONG LATINOS

Marisol Lara, Maud Joachim-Celestin, Lauren Miller, Simone DeShields, Shevel Dacosta-Davis, Susanne Montgomery, Camille Clarke

School of Medicine, Loma Linda University, Loma Linda, CA

Latinos, the largest ethnic minority in the US, disproportionately present with overweight/obesity and, as a consequence, have high rates of diabetes. They are also less likely to participate and/or complete weight loss programs due to complex cultural and socioeconomic barriers. Community health workers (CHWs) have been successfully used to bridge the cultural gap and optimize programs for Latinos. Their insights about perceptions, beliefs, and attitudes regarding obesity within the Latino community has proven critical in gaining a better understanding of obesogenic behaviors. This poster documents the cultural and contextual adaptation of the Full Plate Diet (FPD) program which occurred in partnership between health professionals and Latino CHWs. As part of a community-based participatory research project, a bi-lingual physician led Spanish-language discussions to adapt the FPD through the use of popular education methods of co-learning between medical students (N=3) and CHWs (N=5) over a two-week period, followed by a CHWs-led pilot test of the FPD program. A training pre/posttest and post experience focus group were conducted and analyzed. Participants reported liking the simplicity of the curriculum, the adapted program's focus, relevance to the Latino community, the ability to adapt meals to fit their and their families' expectations, and the effectiveness they experienced when following the program. At post-assessment, all reported being likely or very likely to use the skills learned in the program, and all CHWs lost weight. The augmented FPD, named "My Full Plate" ("Mi Plata Completo") by the CHWs is a promising lifestyle program for Latinos with potential positive long-term health benefits. The use of a non-diet approach that incorporates culturally acceptable healthy dishes, and education on obesity prevention with solutions to specific barriers Latinos face, resulted in a program that is seemingly simplistic, easy to follow, and uses resources readily available to the community it is intended to reach.

# NIPHER MALIKA

## BEHAVIORAL HEALTH PARTICIPANT 2018

I am a PhD student in the Social Policy and Social Research program in the School of Behavioral Health at Loma Linda University. Through previous training in global health and epidemiology and work with the LLU Institute for Community Partnerships (ICP), I was able to apply my skills in the health disparities field including utilizing Community-Based Participatory Research methodologies in academic, county, state, and non-profit settings. My interests lie in how immigrants and low-income families and communities navigate social systems and supports, including education, health, child welfare, juvenile/criminal justice, and the social safety net. My background along with my desire to bring about change in communities has allowed me to work on diverse projects tackling obesity, incarceration, environmental health, education, and at-risk populations.

Under the mentorship of Dr. Susanne Montgomery, my research focus has been on identifying whether the Kessler 6 Psychological Distress scale, a world-used measure for identifying mental distress, can accurately identify psychological distress among low-income minority students. Most interesting is working on something current, relevant, and a point of discussion in our world today. Mental health disorders commonly occur and become a financial impairment to many countries. Therefore, identifying the best way to recognize early onset and intervene is of great importance to public health.

Aside from research, I volunteer at Youth Hope, a non-profit helping homeless, runaway, and at-risk youth in Redlands and the Inland Empire. My role at Youth Hope is to help these youth attain their GED and pursue higher education if they desire. When I am not doing research, volunteering, or in class, I love hiking, running, doing kettlebells, and watching movies.

I would like to thank Dr. Montgomery for support, guidance, and giving me the freedom to run with a hypothesis I was curious about.

# THE RELIABILITY AND VALIDITY OF K6 AMONG MINORITY ADOLESCENTS

Nipher Malika, Juan-Carlos Belliard, Susanne Montgomery

The Institute for Community Partnerships and Behavioral Health Institute,
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Mental health disorders are common and place financial burdens on many countries throughout the world. Identifying these disorders early in order to address them at their onset is crucial. One of the most widely used scales, the Kessler Psychological Distress scale (K6), has been noted for its high specificity and sensitivity in identifying cases of mental illness among adults. However, findings regarding its reliability and validity among adolescents, especially low-income minority youth, are limited, an issue of importance since it is well established that reactions to stressors are different across racial and socioeconomic groups. Since cultural and social factors contribute not only to the causation of anxiety and depressive symptoms but are also related to coping styles and likelihood of seeking treatment, this study aimed to evaluate the psychometric properties of the K6 in a predominantly low-income, minority, school-based population. A cross-sectional study was conducted on youth (N=24,377) grades 5$^{th}$ through 12$^{th}$ grade from an inland Southern California low-income school district (>78% free lunch eligible). The confirmatory factor analyses conducted with EQS version 6.3 revealed that the K6 scale consisting of one factor was not a good fit, suggesting that the scale is not a suitable screening tool for depression in this low-income, minority population. It is possible that the items in the scale tap different constructs when used among minority adolescents. Indeed, it has been argued that depression among minorities presents differently in comparison to Caucasians. Because most mental disorders have been shown to have an early age-of-onset and are significantly associated with adverse societal costs, better screening scales that more accurately aid in the early identification of psychological distress among minority adolescents are needed.

# AMANDA L. MENDEZ

## BEHAVIORAL HEALTH PARTICIPANT 2018

As a naturally curious person, learning and growing in my graduate program at Loma Linda University (LLU) has been an adventure for me. I entered my PsyD program in the School of Behavioral Health in the fall of 2015 and have practiced therapy as a student psychologist for two years during which I have been stretched and developed into a creative, sensitive, and attuned clinician. In addition to clinical work, research remains an integral piece of my education and my contribution to the field of psychology.

I have had the pleasure and honor of joining the Stage 2 Outpatient Adolescent Recovery (SOAR) research lab at LLU´s Behavioral Health Institute. SOAR is an adolescent outpatient program utilizing intensive Dialectical Behavior Therapy (DBT) Plus. SOAR was developed to help support adolescents who experience emotional dysregulation and have a history of self-injurious or suicidal behavior. We are currently in program development stages to create a multi-level intervention addressing emotional and behavioral difficulty while maintaining DBT skills. In this lab, I have met outstanding researchers, both well-established and beginners like me. This introduction has taught and inspired me to participate in translational research that can inform and shift the treatment to community-based settings more accessible to people in need. Practicing with LLU's philosophy of whole-person care–following the biopsychosocial-spiritual model–has transformed how I look at healthcare and the relationships with my fellow providers and patients.

My interests outside of graduate school include volunteering in ministry at my church, weightlifting in my home-gym, cooking with my husband, and spending time with my family and 5 pets.

I want to thank Dr. Bryan Cafferky for his leadership and support in our lab and Dr. Susanne Montgomery for her expertise and guidance as a leader in her field.

# HIGHER LEVELS OF AGREEABLENESS ARE ASSOCIATED WITH HIGHER RATINGS OF THERAPEUTIC ALLIANCE

Amanda L. Mendez, Michael Finlay, David Vermeersch, Susanne B. Montgomery

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The relationship between therapeutic alliance and psychotherapy outcomes has been well documented in the literature. Therapeutic alliance is considered a "main curative component" in the interpersonal process of therapy and is the foundation necessary for successful therapy outcomes across various orientations of psychotherapy. Still, far less research has examined the relationship between specific therapist personality characteristics and the quality of the therapeutic alliance. The current study aimed to examine the relationship between several therapist personality traits and the therapeutic alliance. The study utilized the Working Alliance Inventory Short-Form (WAI-S) to measure client-reported therapeutic alliance and the NEO-FFI to measure therapist personality. A one-way ANOVA was conducted to compare the relationship of agreeableness to the therapeutic alliance in groups of highly rated, average rated, and low rated working alliance. Therapists were grouped by the quality of their working alliance score and the scoring profile associated with each factor. On the NEO-FFI, agreeableness is divided into levels of low (*T= 35-44)*, average (*T= 45-55)*, high (*T= 56-65)*, and very high (*T > 65).* Those who scored in the high range *(T> 56)* of agreeableness demonstrate the highest levels of warmth, empathy, honesty, and trustworthiness. Results indicated that agreeableness was found to be significantly related to the quality of the therapeutic alliance ($F [2, 39] = 7.09$, $p < .00$). Overall, higher levels of agreeableness were associated with higher ratings of therapeutic alliance as well as the highest level of participation in the study. These findings suggest that therapist agreeableness is one important ingredient in strengthening the therapeutic alliance and reducing premature dropout. These findings also suggest that it is important for therapists to better understand their degree of agreeableness and, if necessary, work to develop greater agreeableness for the purpose of strengthening their therapeutic alliances with patients.

# LAUREN MILLER

## BEHAVIORAL HEALTH/PUBLIC HEALTH PARTICIPANT 2018

I have always been fascinated with the profession of healing and had a passion for lifestyle medicine. My interest for the two was especially piqued while serving at a medical missionary training institute in 2012. Here I saw many doctors volunteering time and talent to help the community incorporate principles of nutrition, exercise, mental health, and spiritual health into their lifestyles, which helped many people increase their quality of living and greatly reduce their usage of certain medications. These testimonies inspired me to also pursue a course in medicine, and I am thankful to have recently completed my first year of medical school at Loma Linda University.

Before arriving at Loma Linda, I graduated in 2015 from the University of Nevada Reno with a Bachelor's degree, *In Cursu Honorum*, in nutritional sciences and was awarded Student of the Year in that department. During my time in undergrad, I continued to cultivate my interest in lifestyle medicine by volunteering for many health fairs, cooking schools, and massage clinics organized by my local church. When not volunteering with my church as prayer meeting leader, Sabbath school teacher, teen mentor, or board member, I worked as a medical scribe in a local emergency department as well as a snowboard instructor during the winters.

In the future I hope to pursue a residency in either preventive medicine or orthopedic surgery, incorporating what I have learned about the importance of the mind-body connection in the treatment of my patients. I am thankful to Dr. Camille Clarke, Dr. Maud Joachim-Celestin, Dr. Susanne Montgomery, and the rest of our team for the opportunity to get hands-on experience in our research project incorporating "The Full Plate Diet" and the community resiliency model into the Latino community.

# EVALUATING THE INFLUENCE OF NATIVITY, LANGUAGE, AND FAMILIAL SUPPORT ON UNHEALTHFUL FOOD AND BEVERAGE CONSUMPTION AMONG LATINOS IN SOUTHERN CALIFORNIA

Lauren E. Miller, Shevel S. DaCosta-Davis, Simone Deshields, Maud Joachim-Célestin, Marisol Lara, Susanne Montgomery, Camille Clarke

School of Medicine, Loma Linda University, Loma Linda, CA

Increased acculturation among Hispanics has been associated with a decrease in the quality of dietary habits and an increase in the prevalence of obesity. The aim of this study is to compare the consumption of fast/processed foods and sugary beverages in Spanish speaking vs. non-Spanish speaking Hispanics and non-US natives vs US natives. We also explored the degree of familial support individuals received for incorporating healthy lifestyle habits, depending on acculturation. Surveys were completed by fifty (N=50) Hispanic community participants residing in Southern California. Questions pertaining to acculturation, eating habits, and familial support were analyzed for frequency and statistical correlational significance via SPSS v. 24. ANOVA analyses revealed a statistically significant difference in the frequency of consumption of fast food/packaged food between those born in the US vs. foreign-born participants and between those who spoke predominantly Spanish vs. those who spoke predominantly English (both $p < .000$) in that foreign-born and less acculturated Hispanics eat less fast/processed food. Although only marginally significant, we also found the same pattern for sugary drink consumption ($p=.055$). On the other hand, the amount of familial support for physical activity/dietary habit changes was independent of language spoken and country of birth (no statistical differences). This study confirms previous research that demonstrates that as Latinos acculturate, they are more likely to consume fast/processed foods and sugary drinks to a lesser degree. Unlike other studies, however, our research does not suggest that acculturation impacts the likelihood of receiving more or less familial support for adopting healthy lifestyle habits. Further studies should seek to evaluate the efficacy of culinary intervention in decreasing the consumption of processed foods in acculturated Latino Americans.

# NAVDEEP RANDHAWA

## BEHAVIORAL HEALTH PARTICIPANT 2018

I graduated from a small high school in Hemet and went to the University of California, San Diego (UCSD). I recently graduated with my Bachelor of Science in Cognitive Behavioral Neuroscience. Although I am excited about what I have been able to accomplish so far, my real journey in pursuing medical interests is just beginning. I am currently working as a medical scribe in the emergency department at Palomar Medical Health while preparing to attend medical school next year.

I have always been interested in medicine since several of my family members attended medical school. However, my own motivation was truly sparked when I took a medical trip to Cusco, Peru. There I met the beautiful Peruvian culture and its people, and my direction to pursue medicine was confirmed. I could see how privileged we (Americans) are living in a westernized society with access to basic medicines, health professionals, and preventive care. Access to healthcare should not be limited. My experiences in Cusco, studying as a cognitive science major, and working in this summer internship made me see health disparities from a new perspective. There is more to medicine than identifying and curing illness. Practicing medicine includes being aware of the connection one is making with individuals and communities not only physically but also mentally-emotionally. I use these experiences and lessons as a motivating force to further my academic training and hope to one day be able to use them to help others.

I am excited about the research and academic training experience given to me throughout the summer working with Dr. Susanne Montgomery's group. As my knowledge and understanding of health disparities research grows, I look forward to being able to put this knowledge into practice as a future physician.

# REPRODUCTIVE DECISION-MAKING IN CALIFORNIAN PUNJABI SIKH IMMIGRANT WOMEN

Navdeep K. Randhawa, Akinchita Kumar, Lisa Roberts, Susanne Montgomery

School of Behavioral Health, Loma Linda University, Loma Linda, CA

Punjabi Sikhs make up a significant portion of a large and growing subgroup of Asian Indian (AI) immigrants in the United States, yet little is known about the factors that influence their reproductive decision making. Moreover, Sikhs are known to be a highly familial and religious community. In this context, our aim was to explore the influence of living in an extended family and religious coping among women who did (*N*=92, 70.7%) or did not (*N*=38, 29.2%) get to choose family planning methods (FPM). A self-administered anonymous survey was given to Punjabi Sikh women (*N*=130) in California. Participant women were on average 36 years old, lived in the US for 18 years, and most were married (85%). Religious coping was measured using the Brief RCOPE scale, assessing positive (PRC), negative (NRC), and overall religious coping strategies. At the bivariate level the ability to choose FPM was positively correlated with employment, being married, and living with extended family but was negatively correlated if they had more daughters. A simple linear regression that included religious coping was run to explore being able to choose FPM. Results verified that living with extended family was positively associated while a higher number of daughters was negatively associated; religious coping was not significant ($R^2$ -22%). When discussing FPM with Punjabi women, healthcare professionals may be missing critical opportunities to discuss reproductive choices with their patients' extended family or significant others by assuming that the women make their choices autonomously. Moreover, it is critical to understand that in Sikh culture, the expectation of a son remains high and, therefore, if a women has previously had one or more daughters, this fact may impact her family planning autonomy. When serving diverse populations, such as immigrant Punjabi Sikhs, healthcare providers need to be aware of their patients' cultural context and be prepared to explore a broader set of questions to best understand women's FPM decisions.

# RAJHVIR SINGH

## BEHAVIORAL HEALTH PARTICIPANT 2018

I am a recent graduate with a Bachelor of Science in Biology from the University of California, Riverside. I plan to attend medical school so I can fulfill my commitment of serving our local area and the community I grew up in. In my time as an undergraduate, I had the opportunity to volunteer in multiple programs, including in the emergency department at St. Mary's Medical Center, the Flying Samaritans free clinic in Mexico, and Kindling Intellectual Development in Riverside. This work helped me expand my understanding of the many health disparities and barriers low-income communities face on a daily basis. While this work in general has further motivated me to pursue a medical career, it has also deepened my commitment to returning to the Inland Empire as our community is home to many who are underserved and underrepresented and deserve a locally committed advocate.

I am grateful to work as a research assistant with Drs. Susanne Montgomery and Lisa Roberts to support their research on mental health disparities in Punjabi Asian-Indian communities in southern California. Sadly, the stigma of and awareness about mental health is strong in my community, and as a Punjabi male, this research is close to my heart as I have witnessed the immense mental needs in my community first-hand. As part of my summer project, I am eager to explore the Punjabi young male experience regarding mental health needs, stigma, and help-seeking in a cultural context that favors males on one hand but then also burdens them with additional expectations.

I plan to continue my work in Drs. Montgomery and Roberts' lab and am excited to explore the data we collected during this past year, hopefully resulting in publications. I thank them both for their guidance and mentorship.

# EXPLORING THE INFLUENCE OF ANXIETY, DEPRESSION, & DISCRIMINATION ON LIFE SATISFACTION AMONG PUNJABI SIKH MEN IN CALIFORNIA

Rajhvir Singh, Amitoj S. Randhawa, Akinchita Kumar, Lisa Roberts, Susanne Montgomery

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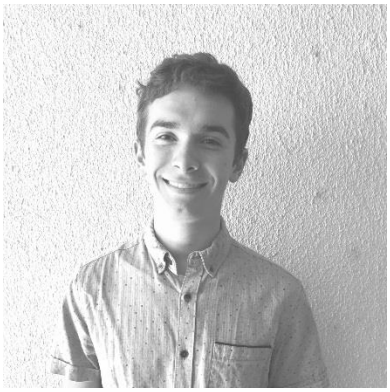
In the US, Punjabi Sikh Asian Indian (AI) men are part of an ever-growing population emigrating from India, yet there is little literature on the subjective mental health and well-being of this subgroup. Our aim was to explore the relationship between discrimination, anxiety, depression, and its influence on satisfaction with life among Punjabi Sikh AI Men in California. A self–administered, anonymous survey ($N$ =155) that included the following standardized measures: Patient Health Questionaire-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7), Satisfaction with Life Scale (SWLS), and a measure for discrimination which was given to Punjabi Sikh AI Men ages 18-81 in either English or Punjabi. Our results indicated low to mild anxiety ($M$= 5.29, SD 5.06), low levels of depression ($M$= 4.56, SD 5.07), mild to moderate levels of discrimination ($M$= 17.88, SD 5.56), and above average levels of life satisfaction ($M$= 26.08, SD 6.99). Further, life satisfaction was significantly correlated with being married, older age, and employed. Simple linear regression results revealed that employment, anxiety, and discrimination significantly contributed to the model, explaining 29.6% of the variance. In a group of AI men that generally had high levels of life satisfaction, anxiety and discrimination were significant barriers to having higher levels of life satisfaction. Experiencing discrimination and anxiety, not unexpectedly, resulted in fundamental obstacles towards achieving the life satisfaction many envisioned by emigrating. This evidence of discrimination and mental health challenges experienced by some Punjabi Sikh AI men underscores a critical need for efforts to better understand and respond to the unique challenges of this little studied minority immigrant group. This is important as the literature indicates a strong stigma against discussing mental health or discrimination as a public discussion might contradict the model minority reputation that the larger Sikh community so highly values.

# Summer Undergraduate Research Program (SURF)

Nicolas Belliard
Jennifer Gallardo
Bria Gamble
Author Goyne
Matthew Kimble
Nathan Leigh
Elaine Leslie
Vanessa Lopez
Crystal Mariano
Samantha Palahnuk
Patricia Principe
Kari Roberts
Matthew Shankel
Jacob White

# NICOLÁS BELLIARD

## SURF PARTICIPANT 2018



Each person, regardless of the field of work, has an educational journey unique to his or her own experience. Whether it be countless years of academic study or a lifetime of vocational experience, the learning process is continuous. My own educational journey has taken its various turns, and although my end goal has not always been clearly laid out, I have learned many invaluable things throughout the journey. Thanks to some of my teachers, my appreciation for science has grown over the years. From Newton's clear-cut laws of motion to the massively complex nature of our nervous system, I have found myself in awe as I study the way our universe works. Research, as I see it, is a way to turn this love for science into a professional career. This conclusion is what has motivated my interest in research. I am currently pursuing a degree in bioengineering at Walla Walla University, located in southeastern Washington, and aside from school, I am most likely found enjoying God's incredible creation or playing my cello.

For my future plans, I am considering a career in research, medicine, or the bioengineering industry. As this is my first research experience, I hope this summer will provide a clearer picture of what I want to pursue in my future educational endeavors. Regardless of where I end up, I know a love for learning and science will always remain an integral part of the work I do.

I would like to specifically thank Dr. Julia Unternaehrer and her lab for being patient with me as I learn, instructing me in the details of research, and making the lab an intellectually stimulating yet fun place to be.

# LOCATION OF THE SNAI1 TRANSCRIPTION FACTOR BINDING SITE ON THE LET-7 MICRORNA PROMOTER IN OVARIAN CANCER CELLS

Nicolás Belliard, Hanmin Wang, Evgeny Chirshev, Julia J. Unternaehrer

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Our objective in this study is to locate the site where the SNAI1 (Snail) transcription factor binds on the let-7 promoter. We hypothesize that by mutating different E-box binding sites on the let-7 promoter, we can identify the exact location of Snail binding. An important part of cancer metastasis is epithelial-mesenchymal transition (EMT), a process where cells lose their adhesive properties and gain the ability to migrate and invade. Additionally, a subset of cancer cells known as cancer stem cells (CSCs) is capable of self-renewal and differentiation. Previous studies have shown that, in addition to invasiveness, EMT is linked to stemness. It is also known that EMT is mediated by Snail and several other transcription factors. We are interested in the connection between Snail and let-7, a family of microRNAs that are expressed at low levels in many types of cancer. Although a correlation between Snail and let-7 is known, the mechanisms behind their relationship are not. To investigate this, we are using techniques including transfection, quantitative reverse transcriptase PCR (qPCR), mutagenesis, luciferase assay, and chromatin immunoprecipitation (ChIP) assay. Our results have shown a correlation between high Snail expression and low let-7 expression in addition to evidence that Snail binds the let-7 promoter. We now aim to take this further and identify the exact Snail binding location on the let-7 promoter. We are currently preparing a mutated let-7 promoter for analysis that will allow for identification of the Snail binding site to test our hypothesis. These results will deliver insight into let-7 regulation which will allow for restoration of let-7 expression, reversal of CSC stemness, and ultimately lead to an advancement of cancer therapies that can reverse the deadly effects of metastasis.

# JENNIFER GALLARDO

## SURF PARTICIANT 2018

Research is fundamental as it allows us to create innovative ways to improve lives. This profound discovery changed my career path as I have known I wanted to help people through medicine but had only considered this being possible as a doctor. Conducting research at California State University, San Bernardino, where I am majoring in biology, has allowed me to develop a foundation which I continue to build on in order to gain the knowledge and skills I need to pursue a research career. My interests lie in discovering the mechanisms diseases use to infect our bodies and how they can be reverted. My goal is to create a vaccine or treatment that can be taken to remote parts of the world to help improve people's daily lives.

As a first-generation college student whose parents migrated from El Salvador, my parents always encouraged me to surpass expectations, but I never imagined all the opportunities God would allow me. Being a student mentor to freshmen and transfer students as well as being part of the biology club has made me aware of how important communicating our knowledge is so others succeed as well. Whether a scientist or not, I believe it is important for everyone to understand the impact science has in our daily lives.

Through this summer program, I worked with Dr. Eugenia Mata-Greenwood and Wendy Chow to gain a better understanding of different molecular techniques and programs. I am truly thankful for Dr. Mata-Greenwood's mentorship and encouragement. Her knowledge and patience enabled me to grow both academically and personally. From this experience, I have gained further confidence and desire to pursue research and find answers to aid my community in living better and healthier lives.

# RENAL CHANGES IN TRANSCRIPTOME IN RAT MODELS OF HEALTHY AND COMPLICATED PREGNANCIES

Jennifer V. Gallardo, Eugenia Mata-Greenwood

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Pregnancy is characterized by hormonal changes that alter key biological systems. We have characterized the CD1 rat as a healthy pregnancy model and the Brown Norway (BN) rat as a model of preeclampsia, a disease characterized by high blood pressure and proteinuria. To further understand the differences between these models, we studied the renal transcriptome in CD1 and BN rats at non-pregnant and pregnant. A sub-aim was to identify genes that could contribute to the mechanism by which vitamin D is increased in CD1 pregnancy and decreased in BN pregnancy. The hypothesis is that BN pregnant rat kidneys would show activation of pro-inflammatory and glomerulonephritis gene pathways compared to CD1 pregnant rat kidneys. Age-matched non-pregnant and pregnant (day 18) CD1 and BN rats (n=5 per group) were sacrificed to collect the kidneys and plasma. We confirmed increased vitamin D status in pregnant CD1 and vitamin D deficiency pregnant BN rats. Renal RNA was isolated, purified, and sent for mRNA sequencing. 67 genes were significantly different among all groups while 474 genes were significantly different between pregnant BN and CD1. To validate these data, 26 SYBR green primer pairs were designed using the NCBI database. PCR efficiencies were performed on all primers, and a set of 15 primer pairs were selected for further studies. Sybr green real time PCR was then performed on all 20 samples (5/group). We validated differences between pregnant BN and CD1. Kidney androgen regulated protein (Kap), polymeric immunoglobulin receptor (Pigr), and aldoketoreductase 1 member c2 (Akr1c2) were significantly higher in BN rats compared to CD-1 rats particularly at pregnancy stages. In contrast, dihydrofolate reductase (Dhfr) and interferon alpha inducible protein 27 (ifi27) were significantly higher in pregnant CD1 compared to pregnant BN1 rats. Ingenuity pathway analysis reveals major difference between rat strains on immune gene pathways. We conclude that our hypothesis was correct and that pregnant BN kidneys show activation of immune and pro-glomerulonephritis gene pathways.

# BRIA GAMBLE

## SURF PARTICIPANT 2018

My time so far as an undergraduate student has been a fulfilling, fun, and enriching experience. I recently finished my sophomore year at Oakwood University in Huntsville, AL. During that time I was involved in our biomedical club, an outreach/mentoring club called REACH, and the University's senate.

My goal is to earn my MD/PhD. By combining these degrees I will be able to define mechanisms, find cures as a researcher, then use that information during my practice as a physician. As science evolves, I want to be at the forefront of these changes. I specifically want to focus my efforts as a researcher on the health of the African American community. I realize that there are many discoveries to be made in other areas, but health disparities are where I would like to focus. There is a lack of African American (AA) women researchers in the biomedical sciences; less than 2% of PhDs are AA women. I would like to be a servant and role model to my community.

Being in the SURF program has helped me to apply the facts I have learned in the classroom in a practical way. This program has also given me the chance to learn new scientific techniques, improve my scientific writing, and gain a better understanding of what it means to be a good researcher. I will be able to go back to Oakwood with a plethora of new skills that I can use as a lab instructor and TA. I am grateful to my PI Dr. Kylie Watts, Dr. Emilie Orillard, and the whole team for opening up their lab to me and being patient when teaching me new concepts. I will be forever grateful for the wisdom and insight I have gained during my time here.

# SEARCHING FOR MEMBRANE-LOCALIZING PARTNERS OF THE AER2 RECEPTOR FROM *PSEUDOMONAS AERUGINOSA*

Bria Gamble, Emilie Orillard, Kylie J. Watts

Division of Microbiology and Molecular Genetics, School of Medicine,
Loma Linda University, Loma Linda, CA

*Pseudomonas aeruginosa* is an opportunistic pathogen and ubiquitous Gram-negative bacterium. It relies on four chemosensory systems to sense and respond to environmental stimuli: Che (chemotaxis), Wsp (biofilm formation), Pil-Chp (twitching motility), and Che2 (unknown function). The Che2 system contains one chemoreceptor called Aer2 that senses oxygen via its PAS-heme domain. This oxygen binding modulates autophosphorylation of the CheA2 kinase that in turn phosphorylates CheY2, prompting an unknown cellular response. The Aer2 receptor is soluble, but it localizes to the cytoplasmic membrane where it forms protein arrays that follow the contours of the membrane. The aim of this study is to determine how soluble Aer2 localizes to the membrane and whether protein partners could signal through Aer2. We hypothesize that Aer2 interacts with either the membrane or a membrane protein via its N-terminal domains (NHAMP). To identify potential NHAMP protein partner(s), we used a bacterial adenylate cyclase two-hybrid (BACTH) approach and screened *P. aeruginosa* PAO1 genomic libraries. After co-transformation in *Escherichia coli* BTH101, we selected for colonies exhibiting functional complementation on MacConkey agar (dark red-pink colonies, representing reconstitution of adenylate cyclase and lactose fermentation). A total of 336,000 colonies were screened, and 564 (0.001%) potential hits were recovered. Only 70 (12.4 %) passed the first verification step and were analyzed further. We extracted plasmids containing potential partners and checked for interaction specificity by co-transforming with the empty vector or with the plasmid encoding NHAMP. These experiments are ongoing. Proteins that specifically interact with NHAMP but not with the empty vector will be sequenced to identify interacting partners. Newly identified protein partners may help explain how soluble Aer2 localizes to the membrane and may help clarify the role of the Che2 system in *P. aeruginosa*.

# ARTHUR GOYNE

## SURF PARTICIPANT 2018

I am a freshman mechanical engineering major at Valparaiso University located in Indiana. The main reason why I chose to pursue engineering is because of how appealing the idea of using math and science to solve practical problems to serve others is. This goal is very similar to the goal of a researcher but different in a way that a researcher answers questions that have never been answered by anyone else. I want to use the opportunity of the SURF program to determine if research is a worthy goal to pursue.

The research question I was put on this summer was to determine if a significant amount of the toxic Teflon coating on guidewires is rubbed off into the body during percutaneous nephrolithotomy surgery. The way this outcome was determined was by measuring how much teflon rubbed off in silicone models of the renal pelvis of the kidney. My role in the project was to create 3D models using CAD software and 3D print molds that the silicone could be poured into to make an anatomically correct kidney model. The most interesting part of this research was learning about how 3D printers work and how to use them in a practical setting. As a mechanical engineer, it was also refreshing to learn about the basic anatomy of the kidney for the first time since freshman year of high school.

I thank Dr. Duane Baldwin's lab for enabling me to pursue this important learning experience and teaching me.

# DEVELOPMENT OF A TECHNIQUE TO CREATE ANATOMICALLY CORRECT UROLOGIC ORGANS USING A CONVENTIONAL THREE DIMENSIONAL PRINTER

Arthur Goyne, John Smith, D. Daniel Baldwin, D. Duane Baldwin

Urology Department, School of Medicine, Loma Linda University, Loma Linda, CA

Currently studies testing surgical instruments and tools are limited by the need to sacrifice animals and a lack of realism due to anatomic differences between animal and human anatomy. There is a need to create anatomically accurate replicas of human organs for use in a variety of benchtop studies. The purpose of this project is to develop and perfect a technique to use 3D printing to create anatomically correct kidneys and bladders for benchtop studies in the urology research lab. Realistic organs were required in three urologic studies of guidewire teflon adherence, stent knotting, and bladder stone fragmentation. Initially, actual contrast-enhanced renal Computed Tomographic (CT) scans were converted into .STL files using Embodi3d.com and edited with Meshmixer. Then using Autodesk inventor, the collecting system was cut in half, and a backplate was extruded from both halves. The parenchyma was cut out of a block and then bisected. The files were then exported as an .STL file to the Cura software for the Ultimaker 3 printer and then converted into G code and printed. Next a 50-50 mixture containing Platinum-Siloxane Complex and Amorphous Silica were combined to create a dragon skin (Smooth-On, Macungie, PA) anatomically correct kidney. The ureter was created by drying dragon skin onto a rotating metal dowel. Bladder construction was similar to the process required for creation of the kidney. Two large hydronephrotic kidneys, one normal-sized kidney with ureter and one anatomically correct bladder were created. In addition, 20 different ureters were created. These anatomically correct specimens were used successfully in three different studies in the urology research lab and functioned well. A technique for creation of anatomically realistic urologic organs was developed and perfected in this study. Use of these anatomically correct models will prevent unnecessary sacrifice of animals or the use of cadavers and allow more realistic testing of surgical devices and techniques.

# MATTHEW KIMBLE

## SURF PARTICIPANT 2018

As I grew up, I began to make assumptions about the world around me. Whether these assumptions were generated from a fleeting thought or influenced by others is left to my own speculation. However, they did serve a purpose as these assumptions left me with a desire to seek the truth.

Within my pursuit, I found the human body to be the ultimate mystery. *Who are we*? *Where did we come from*? *What are we*? These questions swirled in my mind and drove me to pursue a career in medicine. At first, I had no idea where to begin. Was I seeking prestige, discovery, or the unknown? How did I want to be remembered? It was not until I found myself in an operating room observing surgery that I found my answer. I want to pursue a career in medicine so I may gain the knowledge and skills necessary to help those in my community. I want to become a surgeon so that I may explore the human body in a way that no one else can, understand how and why things go wrong, and, above all, assist those in need.

This summer, I had the opportunity to work with Dr. David Hessinger studying satiation in the sea anemone. Initially, I was skeptical of my project. However, I quickly learned it is often necessary to take a step back and appreciate the subtleties in life. Sometimes what appears to be the simplest biological process on the surface can be far more complex if one delves a little deeper. Using this experience I plan to reach for my goals and be ever observant in my endeavors. I'd like to thank Dr. Hessinger for opening his lab and mentoring me along my journey.

## TRPV4 CHANNELS INVOLVED IN NEMATOCYST-MEDIATED PREY KILLING

Matthew Kimble, Rosalia Marenco, Selorm Quarshie, David A. Hessinger

Center for Health Disparities and Molecular Medicine, Division of Physiology and Pharmacology, School of Medicine, Loma Linda University, Loma Linda, CA

Three types of cnidocyte supporting cell complexes (CSCC) regulate and trigger nematocyst discharge against prey in sea anemone. Prey trigger discharge from Type Cs by directly stimulating a contact-sensitive mechanoreceptor (CSM) in order to trigger discharge. In Type Bs, prey must first chemosensitize the CSM to trigger discharge. Type As must undergo both chemosensitized and tune vibration-sensitive mechanoreceptors to trigger CSMs. Type As are inhibited by streptomycin and by N-acetylneuraminic acid-proline (NANA-Pro). While CSMs require $Ca^{2+}$ that work instantaneously, their identity is unknown. We suspect TRP channels function as CSMs because they conduct $Ca^{2+}$ and are known to be mechanically gated. Two TRP channel blockers, gadolinium ($Gd^{3+}$) and GSK2193874, dependently inhibit most, but not all, prey killing. $Gd^{3+}$ broadly inhibits TRP channels, but GSK is specific for TRPV4 channels. We hypothesize the unaffected CSCCs are Type As. We reason that if $Gd^{3+}$ and GSK inhibit Types B+C and not A, then we should achieve full inhibition in the presence of streptomycin or NANA-Pro. Using monoclonal *Haliplanella luciae* in a quantitative feeding assay, Gd+NANA-Pro and Gd+streptomycin fully inhibit, but GSK+streptomycin did not. Thus, GSK inhibits TRPV4 channels on either Types A+B or Types A+C. To test this, we utilized tetrodotoxin (TTX) together with GSK. Because TTX inhibits Types A+B, combining TTX and GSK will give less than full inhibition. Albeit, if GSK operates on Types A and C, then it will present full inhibition. Utilizing the feeding assay GSK with TTX, we conclude that GSK inhibits TRPV4 on Types A and B CSCCs.

# NATHAN LEIGH

## SURF PARTICIPANT 2018

In a small high school in Litchfield, CT, I discovered my love for science on the first day of an AP Biology course that covered the many facets of biology in great detail. Ever since that day, I knew I had a passion to pursue biology in college and beyond. I currently attend The Master's University in Santa Clarita, CA, majoring in molecular and cellular biology.

As my love for science grew, I was given the privilege to begin research of my own at Master's and just recently presented my research at the WCBS Undergraduate Research Conference. This research and presentation experience increased my desire to pursue research in the coming semesters as well as in my career.

Consequently, my future career goal is to pursue a PhD and study microbiology and immunology in an effort to help cure hurting patients afflicted by disease. Having been selected as part of the SURF program has been an amazing opportunity to train for that future. I am so thankful to my mentor, Dr. Charles Wang, for the privilege to learn and experience research science in his laboratory. I have worked very closely with Dr. Zhong Chen on the GRASP project as well as having had the amazing privilege to learn machinery operation, data analysis, and techniques for next generation sequencing.

In the end, this program has taught me the importance of communication and asking questions in research. The only question that is not useful is one that is asked too late for an experiment to be salvaged. Despite someone's expertise and individual merit, seeking another person's perspective and collaboration between disciplines is the only way we can do science well.

# SINGLE NUCLEOTIDE POLYMORPHISM ANALYSIS OF ALZHEIMER'S DISEASE RISK ALLELES IN RELATION TO DIET

Nathan Leigh, Zhong Chen, Tiantian Liu, Jennifer Paul, Grace Lee, Nicole Gatto, Charles Wang

Center for Genomics, Department of Basics Sciences, Loma Linda University, Loma Linda, CA

The overall goal of this study is to investigate Alzheimer's disease (AD) risk genes associated with single nucleotide polymorphism (SNP) alleles in relation to dietary pattern (Vegetarian (V) vs. Non-Vegetarian (NV)). The population is composed of 101 subjects derived from the Adventist Health Study 2 (AHS-2) cohort, a population of SDA church members in the US and Canada. Our aim was to determine how diet relates to AD's allele risk factors in the participants. For this purpose, an experiment was designed to genotype ten SNPs (eight genes) by qPCR to identify the possible risk alleles associated with AD in two different diet groups. A one-way ANOVA was completed to ensure no significant differences between AHS-2, global, and American allele frequencies for homozygous allele 1 ($F(2, 18)=0.023$, $P=.978$), homozygous allele 2 ($F(2, 18)=0.064$, $P=.938$), and heterozygous allele ($F(2, 18)=0.093$, $P=.911$) variants. Odds ratio risk factors were acquired from the literature and combined for subject risk from 43.11 (extreme risk) to 8.93 (low risk) of developing late onset AD. Each of the ten SNPs were utilized to compare the V group with the NV group to assess risk. Our results showed SNP 3 (rs9331896, $P=.0027$) and SNP 4 (rs11136000, $P=.0128$) had a significant difference in risk between V and NV for the CLU gene. Thus, these two SNPs might play a protective role for the NV group from developing AD. The CLU gene codes for clusterin proteins that assist in the clearance of Amyloid beta (Aβ) from brain tissue and apolipoprotein that transport lipids. With future testing and a larger sample size, V group risk for CLU malfunction could suggest increased susceptibility for AD due to Aβ and lipid buildup in the brain. In future studies, genetic risk data combined with our current AHS-2 epigenetic study of miRNA in plasma can relate diets' effect on risk alleles' expression to cognitive degeneration.

# ELAINE LESLIE

## SURF PARTICIPANT 2018

I am relatively new to the world of research, but I am thrilled to be a part of SURF this summer. I grew up in an area in which academic opportunities were relatively sparse, and this program has truly been a blessing in putting me on the path to reaching my future career goals. Nothing is more exciting to me than the prospect of spending my life contributing to mankind's well of knowledge. In these uncertain times, I feel science can be our greatest asset to understanding the world and one another. In the words of Marie Curie, "Nothing in life is to be feared, it is only to be understood. Now is the time to understand more, so that we may fear less."

This fall I will be a junior at University of the Cumberlands, a small private college in eastern Kentucky. I am majoring in biology and minoring in Spanish language. In the future, I plan on earning a PhD in microbiology and acting as an advocate and role-model for young women in STEM. My dream job would be to work on something akin to the Human Microbiome Project and apply that knowledge to health issues such as Alzheimer's disease and mental illness.

I would like to thank Dr. Ryan Sinclair for welcoming me into his lab this summer and Thomas Hile for being an excellent colleague and teacher.

# SURVIVAL RATES OF *E. FAECALIS* AND *P. AERUGINOSA* ON SILVER TREATED FABRIC WHEN SUBJECTED TO A COLD-WATER WASH

Elaine Leslie, Alexis Townsend, Ryan Sinclair, Christopher Perry

Center for Health Disparities and Molecular Medicine, School of Medicine and School of Public Health, Loma Linda University, Loma Linda, CA

Fabrics containing small amounts of silver are known to have antimicrobial properties. If they are used in cold water laundering, these fabrics could offer an energy-efficient alternative to hot water washes and traditional disinfectants. The purpose of this study was to test the survival rates of various microorganisms (*Enterococcus faecalis* and *Pseudomonas aeruginosa*) on silver-treated fabric in a cold-water household washing machine. The fabrics used were 12.5% silver-treated pillowcases, 30% silver-treated privacy curtains, and control non-Ag sheets, all cut into 3 $in^2$ swatches. The swatches were inoculated with a known bacteria concentration and then washed in a cold water cycle with three sterile 1 $m^2$ ballast white bed sheets (non-Ag) and one artificially soiled 1 $m^2$ bed sheets (non-Ag). Results were collected by comparing colony growth by number of colonies on an initial concentration, pre-wash, washed, and air-dried samples. Our results showed a 4 log reduction (LR) on the 30% curtain and a 0.8 LR on the 12.5% pillowcase in the concentration of the gram positive *E. faecalis* after the wash. The gram negative *P. aeruginosa* showed a 7.74 LR and did not survive on silver-treated fabric in a cold-water wash; however, the washing machine without the silver had a similar LR on *P. aeruginosa*. Our work suggests that silver treatment and cold-water washes may be a suitable alternative to using expensive heat and disinfectants for cases when *P. aeruginosa* and low contamination of *Enterococcus* (also VRE) are of concern. Future ongoing work is using silver-treated ballast fabric in the washing machine to increase the ratio of silver-treated to non-silver-treated fabrics in the wash. This change and a longer wash time may prove to have greater antimicrobial effects.

# VANESSA LOPEZ

## SURF PARTICIPANT 2018


I am a senior biochemistry major at Occidental College interested in public health, specifically epidemiology. Among the many scientific areas that captivate me as a student is nutritional science. From the moment I took my first nutrition course in college, I knew I belonged there. My biochemistry background allowed me to really appreciate the metabolic processes and physiological impact of nutrition, but studying diverse diets and some of the health disparities of certain cultures finally tied in some of the public health issues I cared about, mainly Type 2 diabetes.

I was lucky to speak at a hypoxia-related Featured Topics Session at the 2018 Experimental Biology Conference in San Diego, presenting my summer research to a crowd of incredible scientists all united for a common physiological issue. This meeting was an impactful and almost uplifting experience for me that will always keep me motivated.

This summer will be my second researching with Dr. Sean Wilson in the perinatal biology department, working on a metabolomics project. Our aim is to understand how high-altitude hypoxia impacts levels of oxylipins and endocannabinoids–both derivatives of polyunsaturated fatty acids–in venous and arterial plasma from fetal and newborn sheep. As these lipid molecules are potential biomarkers for the oxidative stress and inflammation associated with hypoxia, finding the metabolic step or enzyme that is affected is a crucial step into understanding the physiological response to hypoxia. I would like to thank him for the guidance and instruction he has given me throughout the process.

Some of my favorite past-times are dancing to Latin music and painting. I wish to pursue an MD/MPH in the future, hopefully then adding to some of the scientific discoveries in these research areas I care about.

# LONG-TERM HYPOXIA REDUCES LEVELS OF OXYLIPINS IN PULMONARY ARTERIES AND VENOUS PLASMA OF FETAL HYPOXIC SHEEP

Vanessa Lopez, Michael La Frano, Remy Bosviel, John Newman, Richard Thorpe, Oliver Fiehn, Lubo Zhang, Tyler C Hillman, Sean M. Wilson

Center for Perinatal Biology, School of Medicine, Loma Linda University, Loma Linda, CA

High-altitude hypoxia compromises the development and function of the pulmonary vasculature in the fetus and later in the newborn. Gestational hypoxia may result in growth restriction and premature pulmonary hypertension during a crucial transition of the neonate. While the physiology regarding hypoxia is more well-known, the dysregulation that takes place on a molecular level is not yet completely understood. To fully understand its etiology, a metabolomic approach is advantageous in understanding underlying symptoms of hypoxia, two of which are oxidative stress and inflammation. Possible regulators of these stressors are oxylipins and endocannabinoids, products of polyunsaturated fatty acid (PUFA) oxidation. We hypothesized that high-altitude hypoxia would reduce the levels of oxylipin and endocannabinoids of pulmonary arteries and plasma in fetal sheep. We further aimed to find possible biomarkers of the disease that may be key in treating the disease. To test the hypothesis, we took samples of plasma and pulmonary arteries from fetal normoxic sheep and fetal hypoxic sheep raised at 3,800 m. altitude starting gestation day 30. We quantified metabolite levels using ultra performance liquid chromatography- tandem mass spectrometry (UPLC-MS/MS). These lipid profiles were analyzed with chemical similarity enrichment analyses and then visualized by applying pathway analyses. Our results support our hypothesis that oxylipin concentrations were reduced in both venous plasma and pulmonary arteries. Omega-3 PUFAs alpha linolenic acid (ALA) and eicosapentaenoic acid (EPA) were reduced in both plasma and pulmonary arteries. 15-HEPE and 12-HEPE, derivatives of EPA and mediators of inflammatory response were also significantly lower in fetal hypoxic animals than in normoxic fetal animals. By studying the metabolome, the neonate's physiological response can be predicted and treated ahead of time. This is important when it comes to treating gestational hypoxia, a disease that affects numerous newborns worldwide.

# CRYSTAL ABUTIN MARIANO

## SURF PARTICIPANT 2018

As an incoming fourth-year undergraduate at the University of California, Riverside's (UCR) bioengineering program, I have been blessed with the opportunity to explore the complexity of the brain and its functionalities as it pertains to my passion in being involved with degenerative disease research. As a cofounder of the Undergraduate Research Club at UCR, I understood the importance of inspiring our youth to find their passion by providing both a bridge in educating them on the different fields of STEM and by stressing the impact an individual in research can achieve, which this program has done for me.

The SURF program at Loma Linda University has allowed me to follow my aspirations in delving deeper into the causes of degenerative diseases by understanding the body's behavior at a cellular level. It has taught me the value of seeking answers to what has not been previously answered by focusing on the promise of what the outcome can achieve, and in this hope, I would be grateful to provide not only hope but a solution or an additional step closer to assisting those who are directly affected by these diseases within this work and future work I may be involved with.

I would especially like to give thanks to Dr. Shu-Wei (Richard) Sun for not only becoming a valuable mentor in my life throughout this program and constantly challenging me, but by giving me this opportunity to grow as an individual and learn what I am truly passionate about as I hope to continue to pursue this research path in my endeavors to earn my Master's and PhD degrees in the near future.

# EARLY DETECTION OF RETINODEGENERATIVE DISEASES USING INTRARETINAL IMAGING ANALYSIS

Crystal Mariano, Shu-Wei (Richard) Sun

Department of Physiology, School of Medicine, Loma Linda University, Loma Linda, CA

Retinodegenerative diseases are the major causes of blindness, known to cause damage in the visual pathway as it progresses. With the use of clinically available optical coherence tomography (OCT), we are able to synthesize a computational program on MATLAB. We use these techniques in conjunction with mathematical models in order to analyze the retinal layers to determine if there are any significant patterns to be observed. In doing so, we are able to test the hypothesis of early detection of these retinodegenerative diseases through the use of image processing. We begin by retrieving a .tif image using the optical coherence tomography. Focusing on just the retinal layers, we then convert the image into a binary format using MATLAB in order to gather the relevant data to be linearly fit. Once fitted, we are able to mathematically calculate the angle at which the image is needed to be rotated in order to straighten out for a more accurate representation of the layers' intensity profiles. These intensity profiles gathered will be compared to different images of the retinal layers at different points of progression of a disease to determine if there is an evident pattern in our findings. As a result, we may use the patterns observed to identify early progression of a retinodegenerative disease. Our work demonstrates that intraretinal imaging analysis can be a new alternative process of detection for diseases otherwise unable to be predicted at its early stages.

# SAMANTHA PALAHNUK

## SURF PARTICIPANT 2018

My earliest memories as a child involve constantly exploring the outdoors and inquiring about the natural world. An extremely observant and creative individual, I spent the majority of my childhood drawing the local flora and fauna. As I grew up, I committed myself to learning the art of hyper-realistic illustration while challenging myself with advanced math and science courses. I knew that I would forever be left with the question "what if…?" if I left either art or science behind.

I ultimately decided to combine my passions for both biology and art by earning a BS in Biology with a concentration in Biomedical Illustration at The College of New Jersey. I plan to continue my education by earning both a Master's in Biomedical Illustration and a PhD in Science Communication.

As an artist, biologist, and lifelong student, I strive to become as well rounded as possible through my pursuit of a career that requires the illustrator to understand several fields of science. I enjoy investigating experiment-based research questions, and I always aim to understand material at a level beyond what is required in my courses. In my biology classes, I rely on visuals to learn the information presented. Whenever I find a figure that is confusing, I ask myself, how could I present this information in a more efficient manner? My career goal is to communicate science by creating visuals both aesthetic and educational in order to optimize the learning experience of future scholars. I hope to use my interdisciplinary skills to one day lead my own biomedical illustration business.

I'd like to thank Dr. Chris Wilson for being an extraordinary mentor this summer and for providing me with the tools I need to grow as both a biological researcher and illustrator.

# COMPREHENSIVE DISSECTION PROTOCOL FOR PREPARATION OF RHYTHMICALLY-ACTIVE *IN VITRO* NEONATAL RODENT BRAINSTEM-SPINAL CORD AND THIN SLICE

Samantha Palahnuk, Christopher Wilson

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The central respiratory rhythm-generating network includes a group of rhythmically active neurons located in the rostral ventrolateral medulla in the brainstem. Mammalian inspiratory rhythm is believed to be generated from a neuronal network in a region of the medulla called the preBötzinger Complex (pBC). Respiratory signals generated by the pBC drive the rhythmic contraction of inspiratory muscles. Rhythmic neural activity generated in the pBC and carried to other neuronal pools to drive the musculature of breathing may be studied using various approaches, including *en bloc* nerve recordings and transverse slice recordings. However, previously published methods have not extensively described the brainstem-spinal cord dissection process in a transparent and reproducible manner for future studies. Here, we present a comprehensive overview of our laboratory's method to reproducibly cut rhythmically active slices containing the necessary and sufficient neuronal circuitry for generation and projection of inspiratory drive. This work builds upon previous brainstem-spinal cord electrophysiology protocols to enhance the likelihood of reliably obtaining viable and rhythmically-active slices for recording neuronal output from the pBC, hypoglossal premotor neurons (XII pMN), and hypoglossal motor neurons (XII MN). We have expanded upon previous work by our lab and others by providing detailed, step-by-step illustrations of the dissection, from whole rat pup, to *in vitro* slice containing the XII rootlets.

# PATRICIA PRINCIPE

## SURF PARTICIPANT 2018

I am originally from Peru, my favorite hobby is traveling, and I love learning. I am finishing my last year at Southwestern Adventist University majoring in biology with emphasis in biomedical sciences. After graduation, I look forward to attending graduate school as part of an MD/PhD program. I would like to play an active role in biomedical research as well as interacting with patients as an internist.

For the past six years I spent my summers as a literature evangelist in different places, and although this summer has definitely been different than the previous ones, spending this summer as an intern at Loma Linda University has motivated me to keep dreaming big for God. Resilience, patience, and perseverance have still been part of my everyday lessons applied during this summer as I have found myself making mistakes many times. However, as someone once said, "Our greatest weakness lies in giving up; the most certain way to succeed is always to try just one more time."

I want to thank Dr. Xiao-bing Zhang for giving me the opportunity of working in his lab during this summer as part of the Department of Regenerative Medicine and also express my deepest gratitude to Leslie Aranda, Yawen Fu, Gou-hua Li, and Dr. Juan Fu for their support, time, and friendship during this summer.

## EFFICIENT PRECISE KNOCK-IN IN iPSCs WITH A DOUBLE CUT HDR DONOR AFTER CRISPR/CAS9-MEDIATED DNA CLEAVAGE

Patricia Príncipe, Yawen Fu, Guohua Li, Leslie Aranda, Xiao-Bing Zhang

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The ability to precisely edit genomes gives a powerful tool to study the functionalities of any pieces of DNA in the genome, and it may also lead to the development of new therapies that can potentially cure numerous genetic diseases. The combination of genetic editing and induced pluripotent stem cells (iPSCs) is providing unprecedented opportunities to study biological principles and holds promise especially in regenerative medicine. The Clustered Regulatory Short Palindromic Repeats (CRISPR) system is currently at the forefront of genome editing technology as it is much more precise and efficient than other methods. However, knock-in efficiency mediated by homology-directed repair (HDR) in iPSCs by the CRISPR/Cas9 system is still a challenge in genome editing. Here we hypothesized that *in vivo* cleavable donor plasmid can increase HDR, achieved by flanking the targeting vector with two sgRNA recognition sites identical to the sgRNA target site on the genome. To test this hypothesis, we compared HDR efficiency using four types of plasmid combinations targeting EEF2 locus on iPSCs: a control without any sgRNA plasmid, no genome-cutting sgRNA, no sgDocutRNA, and double cut. Three days after electroporation, cell populations were assessed by flow cytometry. FACS data showed that a double cut HDR donor increases HDR efficiency by fivefold to tenfold relative to circular plasmid donors at EEF2 locus in iPSCs. Synchronizing the demand and supply of homologous sequences provides a striking increase in knock-in efficiency of up to 50%. Our work provides guidance for the design of HDR donor vectors; improved targeting strategies are broadly applicable in generating precise knock-in for basic research and disease modeling.

# KARI ROBERTS

## SURF PARTICIPANT 2018

I recently graduated from Point Loma Nazarene University (PLNU) in San Diego where I majored in biochemistry. While there, I worked two part-time jobs as both a teacher's assistant in the biology lab and as a babysitter. I volunteered at University of California San Diego's Medical Center, the San Diego Humane Society, and my church's nursery. Though I attended college in San Diego, Yucaipa, CA, is where I call home. Whenever I was home, I spent my spare time volunteering at Loma Linda University Children's Hospital. Since graduating from PLNU in May, I have moved back home with my family in Yucaipa.

My experiences thus far have been preparing me for my future aspirations. In the fall, I will be embarking on my first year at Loma Linda University School of Medicine. I yearn to be a physician who treats patients beyond their physical symptoms and considers their body, mind, and soul. Patients are multifaceted, and, therefore, they deserve care that can accommodate that complexity. I believe Loma Linda University will help me best pursue this dream. However, after my experiences in the lab these past two summers, I have also gained a greater fascination for research. Upon completion of my MD, I am interested in exploring options to receive a PhD in biomedical sciences.

It has been a great privilege to work in Dr. Kerby Oberg's lab and gain insight into a different side of medicine. I have shadowed many doctors in clinic, but it has been another experience entirely to catch a glimpse of the bench research that goes into the treatments that take place at the bedside. I'd like to thank Dr. Oberg, Charmaine Pira, and the rest of my team for helping me learn, grow, and challenge myself this summer.

# FGF REGULATES LHX2 EXPRESSION THROUGH AN ASSOCIATED *CIS*-REGULATORY MODULE

Kari D. Roberts, Neera M. Shah, Billy A. Watson, Charmaine U. Pira, Kerby C. Oberg

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Limb development occurs along three major axes – proximal-distal, anterior-posterior, and dorsal-ventral. Fibroblast growth factors (FGFs) secreted by the apical ectodermal ridge (AER) and sonic hedgehog (SHH) released from the zone of polarizing activity (ZPA) are responsible for proximal-distal and anterior-posterior development, respectively, and maintain each other through a positive feedback loop. This reciprocal loop is critical for proper limb development and may function in regenerative wound healing. Though the molecules involved in the FGF to SHH regulatory pathway are still under investigation, LIM homeobox 2 (LHX2) has been identified as an intermediate in FGF-mediated *SHH* expression. There are several conserved regions of non-coding DNA associated with the LHX2 gene locus that could serve as regulatory modules and be targeted by FGF signaling. We hypothesize that FGF regulates LHX2 through at least one of these potential *cis*-regulatory modules (PCRMs). To identify an FGF-targeted PCRM regulating LHX2 expression in the limb, we screened for the activity of 10 PCRMs within the LHX2 expression domain (distal mesoderm subjacent to the AER). Each PCRM was linked to the p*TK*-GFP reporter construct and electroporated into the distal mesoderm of HH20-23 chicken embryo wing buds subjacent the AER. PCRM activity was determined 24 hours later using fluorescence microscopy. Our results indicate that at least three of the PCRMs investigated (PCRM (-19), PCRM (-2), and PCRM (-1)) display activity coincident with LHX2 expression in the chicken wing bud. The interaction between these three *cis*-regulatory modules (CRMs) and the promoter needs to be determined via 3C to confirm LHX2 regulation. We will also confirm FGF activation of the CRMs through application of FGF-soaked beads to chicken wing buds containing the CRM-reporter constructs. Our work provides insight into the mechanisms regulating limb development and possibly regenerative wound healing.

# MATTHEW SHANKEL

## SURF PARTICIPANT 2018

Science has always been a source of fascination and interest for me. It provides both a challenge and a reward unlike any other subject I have studied. Research this summer provided an incredible opportunity to observe and participate in the application of science and discover the driving factors behind new information. I appreciate both the knowledge and skills I have already learned and look forward to the rest of this summer.

I am currently attending Walla Walla University as a senior bioengineering student. Last year, I went as a student missionary to teach on the island of Majuro. While there, I learned more about myself, and I discovered a passion for education and service. I returned from my year abroad and became more involved on campus through a Resident Assistant job and a position in Engineers Without Borders. This next year I will serve on the Student Missions team as the programming coordinator. I hope to use these experiences and the knowledge I have gained to pursue a PhD and teach at the collegiate level in the future. This drive comes from my belief in the impact teachers and education have on students' lives and their futures.

I am greatly appreciative towards Dr. Kerby Oberg and Charmaine Pira for accepting me into their lab. They are both extremely helpful and available and answer questions patiently. I have had an incredible summer while learning from them.

# CHARACTERIZATION OF A GDF5 ASSOCIATED ENHANCER

Matthew Shankel, Charmaine Pira, Kerby Oberg

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Growth differentiation factor 5 (GDF5) is a secreted protein that regulates joint development and maintenance. Reduced levels of GDF5 are associated with accelerated degradation of joint cartilage, a disease called osteoarthritis. A GDF5 Associated Regulatory Region (GARR) has been previously identified as a 900 base pair enhancer located 78 kb downstream of GDF5. GARR contains a number of potential transcription factor binding sites, including two sites for odd-skipped related (OSR) zinc-finger transcription factors. OSR1 & 2 have been reported to control joint formation, and we hypothesized that one of their roles in joint formation would be the regulation of GDF5. To identify whether an OSR transcription factor contributes to GARR activity, we performed site-directed mutagenesis on both OSR binding sites (moGARR). We used targeted regional electroporation (TREP) to introduce GARR and moGARR reporter constructs into Hamburger Hamilton stage 23 chicken limb buds. Transfection efficiency was determined by co-transfection with a beta-actin promoter-driven RFP construct. Following transfection, activity was determined by fluorescence microscopy. Limbs with sufficient targeted transfection underwent further detailed analysis. Comparison of GARR and moGARR demonstrated similar spatial activity with similar intensity. Our data suggests that mutation of the OSR binding sites alone was insufficient to dramatically alter GARR activity although subtle changes may not be evident within these studies. Additional binding sites will be evaluated independently and in combination with the OSR sites to determine the factors that contribute to GARR activity.

# JACOB WHITE

## SURF PARTICIPANT 2018

Since childhood, I have possessed a desire to pursue a career in science. My passion for scientific inquiry was developed through experiences with my marine biologist father, such as collecting water samples and identifying organisms. As an adolescent, I became enthralled with mycology after observing different mushroom species and reading medicinal mycology textbooks. During this period, I decided to work towards a PhD in either mycology or marine biology. However, as a first-year student in college, I became captivated with the complexity of neurobiology, especially the mechanism of action potentials in neurons. My scientific interests culminated in my current goal of receiving an MD/PhD in neurobiology. After receiving an MD/PhD degree, I plan to work towards developing and applying novel therapies for Charcot-Marie-Tooth disease, a common hereditary neuropathy.

I am currently a senior biology student at Southern Adventist University (SAU) in Tennessee. Attending SAU has allowed me to work towards achieving an MD/PhD degree through learning laboratory techniques and conducting research on *Latrodectus hesperus* silk under the direction of Dr. David Nelsen. I am highly grateful that God allowed me to be selected to participate in Loma Linda University's Summer Undergraduate Research Fellowship (SURF) program as I have not had the opportunity to work in a biomedical research laboratory before. I also greatly thank my mentor, Dr. Erik Behringer, for allowing me to work in his laboratory as well as Phoebe Nye for mentoring me through the SURF program.

# GENETIC EXPRESSION OF CEREBROVASCULAR ENDOTHELIAL GPCRS, ION CHANNELS, AND CONNEXINS DURING ADVANCING AGE AND ALZHEIMER'S DISEASE

Jacob B. White, Phoebe P. Nye, Erik J. Behringer

Department of Basic Sciences, Division of Pharmacology, School of Medicine, Loma Linda University, Loma Linda, CA

Aging is a key risk factor for dementia, including Alzheimer's disease (AD). As of 2018, ≈97% of the 5.7 million Americans diagnosed with AD are ≥65 years of age. The development of AD has been associated with decreased perfusion of the brain due in part to cerebrovascular dysfunction. Cerebral arteries coordinate vasodilation and blood flow throughout the brain through endothelium-derived hyperpolarization (EDH), which is modulated by G protein-coupled receptors (GPCRs), ion channels, and gap junctions. Genetic expression of EDH components has not been resolved in cerebral endothelium in the context of aging and AD. Based on our functional data, we tested the hypothesis that GPCR or $K^+$ channel expression may decline with advancing age and AD in mouse cerebrovascular endothelium. Cerebral endothelium was isolated from C57BL/6 mice of three age groups [Young (3-7 mo), Middle-age (12-16 mo), and Old (24-28 mo)], 3 male and 3 female mice/age group, significance at $\alpha = 0.05$]. Quantitative polymerase chain reaction (qPCR) was performed to characterize mRNA expression. Our results showed that the expression of purinergic receptor *P2ry1* and connexin *Gja1* decreased significantly in Old. The expression of $K^+$ channels (*Kcnn3*, *Kcnn4, Kcnj2*), non-selective cation channels (*Trpv4*), and connexins (*Gja4*, *Gja5*) did not change significantly with advancing age. In an AD mouse model (3xTg-AD), preliminary findings reveal down-regulation of inward-rectifier $K^+$ channel (*Kcnj2*) coinciding with the presence of amyloid-β and tau pathology. These data suggest decreased purinergic receptor (aging C57BL/6) or $K^+$ channel (aging 3xTg-AD) expression may contribute to diminished vasodilation responses to neurotransmitters such as ATP, resulting in decreased blood flow throughout the brain. Our results indicate potential pharmacological and genetic targets for treating cerebrovascular disease, which could thereby delay or prevent dementia.

# Guest Participants

Eloisa Lopez
Casey Reid
Christian Westenburg

# ELOISA LOPEZ

## GUEST PARTICIPANT 2018

The Coachella Valley is known for its music festivals, resort cities, and amazing golf courses. In reality, this description only belongs to the western part of the valley. I grew up in the Eastern Coachella Valley (ECV), a region made up of predominantly Latino or Hispanic agricultural working families. Growing up, I never compared the East from the West. I had never heard of health disparities and environmental justice. After leaving the Coachella Valley I realized what those terms meant and that my community had experienced both.

I recently graduated from UC Berkeley with a degree in Public Health. This summer I was offered an internship through Health Career Connections (HCC). Based on my career goals and interests, I was placed with Dr. Ryan Sinclair at Loma Linda University. Working with Dr.Sinclair has been a great learning experience. I conducted data analysis on a 2014-2016 comprehensive 5-area health survey in order to update a health disparities policy brief for the ECV. I also conducted a literature review in order to develop a curriculum for a community science project involving balloon mapping, water quality, and air quality in the Salton Sea.

Through my summer internship I was also able to learn more about environmental justice during community meetings. Attending these meetings was my favorite part of the internship since I was able to connect with community members and realize the application and importance of my work. This summer has reaffirmed my passion for addressing health disparities through research and community activism. I would like to thank Dr. Sinclair for being a great mentor this summer and providing a welcoming space for me to share my ideas.

# CURRICULUM DESIGN FOR A COMMUNITY SCIENCE PROGRAM TO MAP AND DOCUMENT THE ENVIRONMENTAL JUSTICE ISSUES OF THE EASTERN COACHELLA VALLEY

Eloisa Lopez, Ryan Sinclair

School of Public Health, Loma Linda University, Loma Linda, CA

Environmental justice (EJ) refers to the idea that all people should have equal access to environmental protection regardless of their race or socioeconomic status. The Building Healthy Communities Coachella Valley has a current campaign focused on environmental justice problems common in the Eastern Coachella Valley (ECV). The ECV has several environmental contamination and change issues that are not present in the Western Coachella Valley. These issues adversely affect disadvantaged populations who live in that area by degrading the air and water quality. The Building Healthy Communities campaign has outreach strategies for community members to advocate policy changes that would improve their community and their health. Our group has designed a community science method where local youth are recruited to a youth action team that organizes community science. The community science activities are designed to (1) build leadership capacity and knowledge of participants as well as (2) collect relevant environmental data that can be used in the EJ campaign. In order to address the first of these two goals, we realized it is important to engage the youth in discussions about community science and its application to the Salton Sea as well as empower youth through knowledge. For the second goal, it was necessary to conduct a literature review regarding current water and air monitoring at the Salton Sea. This was an important step in determining the best water quality criteria and data collection methods to use with youth. The team plans to map the receding shoreline of the Salton Sea through Balloon mapping, measure water quality of the Salton Sea and of tap water in homes, and measure the air quality using a small wife laser air particulate sensor. By conducting these data collection activities with environmental justice-impacted youth, we hope to empower the local community and reduce the environmental health risks they are exposed to.

# CASEY REID

## GUEST PARTICIPANT 2018

I am currently a second year medical student at the University of Nevada-Reno School of Medicine and have a degree in biology with a pre-medical concentration from California Baptist University. God willing, my plan is to come back down to Loma Linda University for residency to pursue a career in surgery.

I have spent this summer dedicated to both clinical research overseas looking at chronic health conditions in the Dominican Republic and basic science research here at LLU on the effects of long term hypoxia and both fetal and adult basilar arteries. As an MD, I hope to dedicate a large portion of my career to serving those overseas, and research into public health deficits plays a large role in that. For the last 3 years I have been working in Dr. Sean Wilson's fetal hypoxia lab where we learn about the effects of giving birth and living at high altitude as certain communities do around the world.

This experience has been an amazing gateway into the world of research, and Dr. Wilson has been an amazing mentor as he helped get me introduced to, and deeply involved in, research and publication. My time here pushed me to help form a closer relationship between LLU and my alma mater CBU through the creation of a joint research program to give driven biology students the opportunity that I had to get introduced to basic science research as early as possible.

# LONG TERM HYPOXIA NEGATIVELY INFLUENCES $Ca^{2+}$ SIGNALING IN BASILAR ARTERIAL MYOCYTES OF FETAL AND ADULT SHEEP

Casey Reid, Monica Romero, Abigail Dobyns, Lawrence D. Longo, Christopher G. Wilson, David A. Hessinger, Lubo Zhang, Sean M. Wilson

Center for Perinatal Biology, Department of Physiology and Pharmacology, AIM Core Facility, School of Medicine, Loma Linda University, Loma Linda, CA

$Ca^{2+}$ sparks and waves have been shown to play a major role in the regulation of vascular tone. Without the spark's activation of BK channels, vasculature will constrict, and without waves, total cell calcium decreases and diminishes the ability of $Ca^{2+}$ to do work and, therefore, dilates. The impact of long term hypoxia and maturation on calcium signals in basilar arterial myocytes was examined using confocal imaging techniques. In adult animals, LTH decreased spark frequency where fetal LTH animals showed only an increase in spark amplitude. LTH decreases total intracellular calcium from waves independent of age due to a faster decay in the $Ca^{2+}$ signal, decreasing vasoconstriction and increasing cerebral blood flow. Along with producing smaller events, we found that LTH inhibits the cell's ability to respond to depolarization in fetal and adult sheep resulting in basal levels of calcium upon stimulation. LTH and Ontogeny play interconnected roles in signaling as LTH is shown to inhibit distant communication in fetal sheep where in adult sheep, it stimulates both local and temporally similar $Ca^{2+}$ waves. These observations illustrate that both altitude and maturation produce $Ca^{2+}$ signaling changes which play a role in arterial contractility and other mechanisms of cerebral blood flow.

# HANS C. WESTENBURG

## GUEST PARTICIPANT 2018

Medicine has always been extremely important to me because of its impact on human life. This summer has been extremely enlightening because of the opportunity to volunteer at Loma Linda University School of Medicine. I had always wanted to pursue a career in the health sciences, but it was my time in Dr. William J. Pearce's lab that encouraged me to study molecular biology as an undergraduate and hopefully obtain a PhD in molecular biology in the future.

I am currently a senior at Redlands High School with a 4.4 overall GPA, and I engage in numerous extra-curricular activities such as playing the clarinet, volunteering with Kiwanis, and, of course, volunteering at Loma Linda University. While I take pride in these passions, my principal concerns and interests lie with my education to ensure I have the knowledge to accomplish my goals in medicine, and because of my focus on the medical field, I am extremely excited to be taking AP Biology and AP Chemistry this coming year. That being said, my focus on the health sciences has undoubtedly been influenced by my time at Loma Linda University now that I have experienced scientific study firsthand, and I am enthusiastic about my prospects in the medical field.

I would like to thank Dr. Pearce for providing me with the opportunity of working in his lab, and I would like to thank Dane Sorenson and James Williams for mentoring me.

# ACUTE FETAL HYPOXIA ATTENUATES VASCULAR CONTRACTILITY

Hans Westenburg, Dane Sorensen, James Williams, William Pearce

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Various pregnancy complications can lead to acute fetal hypoxia, which can lead to cerebral defects and even death in a fetus. In response to hypoxia, the fetal vasculature undergoes both compensatory and maladaptive changes in vascular structure and function. Myosin Light Chain Kinase (MLCK) is the rate-limiting enzyme vital to smooth muscle cells' ability to contract and maintain vascular tone. Alterations in the expression and activity of MLCK have been linked with several disease states such as severe asthma, sepsis, inflammatory bowel disease, and severe pulmonary arterial hypertension. The aim of this project is to test the hypothesis that acute hypoxia attenuates vascular contractility through increases in proteasomal degradation of MLCK protein. Hypoxic organ-culture of fetal arterial segments followed by a length-tension protocol revealed acute hypoxia attenuates vascular contractility. Subsequent experiments revealed acute hypoxia also decreased the abundance of MLCK protein. Dynamic changes in the abundance of proteins, such as MLCK, are determined by loss in the balance of transcription, translation, and/or degradation. Utilization of qPCR techniques revealed decreased MLCK abundance after acute hypoxia is not due to changes in the level of MLCK mRNA. Organ-culture of arterial segments in the presence or absence of protein synthesis inhibitor cyclohexamide revealed acute hypoxia did not significantly affect the rates of MLCK mRNA translation. Addition of the proteasomal inhibitor epoxomicin during organ-culture indicated the extent of proteasomal degradation, which was less in hypoxic than normoxic arteries. Together, these results suggest hypoxia either promotes a proteasome-independent pathway of MLCK degradation or induces a post-translational modification of MLCK, which inhibits its participation in contraction and renders it unreactive with the antibodies used to detect MLCK. Regardless of the mechanism by which hypoxia promotes decreased MLCK abundance, the results demonstrate that decreased MLCK abundance contributes to hypoxic inhibition of contractility in fetal carotid arteries, and hypoxia does not increase proteasomal degradation of MLCK, which refutes our hypothesis.


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